Friedrich-Alexander-Universität
Medizinische Fakultät

Uniklinikum Erlangen

IZKF Erlangen 2023









interdisciplinary
Center for
Clinical Research

www.med.fau.de

EDITORIAL

Dear Friends and Members of the IZKF,
Dear Readers,

Please find on the following pages the Annual Report 2023 with an overview of the activities, recent developments and funded projects of the IZKF Erlangen. All information is available on our homepage: www.izkf.med.fau.de.

We welcome our three new project leaders in the Jochen Kalden Programme with their innovative research projects. Prof. Caroline Voskens (Department of Dermatology) was accepted to the programme following the call in 2022 and already started her project. Prof. Ricardo Grieshaber-Bouyer (Department of Medicine 3) and Prof. Lydia Meder (Department of Experimental Medicine I) were successful in the 2023 call. We wish much success in the realization of the projects and look forward to exciting results. The next application deadline is November 1st, 2024.

In 2023, synergy projects were established as a new line of funding. They are intended to provide pilot financing for collaborative research and the acquisition of external group funding instruments. In the second call for proposals, two applications were approved after being reviewed first by a local committee chaired by Prof. Reis and then by the Scientific Advisory Board. Funding of €300 thousand over two years was awarded to the following projects:

- TRAIN: Towards Rationalizing Neurodevelopment, Speaker Prof. Dr. D. Chichung Lie
- TAME THE FLAME, Speaker: Prof. Dr. Sebastian Zundler

The call for Synergy project proposals takes place annually. The next application deadline is July 15th, 2024.

Another programme launched in 2023 was "Do I(I)T". It aims to support the initiation of investigator initiated clinical studies. For that purpose, the IZKF provides full-time rotation positions at Ä1/ Ä2 level for up to 3 months to prepare IITs with a focus on drawing up the study plan and obtaining an ethics vote. Already six projects received funding. The application deadlines are published on the homepage.

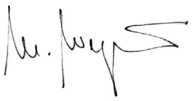
There were also changes within the IZKF committees in 2023. We bid farewell to Prof. Dörthe Katschinski, Prof. Holger Moch and Prof. Gisa Tiegs from the External Scientific Advisory Board and thank them for their years of dedication and support.

Due to his appointment at the Charité, Prof. Gerhard Krönke (Department of Medicine 3) resigned from the ELAN Committee on April 1st, 2023 and was succeeded by Prof. Andreas Ramming (Department of Medicine 3). We wish Prof. Krönke all the best for the future and warmly welcome Prof. Ramming in the ELAN Committee.

After successfully completing the clinician scientist programme, PD Dr. Markus Eckstein (Institute of Pathology) handed over his position as one of the speakers of the CSP Committee to Dr. Alexander Schnell (Department of Paediatrics and Adolescent Medicine). Many thanks to Markus Eckstein for his commitment and dedication.

Currently we are preparing our next IZKF symposium. The 9th International IZKF Symposium „From cells to organs: How interactive networks shape human disease“ takes place on June 20th and 21st, 2024 in Kloster Banz. The programme, including a poster exhibition, promises insightful sessions.

Finally, I would like to thank you for your continued interest in and support of the IZKF. I also want to express my deepest gratitude to all the members of the Administrative Office who contributed once again to the success of the IZKF as a whole - and to the making of this annual report.



Prof. Dr. Michael Wegner
Chairman

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281 IZKF
147 Dr. med.
134 Dr. rer. nat./Dr. rer. biol. hum.
56 participants outside RTG

58 Publications

Cumulative Impact Factor **532.000**
Average Impact Factor per publication **9.172**
Average publications per project **0,8***
16 publications with an IF more than 10

*Based on advanced projects, junior research groups and junior projects

113* Employees of the IZKF

76 Doctoral fellows, Post-Docs and laboratory rotations
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*Based on advanced projects, junior research groups, junior projects and laboratory rotations

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* Project leaders, clinician scientist programme, laboratory rotations and committee members

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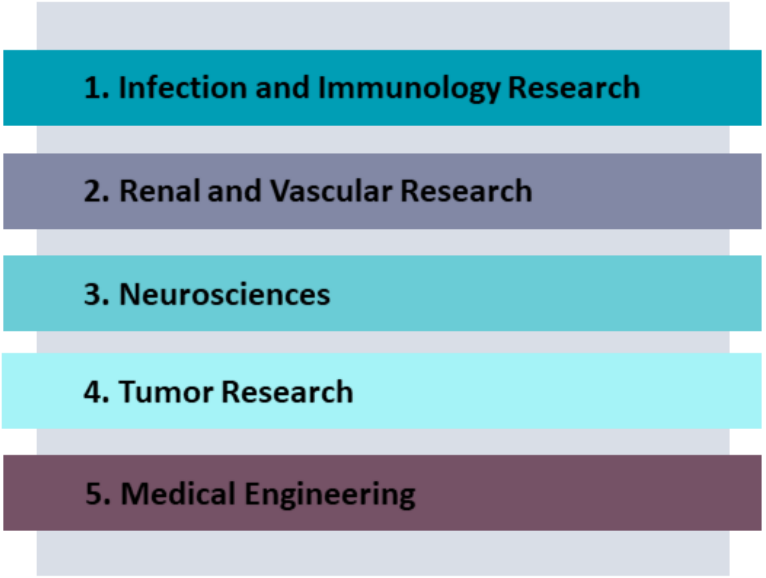
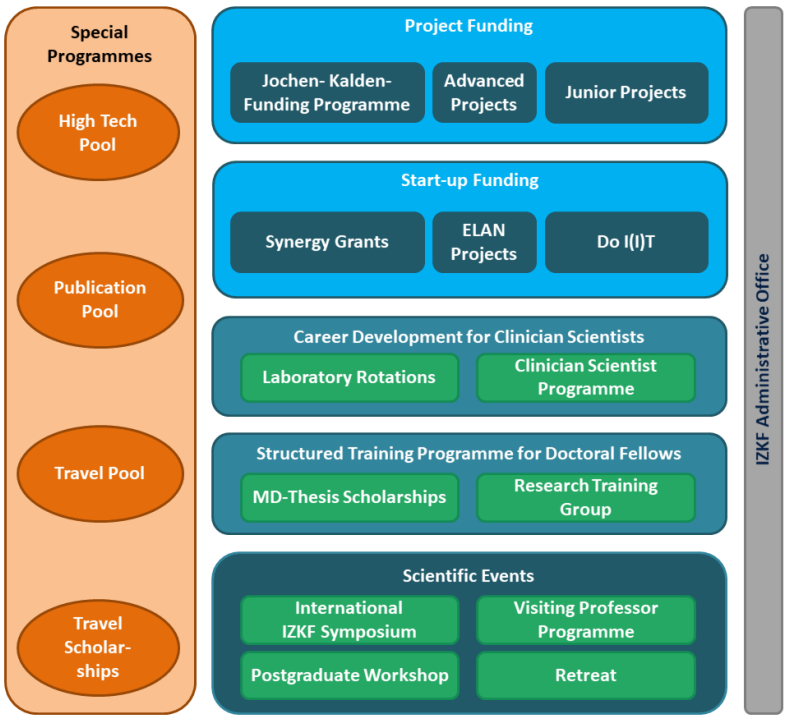
PROGRAMMES

The IZKF is the central structure of research development of the Faculty of Medicine. Its mission is to improve the overall quality of clinical research, to stimulate interdisciplinary research, to advance the careers of young scientists and to foster the acquisition of extramural funds. In order to achieve these goals, the IZKF supports projects in all research areas of the Faculty of Medicine on a strictly time-limited basis. The selection of projects is based exclusively on quality aspects. The various programmes are aimed at physicians and scientists at different stages of their scientific careers. Equip- ped with its own budget and own management structures, the IZKF continuously develops its own funding programmes in line with the needs of the Faculty of Medicine. In addition, the Faculty of Me- dicine also uses the structures established in the IZKF for the allocation and management of funds and avoids the creation of parallel structures.

The IZKF has created more transparency about research activities in the various areas and strengthe- ned cooperation between clinics and institutes, but also between different clinics. The IZKF enables re- search funding beyond budget boundaries and also supports risk projects.



Main research areas of the Faculty of Medicine



Programmes and supporting activities of the IZKF for scientists at all career levels

The IZKF offers research grants in all main research areas of the Faculty of Medicine, i.e. immunology and infection research, renal and vascular research, neurosciences, tumor research and medical engineering. Advanced projects are assigned to one of the five main research areas of the Faculty, which is also encoded in the project number. Junior projects and pilot projects are also assigned to these five main research areas. However, there are some junior and pilot projects that cannot be directly allocated to one of the main research areas. These are grouped under “others”. The project reports in the hind part of this report are initially grouped by funding line, and additionally sorted by project numbers.

In all project lines with age restrictions childcare is taken into account. Periods of childcare are granted on a lump-sum basis without proof of actual periods of absence with two years per child for women and one year per child for men. Upon presentation of proof, additional periods of absence may be taken into account for both men and women. In junior projects the IZKF even offers extra funding under certain circumstances.

The SARS-CoV2 pandemic also had an impact on approved projects. Some asked for a later start due to problems in recruiting staff. The IZKF made it possible to start a project a maximum of one year after assessment. 26 projects could start on time. At the end, only 5 projects had a delayed start (funding period 2020-2023).

Advanced Projects

As already mentioned the IZKF supports clinically relevant projects on all main research areas of the Faculty of Medicine. The project duration is 30 months.

After a single funding period projects should be transferred to extramural funding. If the application for extramural funding was filed (as listed below) within the duration of the IZKF project, the duration of the project will be extended for another six months. The successful participation of doctoral fellows funded in Advanced Projects will also be included as a further criterion for a project extension. In case of a two-stage review process for external funding proposals the full application is required for the extension of IZKF funding.

Project funding is allocated after a stringent peer-review process based solely on scientific criteria. Research grants are approved after a two-stage review process. In an initial step, draft proposals are subject to an internal review by an ad hoc committee consisting of members of the Management Board, the ELAN-Committee and the Junior Scientists Committee as well as other recognized scientists of the Faculty of Medicine based on a written proposal and public presentation. Decisions are reached after internal assessment and are communicated immediately afterwards. Successful proposals are presented in the second stage to the Scientific Advisory Board and peer-reviewed during on-site visits. Projects must start within six months. Over the years funding rates were about 30 - 40%.

Applicants are expected to have an active publication record and own external funding. Preliminary results should promise a successful transfer of the project into external funding after the 30-months term. Within this period an application for funding should be submitted to one of the listed funding institutions. Innovative and original ideas and concepts are especially valued as well as clinical relevance and interdisciplinary approaches. Applicants can be from all clinics, departments and institutes of the Faculty of Medicine and co-applicants from other faculties with no age limit.

Call for proposals	every 3 years
Eligibilty	active publication record and own external funding no age limit
Staff	Single projects: graduate student or technical assistant (one position) Tandem projects: graduate student(s) and/or technical assistant (two positions)
Consumables	Single projects: EUR 15,000 p.a. Tandem projects: EUR 35,000 p.a.
Others	Participation in Travel, Publication, High Tech Pool, and Travel Scholarships (only for graduate students)
Duration	30 + 6 months

LOM weighted 4-fold

- BMBF
- DFG
- EU
- NIH-Grants
- Other Federal and State Ministries

LOM weighted 2-fold

- Alexander von Humboldt-Stiftung
- Bayerisches Staatsministerium für Wissenschaft und Kunst
- Bayerische Forschungsstiftung/ Bayerische Landesstiftung
- Bill & Melinda Gates Foundation
- DAAD
- Deutsche Kinderkrebsstiftung/ HIT Deutsche Kinderkrebsstiftung
- Deutsche Stiftung für Herzforschung
- Dr. Mildred-Scheel-Stiftung/ Stiftung Deutsche Krebshilfe
- Else Kröner Fresenius Stiftung
- Fritz Thyssen Stiftung
- Gemeinnützige Hertie-Stiftung
- German-Israeli-Foundation (GIF)
- José Carreras Leukämie-Stiftung
- Volkswagen Stiftung
- Wilhelm Sander-Stiftung

Jochen-Kalden-Funding Programme

The junior research groups represent a central funding instrument of the IZKF. Every year, two new junior research groups have the possibility to benefit from this attractive career development programme.

The review takes place in a one-step process under the auspices of an ad hoc committee composed of members from the IZKF Management Board, members of the ELAN-Committee and the Junior Scientists Committee and the participation of the speakers of the Scientific Advisory Board.

Over a period of 2 years, each junior research group receives funding equivalent to one graduate student and one technical assistant and consumables in the amount of € 40,000 p.a. as flexible funding. If an application for extramural funding is submitted for external funding agency that is at least LOM-weighted 2-fold a further project year is granted.

Call for proposals	annually (1st November)
Eligibility	Newly appointed W1 / integrated W2 professors or W3- professors with tenure track or a comparable option of consolidation doctorate no longer than 10 years ago (medical doctorate) or no longer than 8 years ago (other doctorates, e.g. life sciences, engineering), based on the application deadline for professorship no significant other funding for a junior research group
Staff	Graduate student Technical assistant
Consumables	EUR 40,000 p.a.
Others	Participation in Travel, Publication, High Tech Pool and Travel Scholarships (only for graduate students) Possibility of providing laboratory space for shared use
Duration	24 + 12 months

Junior Projects

For scientists starting their independent career, obtaining their first extramural research funding is an important step. To aid in this process, the IZKF offers starting grants to young postdoctoral physicians and scientists up to 35 years of age without previous significant external funding. Candidates should have a visible publication record and projects should be based on an original idea with first tangible results.

After this time it is expected that successful candidates submit an external grant application. If the application is filed within duration of the junior project, the spending period will be extended by another 6 months. The successful participation of doctoral fellows funded in junior projects will also be included as a further criterion for the extension period.

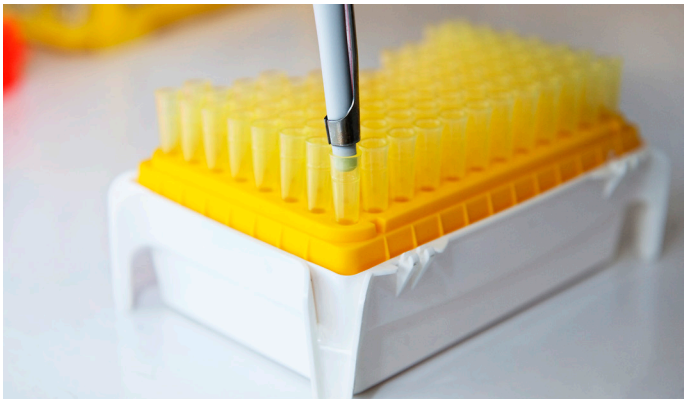
Junior projects are subject to a one-stage internal review only. Full proposals are reviewed by an ad hoc committee composed of members of the Management Board, members of the ELAN-Committee and Junior Scientists Committee based on a written proposal and public presentation. Decisions are reached after internal deliberation and are then communicated immediately afterwards to the proponents. The IZKF expects that at least 25% of the position of the applicant is financed from the budget of the applying institution. The contract should last at least as long as the project runs.

Call for proposals	annually
Eligibilty	for postdoctoral physicians/ scientists up to 35 years of age without previous external funding
Staff	Technical assistant or graduate student
Consumables	EUR 15,000 p.a.
Others	Participation in Travel, Publication, High Tech Pool and Travel Scholarships IZKF laboratory rotations for physicians
Duration	30 months

PILOT PROJECTS

The aim of the ELAN programme is to support scientific projects at a very early stage or under special circumstances and help project leaders to prepare for successful applications for external funding (start-up projects), to support newly established working groups, to develop new innovative ideas (pilot projects) or act as interim funding if temporary gaps arise between individual extramural funding periods. Funding for a period of up to 12 months is primary available to young scientists until the age of 39 (i.e. before the 39th birthday) at the time of application. This does not apply to newly appointed professors who can submit their application regardless of age. In addition, a portion of funds is also available for applicants of all age limits under special conditions such as temporary gaps of funding.

Call for proposals	continuously
Eligibilty	for young scientists until the age of 39 (i.e. before the 39th birthday) at the time of application with a doctoral degree, subordinately also for applicants beyond the age limit newly appointed (W2)-Professors can submit their application regardless of age position of the applicant is financed partly from the budget of the institution
Staff	sum up to one position
Consumables	max. EUR 15,000
Others	Participation in Travel, Publication Pool and Travel Scholarships IZKF laboratory rotations for physicians
Duration	max. 12 months



If a funding application is submitted to an external funding agency within the project period, a bonus (amounting to one third of the approved funds, maximally € 20,000, to be spent within six months of the end of the project) will be granted.

A total of two ELAN projects can be applied for over the course of a scientific career, provided that a publication or a third-party funded project has arisen from the first funding. The IZKF expects that at least 10% of the position of the applicant is financed from the budget of the applying institution.

SYNERGY PROJECTS

In addition to the ELAN-projects, 3-6 applicants from at least three different institutions can jointly apply for synergy projects. The funding line was established as pilot financing for planned group funding initiatives with a maximum volume of € 300,000 per project. Funding can be spent flexibly over a maximum of two years for staff and consumables. The allocation of funds among the applicants can be chosen freely and must be specified in the application. There is no age limit for applicants in synergy projects. Simultaneous funding in another IZKF funding line is possible. An extension of synergy projects is excluded.

Call for proposals	annually (15th July)
Eligibilty	for scientists with a doctoral degree and at least one first author publication no age limit
Funding	max. EUR 300,000
Others	Participation in Travel and Publication Pool
Duration	max. 24 months

DO I(I)T

In addition to the laboratory rotation the IZKF established rotation positions for up to 3 months Ä1/ Ä2 full-time, which can be applied for in preparation for IITs (focus on drawing up the protocol/obtaining an ethics vote). As a rule, they can be divided into up to 6 months, or up to 9 months on justified application.

Applications can be submitted to the IZKF administrative office up to 3 weeks before the respective Management Board meeting. Applications may be submitted by advanced physicians in further training and specialists of all disciplines without age limit.

Call for proposals	twice a year
Eligibilty	advanced physicians in further training and specialists of all disciplines no age limit
Funding	Ä1/Ä2 for 3 months fulltime equivalent
Others	-
Duration	3 to 6 (9) months

Career development for Clinician Scientists

Leave from clinical work for research

Access to protected research time is essential for young clinicians developing their projects. The laboratory rotation positions enable young scientists, who completed their doctorate, to fully devote themselves to a research project.

In the IZKF eight rotation positions are financed continuously and are available as follows. Physicians, who apply for a rotation position as part of a Junior Project, have the opportunity to apply for a rotation position for 12 months full-time or 24 months part-time directly as part of the project application. Within the Clinician Scientist Programme physicians can apply for the Module Step 2 that offers rotation positions for 12 months full-time or 24 months part-time.

In addition to these two programmes, there are rotation positions for flexible use. The positions are available for a period of six months full-time or 12 months part-time, an extension is not possible. Support of up to four rotation projects per year is possible.

Applications may be submitted at any time. There is no age limit, but the planned rotation position must make a suitable contribution to the scientific development of the applicant.

Clinician Scientist Programme

The Clinician Scientist Programme (CSP) is aimed at physicians who are in their specialist training, would like to conduct their own research project and to continue their scientific education within the frame-work of a structured training programme.

The aim of the CSP is to establish a new career path and promotion for Clinician Scientists and to create a structured scientific qualification programme for physicians performing clinical research. The focus is also on strengthening translational research by creating time for scientific work and the preparation for habilitation. The CSP includes professional as well as interdisciplinary further education, mentoring, retreats and regular meetings. At the same time, the physicians conduct their own research project.

The programme at the IZKF has a two-stage structure and is divided into a Step 1 and a Step 2. The Step 1 module lasts two years and requires a proof of the completed doctorate and enrolment in specialist training (already started at the time of joining the CSP).

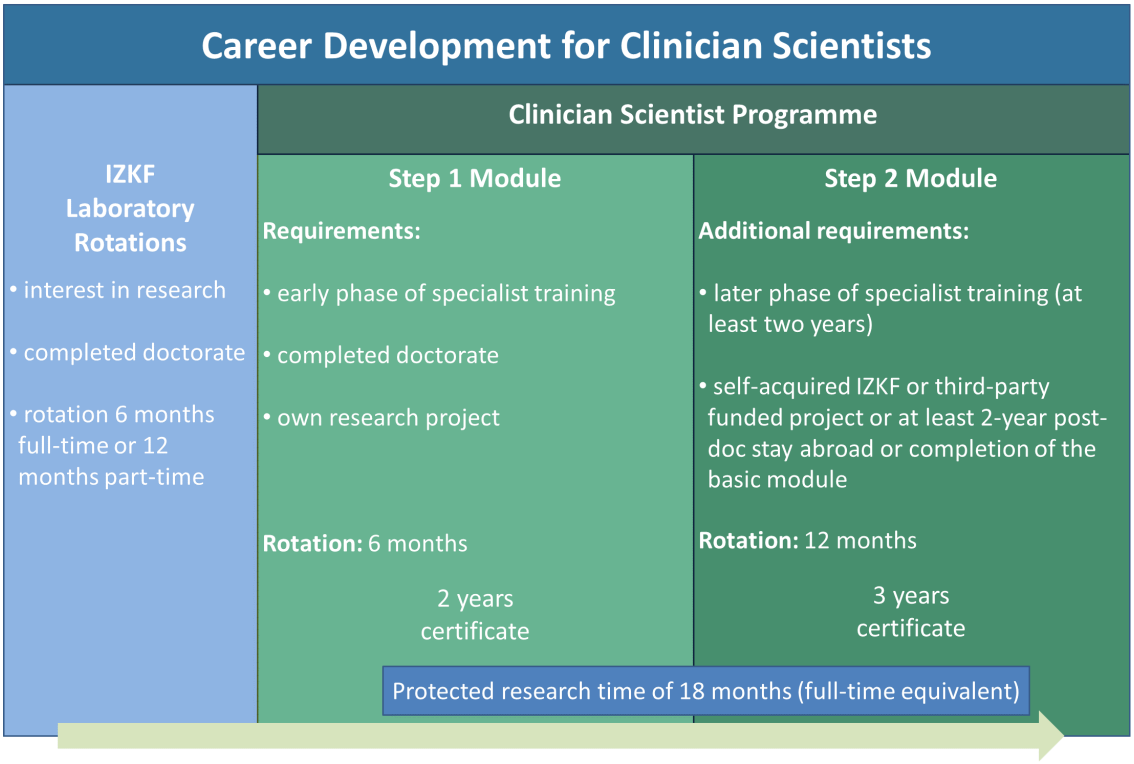
The Step 2 module (duration three years) is aimed at physicians who have already successfully acquired a funding from the IZKF or a third party or the enrolments in the NOTICE Programme. The admission requirement for the Step 2 module is also fulfilled with a postdoctoral stay abroad of at least two years, at least two years of specialist training or with a successfully completed Step 1 module. The leave of absence is 12 months full-time or equivalent part-time via rotation positions. In order to obtain the certificate for the Step 2 module, a leave of absence of a total of 18 months is mandatory, even if the Step 2 was started directly. The department must agree to an additional six months of leave, unless the IZKF (laboratory rotation or Step 1) or other funders have provided funding. The maximum laboratory rotations financed by the IZKF over the entire scientific career is limited to 18 months.

A fast-track change from Step 1 to Step 2 is possible by application, if at least two years of specialist training have been completed and project funding has been personally obtained. Candidates who have been in the habilitation process for more than two years or who have already undergone an interim evaluation by the Fachmentorat cannot be accepted.

Applications for admission to the CSP may be submitted any time. Additionally, the IZKF regularly advertises direct admission to the CSP Step 2 by providing a rotation position.

Clinician Scientist programs financed by third-party agencies can be integrated into the CSP of the IZKF. This means that the participants in the externally funded Clinician Scientist Program have the same rights and obligations as other participants in the IZKF-CSP.

Successful completion of the CSP Step 2 allows admission to the doctoral programme for a doctorate in human biology at the Erlangen Faculty of Medicine.



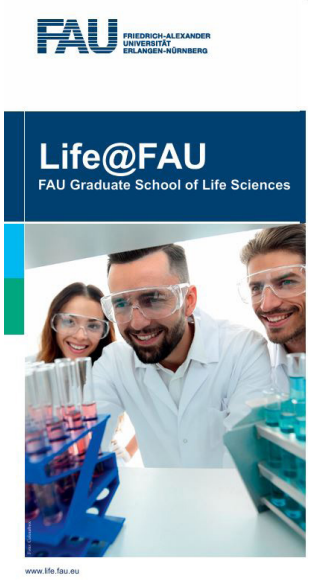
Overview of career programmes for clinician scientists

Structured Training Programmes For Doctoral Fellows At The IZKF

Life@FAU

The Graduate School for Life Sciences (Life@FAU) was launched following an initiative of the IZKF to offer an interdisciplinary structured training programme for doctoral students at the Faculty of Medicine and the Department of Biology. The Faculty of Medicine and the Department of Biology at the Faculty of Sciences are involved on equal footing.

All research training groups of both faculties are members of Life@FAU including the IZKF Research Training Group. The objectives of Life@FAU are to promote and support structured training programmes for doctoral candidates at FAU, to create uniform standards in postgraduate education in the field of life sciences and to ensure the provision of structured training programmes.



MD-Thesis Scholarships

This programme was initiated to arouse interest for science in motivated medical students early on in their career. Medical students are supported in performing an experimental thesis.

Now 30 grants for eight months each are available for medical students with outstanding performance and commitment in studies. The participants have to work full-time in the laboratory and a scholarship is offered during their research activity. Furthermore, the doctoral fellows have to complete defined training modules during the 12 months after start of the fellowship. Training modules include guest speaker seminars, soft skills courses and the continuous supervision by a mentoring committee.

Every participant of the MD-Thesis Scholarship Programme automatically becomes a member of the IZKF Research Training Group and the Graduate School of Life Sciences at FAU (Life@FAU). Thus, the doctoral students can benefit from a structured, interdisciplinary training programme.

Research Training Group

The IZKF runs a research training group for all doctoral fellows and MD-students of the IZKF. Participation is mandatory for all IZKF-funded doctoral candidates in sciences and medicine who are not involved in an alternative structured training programme of the Faculty/ University. Other students may also associate with the research training group.

Aims of the IZKF Research Training Group include fostering networking and scientific self-organisation, methodological competence and soft skills as well as offering insights into other scientific fields and career opportunities. A structured seminar programme, courses in basic methods, in scientific writing and presentation are organised by the IZKF. In addition, the participants of the research training group have to attend guest speaker seminars and participate in the annual internal retreat. Participation in external congresses and in seminars organised by the doctoral fellows are mandatory.

The research training group also offers a mentoring programme for all doctoral fellows. Each doctoral fellow selects three mentors. At least one annual meeting of the doctoral student and the mentoring committee is expected.

The IZKF Research Training Group is divided into five research areas: Jour Fixe Ink (Immunology/infection/renal and vascular research), Jour Fixe Neuro (Neuroscience), Jour Fixe Onco (Oncology), Jour Fixe DigIT (Digital information technology) and the Jour Fixe MedTech (Medical and healthcare technology).

Postgraduate Workshop 2023: Winners of Poster Prizes, Chiara Van Passen and Diana Matthe, Prof. Becker

Special Programmes

The following special programmes provide additional funding for IZKF projects:

High Tech Pool

The IZKF actively encourages the use of modern “omics” technologies in the projects, such as those provided by the Core Unit Next Generation Sequencing. Since these experiments are generally expensive and consumables within IZKF advanced and junior projects are restricted, additional support is necessary. Costs for consumables can therefore be supported upon request with up to € 10,000 per project, provided that the project itself contributes at least 30% of the total sum. Exceptions are services provided by OICE, PIPE and FACS. Services from core units NGS, METAB, MACE and CUBiDA can be covered. The High Tech Pool is primarily for analyses/services of the mentioned core units at the site and not for in-house implementation in the laboratory (e.g. KITs).

The High Tech Pool is also available to active participants of the CSP Step 2 Module.

Travel Funding

To enable IZKF members to present their results to the academic community, the IZKF supports their participation in international conferences. All applicants are expected to give a lecture or present a poster. The subject matter of the event must be related to the IZKF project in order to receive funding. The financial contribution of the IZKF is limited to € 500 for conferences in Germany, € 1,000 in Europe, and up to € 1,500 for conferences outside Europe.

A project-related active participation is required and an application in advance is necessary.

Publication Funding

The publication of results obtained in IZKF projects in scientific journals is actively supported. It is expected that the IZKF funding of the project is acknowledged and the affiliation is Erlangen. IZKF also supports open access publications.

If the IZKF is the only sponsor and the total costs of the publication are below € 3,000, IZKF can cover up to € 1,500. If the total costs exceed € 3,000 a financial contribution of € 2,000 is given by the IZKF. For publications in which the IZKF as well as other sponsors are mentioned, the IZKF contribution is € 500 less.

Travel Scholarships

Travel scholarships allow IZKF's young researchers to spend time in other laboratories in Germany or abroad to conduct important experiments or learn the latest techniques and methods. The programme also allows young scientists to intensify existing collaborations or establish new ones. Travel grants include transportation and accommodation for up to three months. An extension of the travel scholarship for another three months is possible.

IZKF Visiting Professor Programme

To encourage cooperation and to foster the exchange of ideas, IZKF promotes visits of external scientists. Every year approx. 10 scientists from abroad but also from other places in Germany can be invited for a stay of two days - four months. The programme covers an amount of up to € 3,000 for travel and accommodation costs for visiting researchers. Application is restricted to IZKF members and the invited researcher's subject must be related to the IZKF.

Availability of the special programmes in the various funding lines is summarized below.

	High Tech Pool	Travel Pool	Publication Pool	Travel Scholarships
Advanced Projects (Project leaders and scientific staff financed by project)	✓	✓	✓	✓ (only for doctoral students)
Junior Projects (Project leaders and scientific staff financed by project)	✓	✓	✓	✓
Pilot Projects (Project leaders and scientific staff financed by project)	✗	✓	✓	✓ (only for scientists of pilot projects under the age limit)
Syngery Projects (Project leaders and scientific staff financed by project)	✓	✓	✓	✓ (only for doctoral students)
Jochen-Kalden Funding Programm **(former Junior Research Groups)** (Project leaders and scientific staff financed by project)	✓	✓	✓	✓ (only for doctoral students)
Clinician Scientists Programme (active members)	✓ (only for Step 2)	✓	✓	✓
Other IZKF laboratory rotations	✗	✓	✓	✓
MD-Thesis Scholarships	✗	✓	✓	✓
Time frame	only within project period	6 months after the end of the project (MD: 12 months after the end of the scholarship)	12 months after the end of the project	only within project period

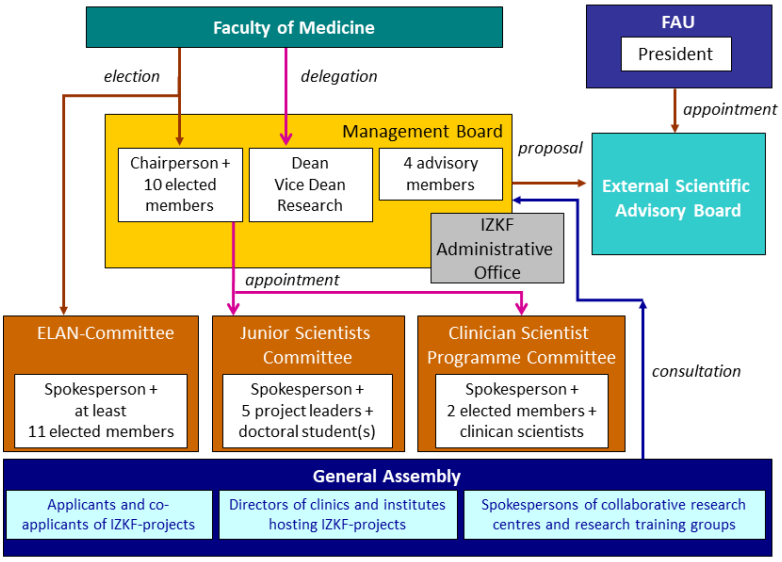
Participants in the Do I(I)T programme do not have access to the special programmes.

The table shows which programmes of IZKF are eligible for using special programmes.

GOVERNANCE

The IZKF is a self-organised structure within the Faculty of Medicine. The IZKF has a set of written rules and regulations approved by the Faculty of Medicine. All rules and regulations are continuously reviewed and revised, if necessary. The Statutes of the IZKF regulate the status, tasks and objectives of the IZKF as well as the responsibilities and composition of the committees. The Rules of Procedure specify the application procedure, the funding and duration of the projects as well as the decision-making process among Chairman, Management Board and the External Scientific Advisory Board. Finally, the Advisory Board regulations regulate the IZKF's cooperation with the Advisory Board in detail. All regulations are available on the IZKF Homepage.

Governing bodies include the Management Board, the External Scientific Advisory Board, the ELAN-Committee, the Junior Scientists Committee, the Clinician Scientist Programme Committee and the General Assembly.



Governance of the IZKF

The Management Board is the general steering committee of the IZKF. It is responsible for developing the scientific programme, controlling the financial framework and allocating resources to projects and ensures that results are reported. Five annual meetings are held and decisions are taken by simple qualified majority. Elected members include the Chairman who is responsible for daily operations with the support of the Administrative Office. Re-election is possible for all members of the Board.

Programmes and the financial framework are reviewed and approved by the External Scientific Advisory Board. This body meets on site every two or three years to oversee the general development of the IZKF and the proposed projects. The Board consists of at least 10 internationally recognized scientists from universities and research institutes led by an elected chairperson.

The ELAN-Committee is responsible for reviewing pilot and synergy projects and its members assist in the selection of advanced and junior projects. It consists of the spokesman for pilot projects (ELAN) and at least 11 further members all elected by the Faculty of Medicine for a period of three years.

The Junior Scientists Committee supports the Management Board in establishing and supervising career development programmes for young scientists. It selects the recipients of the MD-Thesis scholarships and organizes the IZKF Research Training Group. In addition, its members participate in the internal review process for project funding.

The Clinician Scientist Programme Committee (CSP-Committee) accompanies the Clinician Scientist Programme of the IZKF in terms of organisation and content and makes recommendations regarding the admission of new applicants to the Clinician Scientist Programme.

The General Assembly convenes once a year to discuss the annual report of the chairman and the further development of the IZKF. Its members are all project leaders, the directors of clinics and institutes receiving funding, and the speakers of all local collaborative research centers and research training groups.

External Advisory Board (from left to right): Prof. Moch, Prof. Busch, Prof. Mertens, Prof. Kuhlmann, Prof. Tiegs, Prof. Prinz, Prof. Seufferlein, Prof. Kalinke, Prof. Siebert, Prof. Schulz

Management Board

Chairperson

Prof. Dr. Michael Wegner, Institute of Biochemistry - Chair of Biochemistry and Pathobiochemistry


Prof. Dr. Wegner


Prof. Dr. Bozec

Deputy Chairperson

Prof. Dr. Aline Bozec, Department of Medicine 3

Members

Prof. Dr. Christoph Becker, Department of Medicine 1
Prof. Dr. Carola Berking, Department of Dermatology
Prof. Dr. Christian Bogdan, Institute of Clinical Microbiology, Immunology and Hygiene
Prof. Dr. Thomas Brabletz, Chair of Experimental Medicine I (until 04/2024)
Prof. Dr. Johann Helmut Brandstätter, Department of Animal Physiology
Prof. Dr. Dr. Raymund Horch, Department of Plastic and Hand Surgery
Prof. Dr. Dieter Chichung Lie, Institute of Biochemistry
Prof. Dr. Markus Neurath, Department of Medicine 1
Prof. Dr. André Reis, Institute of Human Genetics
Prof. Dr. Mario Schiffer, Department of Medicine 4
Prof. Dr. Friederike Zunke, Department of Molecular Neurology

Consultative Members

Prof. Dr. Joachim Hornegger, President of the FAU
Christian Zens, Head of Administration of the FAU
Prof. Dr. Dr. Heinrich Iro, Medical Director of the University Hospital Erlangen
Dr. Albrecht Bender, Head of Administration of the University Hospital Erlangen


Prof. Dr. Becker


Prof. Dr. Berking


Prof. Dr. Bogdan


Prof. Dr. Brabletz


Prof. Dr. Brandstätter


Prof. Dr. Dr. Horch


Prof. Dr. Dr. Lie


Prof. Dr. Dr. Neurath


Prof. Dr. Reis


Prof. Dr. Schiffer


Prof. Dr. Zunke


Prof. Dr. Hornegger


Zens


Prof. Dr. Dr. Iro


Dr. Bender

Members of the Management Board (as of 31st December 2023)

External Scientific Advisory Board

Chairperson

Prof. Dr. Thomas Seufferlein,
University Hospital Ulm, Internal Medicine I

Deputy Chairperson

Prof. Dr. Tanja Kuhlmann,
University Hospital Münster, Institute of Neuropathology


Prof. Dr. Seufferlein


Prof. Dr. Kuhlmann

Members

Prof. Dr. Dirk Busch, Technical University of Munich, Institute for Medical Microbiology, Immunology and Hygiene

Prof. Dr. Ulf Dittmer, University Hospital Essen, Institute of Virology

Prof. Dr. Anka Dorhoi, Friedrich-Löffler-Institut, Institute of Immunology (since 03/2024)

Prof. Dr. Renate Kain, Medical University of Vienna, Department of Pathology (since 03/2024)

Prof. Dr. Ulrich Kalinke, TWINCORE, Centre for Experimental and Clinical Infection Research

Prof. Dr. Thomas Kamradt, Jena University Hospital, Institute of Immunology

Prof. Dr. Dörthe Katschinski, Göttingen University Medical Center, Department of Cardiovascular Physiology (until 12/2023)

Prof. Dr. Peter R. Mertens, University Hospital Magdeburg, Clinic for Renal and Hypertension Diseases, Diabetology and Endocrinology

Prof. Dr. Holger Moch, University Hospital Zurich, Institute of Pathology and Molecular Pathology (until 12/2023)

Prof. Dr. Jörg Prinz, LMU München, Department of Dermatology and Allergology

Prof. Dr. Jörg B. Schulz, University Hospital Aachen, Department of Neurology

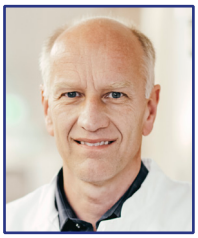
Prof. Dr. Reiner Siebert, University Hospital Ulm, Institute of Human Genetics

Prof. Dr. Gisa Tiegs, Hamburg-Eppendorf University Medical Center, Institute of Experimental Immunology and Hepatology (until 12/2023)

Prof. Dr. Sibylle von Vietinghoff, University Hospital Bonn, Internal Medicine I, Nephrology (since 03/2024)

Prof. Dr. Konstanze F. Winklhofer, Ruhr-University Bochum, Institute of Biochemistry and Pathobiochemistry


Prof. Dr. Busch


Prof. Dr. Dittmer


Prof. Dr. Kalinke


Prof. Dr. Kamradt


Prof. Dr. Katschinski


Prof. Dr. Mertens


Prof. Dr. Moch


Prof. Dr. Prinz


Prof. Dr. Schulz


Prof. Dr. Siebert


Prof. Dr. Tiegs


Prof. Dr. Winklhofer

External Scientific Advisory Board (as of 31st December 2023)

ELAN-Committee

Spokesperson for pilot projects (ELAN)

Prof. Dr. André Reis, Institute of Human Genetics

Prof. Dr. Reis

Members

Prof. Dr. Tobias Bäuerle, Institute of Radiology
Prof. Dr. Caroline Voskens, Department of Dermatology
PD Dr. Simone Brabletz, Chair of Experimental Medicine I
Prof. Dr. Anna Fejtova, Department Psychiatry and Psychotherapy
Prof. Dr. Kristian Franze, Institute of Medical Physics and Microtissue Engineering
Prof. Dr. Claus Hellerbrand, Institute of Biochemistry
Prof. Dr. Miriam Kalbitz, Department of Surgery (until 09/2023)
Prof. Dr. Thomas Kinfe, Department of Neurosurgery
Prof. Dr. Gerhard Krönke, Department of Medicine 3 (until 03/2023)
Prof. Dr. Andreas Ramming, Department of Medicine 3 (since 02/2023)
Prof. Dr. Heiko Reutter, Department of Paediatrics and Adolescent Medicine
Prof. Dr. Veit Rothhammer, Department of Neurology
Prof. Dr. Peter Soba, Institute of Physiology and Pathophysiology
Prof. Dr. David Vöhringer, Department of Infection Biology
Prof. Dr. Maximilian Waldner, Department of Medicine 1

Prof. Dr. Bäuerle

Prof. Dr. Voskens

PD Dr. Brabletz

Prof. Dr. Fejtova

Prof. Dr. Franze

Prof. Dr. Hellerbrand

Prof. Dr. Kinfe

Prof. Dr. Ramming

Prof. Dr. Reutter

Prof. Dr. Rothhammer

Prof. Dr. Soba

Prof. Dr. Vöhringer

Prof. Dr. Waldner

Members of the ELAN-Committee (as of 31st December 2023)

Junior Scientists Committee

Spokesperson for career development programmes

Prof. Dr. Christoph Becker, Department of Medicine 1

Prof. Dr. Becker

Members

Daniel Firmbach, Institute of Pathology (since 12/2023)

Prof. Dr. Thomas Gramberg, Institute of Clinical and Molecular Virology

Prof. Dr. Claudia Günther, Department of Medicine 1

Dr. André Karius, Department of Radiation Oncology (until 11/2023)

Sabrina Kojic, Institute of Biochemistry (since 05/2023)

Prof. Dr. Chichung Lie, Institute of Biochemistry

PD Dr. Adrian Regensburger, Department of Paediatrics and Adolescent Medicine

PD Dr. Ulrike Steffen, Department of Medicine 3

Firmbach

Prof. Dr. Gramberg

Kojic

Prof. Dr. Günther

Prof. Dr. Lie

PD Dr. Regensburger

PD Dr. Steffen

Members of the Junior Scientists Committee (as of 31st December 2023)

Clinician Scientist Programme Committee

Spokesperson for Clinician Scientist Programme
Prof. Dr. Carola Berking, Department of Dermatology


Prof. Dr. Berking

Members
PD Dr. Markus Eckstein, Institute of Pathology (until 10/2023)
Dr. Eva Maier, Department of Oral and Cranio-Maxillofacial Surgery
Prof. Dr. Veit Rothhammer, Department of Neurology
Dr. Alexander Schnell, Department of Paediatrics and Adolescent Medicine (since 11/2023)
Prof. Dr. Maximilian Waldner, Department of Medicine 1


Dr. Maier


Prof. Dr. Rothhammer


Dr. Schnell


Prof. Dr. Waldner

Members of the CSP-Committee (as of 31st December 2023)

Finances

Since 2004, the IZKF has been fully supported by intramural funds. The main financial contribution is given by the Faculty of Medicine. Additional contributions are received from the FAU.

Part of the expenditures of 2023 were financed from residual funds of the previous years.

Revenues	
Support of the Medical Faculty	5,402 K€
Support of the University	368 K€
Other revenues	72 K€
Total revenues 2023	**5,842 K€**

Expenditures	
Advanced projects	1,998 K€
Pilot projects	1,023 K€
Career development	2,378 K€
thereof junior research groups	357 K€
thereof junior projects	986 K€
thereof laboratory rotations	633 K€
thereof Topecs	132 K€
thereof clinician scientist programme	10 K€
thereof MD-thesis scholarships	221 K€
thereof research training groups	39 K€
Central projects	106 K€
Administration	306 K€
Total expenditures 2023	**5,811 K€**

Revenues and expenditures 2023

Output and Evaluation

Various parameters are used to assess compliance with the mission of the IZKF in advancing clinically oriented research at the Faculty. Scientific publications and academic success of young scientists are the most obvious and straightforward ones. Additionally, the acquisition of extramural funding is an explicit objective of the IZKF. Other important parameters for the IZKF are the number of different institutions and scientists, who are involved in the IZKF, the number of interdisciplinary projects as well as the number of joint publications.

In the reporting period 114 scientific projects were actively running: 49 advanced projects, 18 junior projects, 42 pilot projects and five junior research groups. In addition, six junior projects started their work in 2023 (3) or in the beginning of 2024 (3).

49 advanced, 18 junior projects and five junior research groups published 58 original articles in 2023 resulting in an average of 0,8 publications per project. The cumulative impact factor (IF) was 532.000, averaging 9.172 per publication. 16 publications have an IF of more than 10. Additional articles of finalised projects are in preparation, submitted or accepted. Publications that have already been accepted are listed in the corresponding final reports.

Intense academic activity within the IZKF advanced and junior projects is reflected in 6 master theses, 66 doctoral theses and five habilitations that were in progress or finalised in 2023. One professorship to IZKF project leaders were offered. A total of 87 project leaders and 61 employed scientists (PhDs and Post-Docs) are involved in 72 scientific projects (running advanced projects, junior research groups and junior projects 2023) funded by the IZKF.

In many instances funding by the IZKF starts at an early phase of the project, thus it must be considered as a high risk funding programme. It is nevertheless reassuring that most of the projects are successful and many of them are continued after the termination of intramural funding. On the following pages the output of the IZKF-projects is given, supported by figures and results of a detailed.

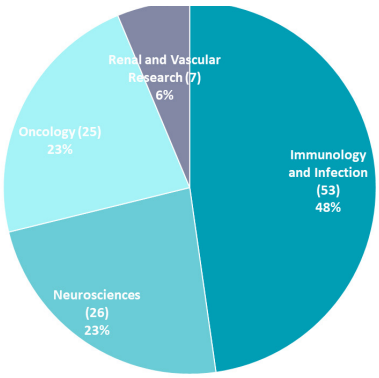
The following table shows all institutions with a running Advanced, Junior or Pilot Project in 2023 and their association to the main research areas of the Faculty. In addition, it can be seen which institution was funded with rotation positions (without assignment to a research area):

Institute	Advanced Projects	Junior Projects	Pilot Projects	Laboratory Rotation
Chair of Experimental Medicine I	O		O	
Chair of Experimental Medicine II	O			
Chair of Pharmacology and Toxicology			N	
Department of Biology – Chair of Genetics	I			
Department of Child and Adolescent Mental Health			S	
Department of Dermatology	I, O		O	X
Department of Immune Modulation	I		I	
Department of Infection Biology			I	
Department of Medicine 1	I, O	I, S, N	I, O	X
Department of Medicine 3	I, O	I	I	X
Department of Medicine 4	R		R	X
Department of Medicine 5	O	I, S		X
Department of Molecular Immunology		I	I	
Department of Molecular Neurology	N	N	N	
Department of Molecular Pneumology	I			
Department of Nephropathology	I, R, O		R	
Department of Nuclear Medicine				X
Department of Obstetrics and Gynecology	O		O, S	
Department of Operative Dentistry and Periodontology		M	N, I	X
Department of Orthodontics and Orofacial Orthopedics	N		N, S	
Department of Orthopaedic and Trauma Surgery				X
Department of Paediatric Cardiac Surgery			R	X
Department of Paediatrics and Adolescent Medicine	O	I, R, M	O, S	X
Department of Plastic and Hand Surgery			O	
Department of Psychiatry and Psychotherapy	N	N	N	
Department of Psychosomatic Medicine and Psychotherapy		S		
Department of Physics – Chair of Biological Optomechanics	I			
Department of Prosthodontics			M	
Department of Radiation Oncology		O		
Department of Stem Cell Biology	N	N	N	
Department of Surgery	O			X
Department of Urology			S	
Institute of Biochemistry - Chair of Biochemistry and Molecular Medicine	O, N, I		O, N	
Institute of Biochemistry - Chair of Biochemistry and Pathobiochemistry	N	N		
Institute of Cellular and Molecular Physiology	R			
Institute of Clinical and Molecular Virology	I	O	I	
Institute of Clinical Microbiology, Immunology and Hygiene	I			
Institute of Experimental and Clinical Pharmacology and Toxicology			S	
Institute of General Practice				X
Institute of Human Genetics	N			X
Institute of Medical Physics	E			
Institute of Pathology	O	O	O	X
Institute of Physiology and Pathophysiology	N			
Institute of Radiology			M	X

I - Infection and Immunology, N - Neurosciences, O - Oncology, R - Renal and Vascular Research, M - Medical Engineering, S - Others, X - Funding of a rotation position, without assignment to a research area

Advanced Projects

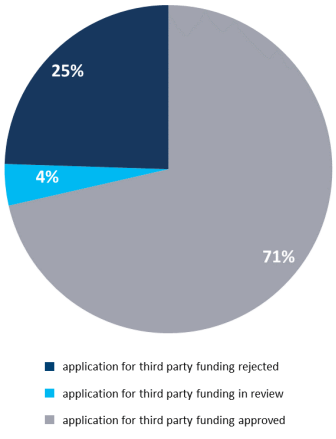
The 41 project leaders of the funding period 2020 - 2023 come from 23 different institutions. 11 (27%) of the project managers are women, 30 (73%) men. Project leaders include 19 (46%) natural scientists and 22 (54%) clinician scientists. In 2022, 25 new projects were approved. Of the 34 project leaders, 6 (18%) are female and 28 (82%) male. 15 (44%) of them are clinician scientists and 19 (56%) are natural scientists.



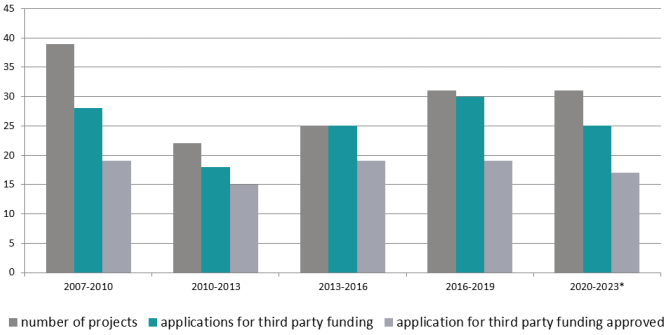
Distribution of advanced projects as per main research area between 2013 and 2022 incl. advanced projects 2022 - 2025

The projects started with the filling of the approved positions or with the first disposition. Due to the SARS-CoV-2 pandemic, the projects had the possibility to start at the latest by January 1, 2021. Tandem projects have the option of filling their positions time shifted and thus do not lose any approved funds for personel. Beginning with the funding period of 2010-2013, grants were awarded for a period of 30 months with an extension by 6 months, if these projects are submitted for external funding. Within the funding period of 2013-2016 all projects submitted external funding applications and therefore received the 6 months funding extension. Of the 31 projects from the 2016-2019 funding period, 30 (97%) have applied for project extensions. From the cohort 2020-2023, 25 (80%) of the 31 projects have successfully applied for an extension.
When considering the last three funding periods (2010-2019), 78 projects were funded by the IZKF of which 73 (94%) submitted external funding applications. 53 of these projects (73%) were granted extramural funding, 20 (27%) were not funded.

Regarding the projects of the period 2020-2023, 17 (68%) of the 25 projects, which applied for external grants, already received funding approvals. Of the projects in the 2023-2025 cohort, 5 (20%) have already stated that they have received approval for external funding in connection with the IZKF project.

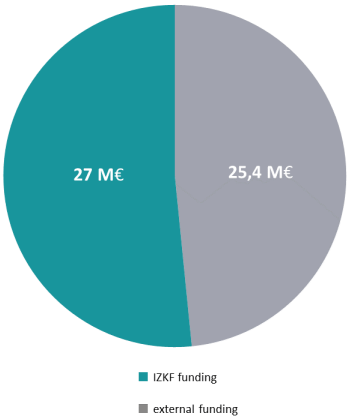


Approved applications for external funding of advanced projects between 2010 and 2023

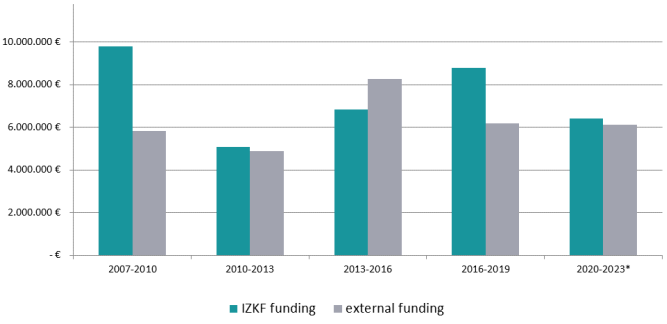


This column graph compares the number of advanced projects with the number of the submitted and approved applications for external funding in each funding period.

* Further applications for external funding agencies are planned.



External funding received from advanced projects between 2010 and 2023



External funding received from advanced projects between 2007 and 2023

* Further applications for external funding agencies are planned.

Jochen-Kalden-Funding Programme

In 2023 there were 5 running junior research groups.

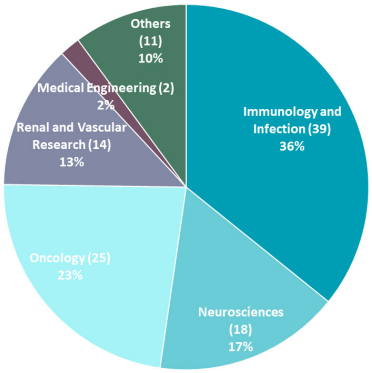
In the first round of applications, Prof. Claudia Günther (Department of Medicine 1), Prof. Janina Müller-Deile (Department of Medicine 4), Prof. Marisa Karow (Institute of Biochemistry) and Prof. Friederike Zunke (Department of Molecular Neurology) were selected as group leaders. All four groups were able to apply for an extension due to applications for extramural funding. Following the call in 2022, Prof. Caroline Voskens (Department of Dermatology) was accepted and already started her project. Prof. Ricardo Grieshaber-Bouyer (Department of Medicine 3) and Prof. Lydia Meder (Department of Experimental Medicine I) were successful in the 2023 call. The next application deadline is November 1st, 2024.

Junior Projects

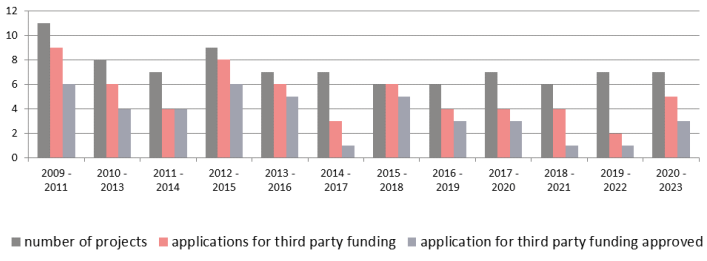
The first call for junior projects was in 2009. Proposals are accepted every year. Overall 109 junior projects were selected for funding between 2009 and 2023. In this period, 45 (41%) physicians received funding and 64 (59%) scientists. 30 (67%) of the physicians requested a laboratory rotation. Of them, 10 (33%) were women and 20 (67%) men. In general, men and women were almost equally supported when assessed over the entire funding period.

53 successful applicants were women and 56 men. The median age was 32 at the time of application, for both women and men. All main research areas of the Faculty are represented with immunology and infection (36%) and oncology (23%) being the most successful over the years. Overall candidates from 27 different institutions within the Faculty of Medicine were selected.

In 2023, eleven proposals were reviewed and six (55%) of them received funding. The approved projects cover the main research areas immunology and infection and neurosciences. The successful applicants work in five different institutions within the Faculty of Medicine. In total, physicians and other scientists were funded equally in this year's call for applications. Four (67%) women received funding and two (33%) men.



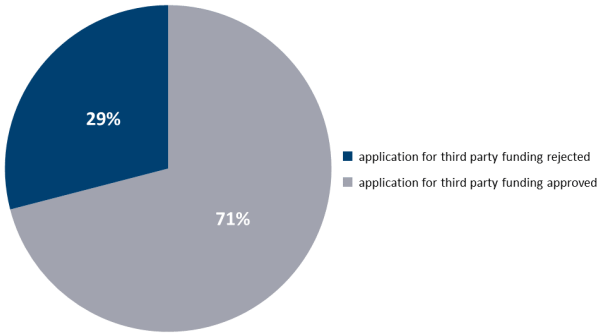
Distribution of junior projects as per main research area of the Faculty of Medicine between 2009 and 2023



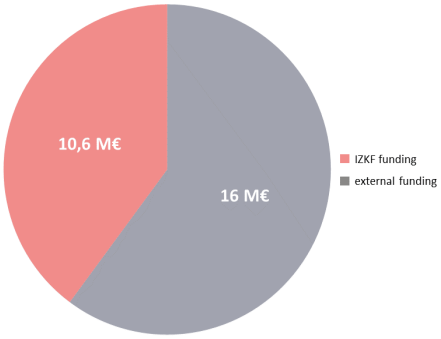
Success-rate of junior projects initiated between 2009-2020

The median age was 33 years.

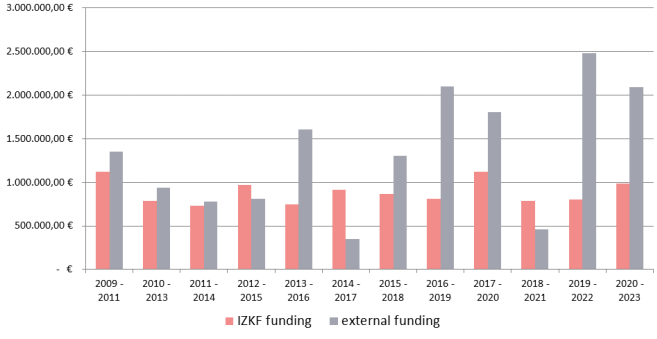
The Junior Projects also perform very well in raising external funding. 71% from the projects that started between 2009 and 2020 applied for third-party funding to an external funding agency. This development has been stable over the entire duration of the programme.



Approved applications for external funding of junior projects (projects initiated between 2009 and 2020)



External funding received from junior projects started between 2009 and 2020



External funding received from junior projects initiated between 2009 and 2020

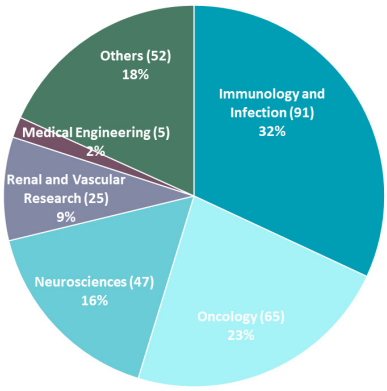
Pilot Projects (ELAN)

Pilot projects are intended to support scientists at an early career stage. Additionally, limited funds are also available for supporting tenured Faculty members in obtaining third party funding.

In the reporting period, 37 proposals were assessed by the ELAN-Committee. Of these, 27 (73%) received funding and one was retracted. The approved projects cover all main research areas of the Faculty of Medicine: immunology and infection (9), oncology (8), neurosciences (4), renal and vascular research (2) as well as medical engineering (2), and two pertained to other research topics. Successful applicants were from 21 different institutions, 19 (70%) being women and 8 (30%) men. Median age was 35 (33 for women and 37.5 for men).

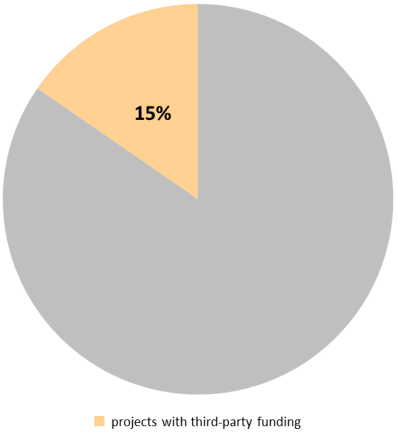
Applications for pilot projects can be submitted electronically via the ELAN-Tool at any time. The ELAN-Committee meets four times a year and selects projects for funding after external and internal peer review. Between 2012 and 2023, a total of 388 proposals for pilot projects were reviewed in the ELAN-programme. Overall, 285 (73%) projects were funded. The gender ratio was even, with 143 women (50,2%) and 142 men (49,8%) being successful, and the median age was 34 years.

All main research areas of the Faculty were represented; with the areas of immunology and infection (32%) and oncology (23%) contributed the majority of successful applications.

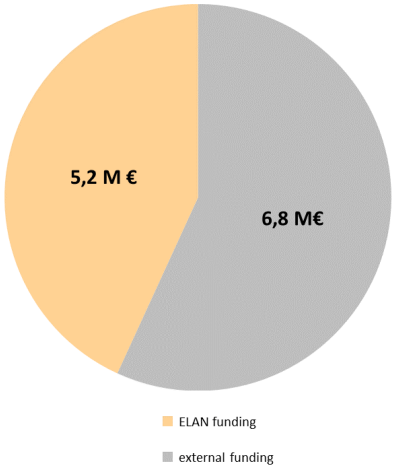


Distribution of pilot projects as per main research area between 2012 and 2023

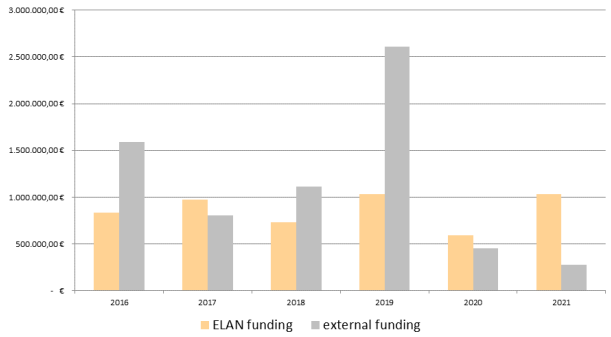
In the following, the success rate of acquiring external funding is summarised.



Pilot projects with external funding (completed projects with approval years between 2016 and 2021)



External funding received from all completed pilot projects (year of approval between 2016 and 2021)



External funding from completed pilot projects started between 2016 and 2021

Laboratory Rotations

In 2023, 30 physicians were funded with a rotation position. In addition to pure laboratory rotations, positions are also open to junior project leaders, participants in the Module Step 1 and Step 2 of the Clinician Scientist Programme. Participants of the DFG-funded NOTICE Programme are funded with 10% of their salary by the IZKF.

Rotations		
Dr. Rebecca Baur	Department of Medicine 5	07/2022 - 07/2023, 50%
Dr. Dennis Kannenkeril	Department of Medicine 4	10/2022 - 09/2023, 50%
Dr. Johanna Kurzhagen	Department of Medicine 4	07/2022 - 12/2022, 07/2023 - 12/2023, 50%
Dr. Harriet Morf	Department of Medicine 3	09/2022 - 08/2023, 50%
Dr. Melissa Pauly	Institute of Human Genetics	07/2023 – 06/2024, 50%
Dr. Kathrin Rottermann	Department of Paediatric Cardiac Surgery	06/2022 - 05/2023, 50%
Dr. Stephanie Sembill	Department of Paediatrics and Adolescent Medicine	09/2022 - 02/2023, 100%

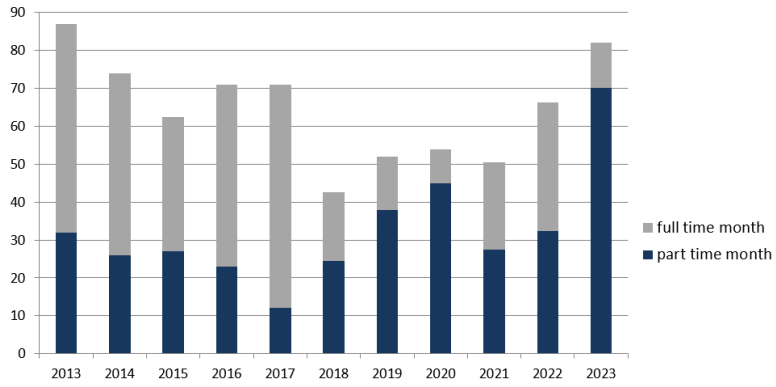
Rotations of Junior Project Leaders		
Dr. Miriam Düll	Department of Medicine 1	04/2023 – 03/2025, 50%
Dr. Alina Hilger	Department of Paediatrics and Adolescent Medicine	10/2022 - 09/2024, 50%
Dr. Benedikt Jacobs	Department of Medicine 5	02/2022 - 01/2024, 50%
Dr. Eva Maier	Department of Operative Dentistry a. Periodontology	03/2023 -02/2024, 100%
Dr. Christian Matek	Departement of Pathology	01/2023 -12/2024, 50%
PD Dr. Adrian Regensburger	Department of Paediatrics and Adolescent Medicine	01/2021 - 05/2021, 01/2022 - 11/2023, 50%

Rotations of successfull applicatants of Clinician Scientists Programme		
Dr. Lisette Warkentin	Institute of General Practice	07/2023 – 06/2025, 50%

Rotations of Clinician Scientists in the NOTICE-Programme		
Dr. Armin Atzinger	Department of Nuclear Medicine	05/2023 – 04/2026, 10%
Janina Auth	Department of Medicine 3	05/2023 – 04/2024, 10%
Giulia Corte	Department of Medicine 3	05/2023 – 04/2024, 10%
Filippo Fagni	Department of Medicine 3	05/2023 – 04/2024, 10%
Dr. Panagiotis Garantziotis	Department of Medicine 3	05/2023 – 04/2026, 10%
Dr. Danilo Hackner	Department of Surgery	05/2023 – 09/2023, 10%
Dr. Anne Jacobsen	Department of Surgery	05/2023 – 04/2026, 10%
Dr. Tilman Jobst-Schwan	Department of Medicine 4	05/2023 – 04/2026, 10%
Dr. Anna Kanewska	Department of Orthopaedic and Trauma Surgery	05/2023 – 04/2026, 10%
Dr. Claudius Mathy	Department of Radiology	05/2023 – 04/2026, 10%
Dr. Maria Gabriella Raimondo	Department of Medicine 3	05/2023 – 04/2026, 10%
Dr. Moritz Ronicke	Department of Dermatology	05/2023 – 04/2026, 10%
Jonas Schmid	Department of Medicine 1	05/2023 – 04/2024, 10%
Julia Scholz	Department of Medicine 5	05/2023 – 04/2024, 10%
Dr. Sebastian Schramm	Department of Medicine 1	05/2023 – 04/2026, 10%
Lukas Sollfrank	Department of Dermatology	05/2023 – 04/2024, 10%

Laboratory rotations 2023 with name, institute, funding period und scope of position

Laboratory Rotations



The table shows the claimed months related to full time for each year. Due to the former duration of 12-24 months, the rotations usually last over a period of 2-3 calendar years.

Clinician Scientist Programme

During the funding period, altogether 29 physicians took part in the CSP. A rotation position within the CSP (Module Step 2) can be applied for. The submission of applications is continuously possible.

In 2023 2 applications were submitted. The Clinician Scientist Programme RECORD has been funded by the Else Kröner-Fresenius Foundation since January 1, 2020 and is associated to the Clinician Scientist Programme.

The following physicians participated in the Clinician Scientist Programme in 2023:

Module Step 1	
Dr. Razvan Marius Brazdis	Department of Psychiatry and Psychotherapy (C)
Dr. Alexander Grotemeyer	Department of Psychiatry and Psychotherapy (S)
Dr. Danilo Hackner	Department of Surgery
Dr. Alaa Hamzeh	Institute of Pathology (S)
Dr. Anna Kanewska	Department of Orthopaedic and Trauma Surgery
Dr. Elias Koch	Department of Dermatology
Dr. Harriet Morf	Department of Medicine 3 (C)
Dr. Melissa Pauly	Institute of Human Genetics (S)
Dr. Maria Gabriella Raimondo	Department of Medicine 3 (C)
Dr. Christina Regensburger	Department of Paediatrics and Adolescent Medicine
Dr. Jan Schaefer	Department of Paediatrics and Adolescent Medicine
Dr. Alexander Schnell	Department of Paediatrics and Adolescent Medicine (C)
Dr. Thanos Tsaktanis	Department of Neurology
Dr. Lisette Warkentin	Institute of General Practice (C)

(S) started in 2023
(C) completed in 2023

Module Step 2	
Dr. Christina Bergmann	Department of Medicine 3
Dr. Miriam Düll	Department of Medicine 1
PD Dr. Markus Eckstein	Institute of Pathology (C)
PD Dr. Ramona Erber	Institute of Pathology (C)
Dr. Ingo Ganzleben	Department of Medicine 1
Dr. Alina Hilger	Department of Paediatrics and Adolescent Medicine
Dr. Benedikt Jacobs	Department of Medicine 5
Dr. Tilman Jobst-Schwan	Department of Medicine 4 (C)
Dr. Johanna Kurzhagen	Department of Medicine 4
Dr. Eva Maier	Department of Operative Dentistry and Periodontology
Dr. Christian Matek	Institute of Pathology
PD Dr. Adrian Regensburger	Department of Paediatrics and Adolescent Medicine (C)
PD Dr. Martin Regensburger	Department of Stem Cell Biology (C)
PD Dr. David Simon	Department of Medicine 3 (C)
Dr. Patrick Süß	Department of Molecular Neurology
Dr. Lisette Warkentin	Institute of General Practice (S)

The third **retreat of the IZKF Clinician Scientists** took place at the Fraunhofer Research Campus in Waischenfeld in mid-October. The participants of the NOTICE-CSP and the mentees from the ARIADNEmed programme were invited for the first time. In total, around 30 young clinician scientists accepted the invitation.

The programme included the participants' own presentations as well as some guest lectures. There were lectures from the fields of preclinical and clinical research from various institutions in Erlangen. On Friday evening, Dr. Teichert from the Department of Palaeoenvironment gave a lecture that was as informative as it was rich in images, taking the participants into the colourful depths of Arctic reefs.

The evening networking around the campfire produced many new insights, ideas and synergies.

Many thanks to the two organizers Eva Maier and Markus Eckstein for their great commitment and the all-round successful event.

Additionally some courses were organized:

Course	Lecturer
Bioinformatics/ data analysis (Basic)	Dr. Fulvia Ferrazzi (Institute of Pathology)
CSP-Kurs Analysis of transcriptomics data in R/Bioconductor	Dr. Fulvia Ferrazzi (Institute of Pathology)
Good Scientific Practice	Dr. Christian Schmitt-Engel (FAU-Graduiertenzentrum)

Courses given in 2023 for participants of the CSP

Life@FAU as structured training programme for doctoral fellows

In 2023, the number of doctoral fellows participating in Life@FAU increased significantly compared to the previous year. In 2022, 511 doctoral fellows took part, in the reporting year there were already 592. The doctoral fellows are distributed between research training groups, research centres etc. as follows:

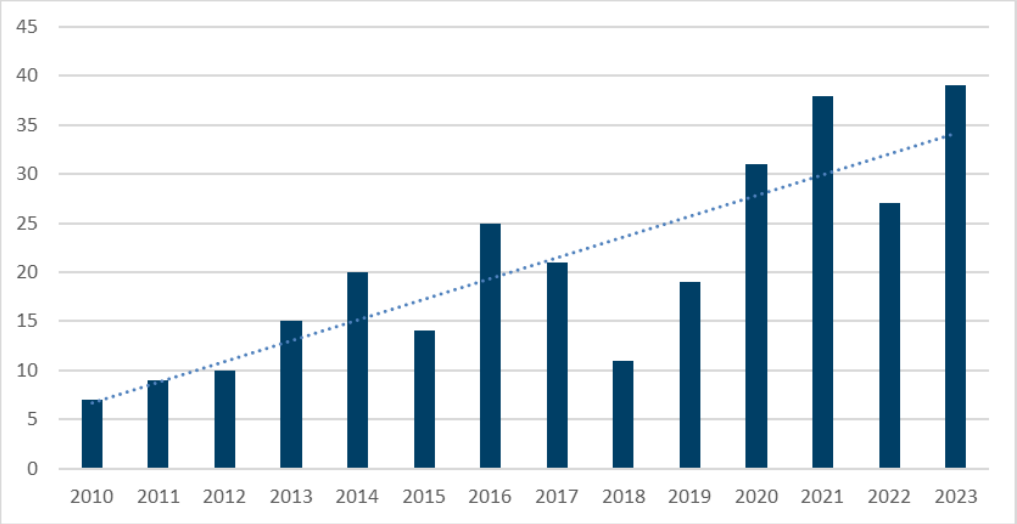
Programme/ Research Training Group	Registered participants	thereof Dr. rer. nat. and others	thereof Dr. med. / dent.
SFB 1181	43	30	13
SFB 1350	2	2	0
GRK 2162	42	30	12
GRK 2504	44	31	13
GRK 2599	22	16	6
GRK 2740	20	16	4
TRR 221	10	7	3
TRR 241	23	23	0
TRR 225	27	18	9
TRR 305	9	8	1
IZKF	44	44	0
IZKF associated	99	90	9
IZKF MD	138	0	138
no connection to RTG	56	52	4
Ongoing	579	367	212
GRK 1962	**8**	**8**	**0**
GRK 1660	**4**	**2**	**2**
TRR 130	**1**	**1**	**0**
Expired	**13**	**11**	**2**
total	**592**	**378**	**214**

Research Training Groups participating in Life@FAU, indicating the number of participants as of 31st December 2023

MD-Thesis Scholarships

In 2023, a total of 57 medical doctoral students from 27 institutions were funded. Due to the fact that some scholarships granted in 2022 ended in 2023, the number of funded doctoral students is higher than the number of scholarships available.

Overall, 47 applications for the MD-Thesis scholarship programme have been received in 2023. The Junior Scientists Committee approved 39 applications (83%), 18 (46%) of the successful applicants were females and 21 (54%) males. The median age was 24 years. Since its inception in 2007, the IZKF supported a total of 328 medical students with a scholarship. Medical students usually initiate experimental work on their doctoral thesis during their studies. They will finish the thesis frequently several years after they graduate. By the end of 2023, 106 (32%) students had already completed their doctoral thesis. Interestingly, 38 students (36%) obtained the highest degree possible, summa cum laude. This compares very favourably to the average 5% of all MD-Theses presented and is testimony to the excellent quality of MD-Theses performed within this programme.



Newly granted MD-Scholarships between 2010 and 2023

The following overview shows all participants of the MD-Thesis scholarship programme with their name, institution and funding period, who had an ongoing scholarship in 2023.

Institute of Biochemistry	
Giese, Sebastian	08/2023 - 03/2024
Hoock, Linus	03/2023 - 10/2023
Lötzsch, Chiara	12/2022 - 07/2023
Ünüvar, Sumeyya	09/2022 - 04/2023

Department of Dermatology	
Arnet, Lisa	10/2022 - 05/2023
Azodanlou, Delara	08/2022 - 03/2023
Karimi, Bita	10/2022 - 05/2023
Meusel, Leonie	11/2023 - 06/2024
Nzirorera, Rayk	02/2023 - 09/2023
Schott, Christian	03/2023 - 10/2023

Department of Medicine 1	
Hindermann, Johanna	08/2023 - 03/2024
Hobauer, Julia	06/2023 - 01/2024
Schwendner, Raphael	04/2023 - 11/2023

Department of Otorhinolaryngology	
Knorr, Sophie	03/2023 - 10/2023
Leischner-Merk, Daria	08/2023 - 03/2024
Löffler, Lisa	03/2023 - 10/2023

Department of Paediatrics and Adolescent Medicine	
Einhaus, Johanna	12/2022 - 07/2023
Fuhrmann, Tobias	08/2023 - 03/2024
Lauter, Luis	10/2023 - 05/2024
Nedoschill, David	06/2022 - 01/2023
Wolf, Ronny	12/2023 - 07/2024
Zeilmann, Markus	04/2023 - 11/2023

Institute of Physiology and Pathophysiology	
Heininger, Hannah	08/2023 - 03/2024
Miering, Tobias	08/2023 - 03/2024
Priller, Christina	08/2023 - 03/2024

Department of Plastic and Hand Surgery	
Englich, Moritz	08/2022 - 03/2023
Kramer, Katharina	08/2023 - 03/2024
Wattenbach, Christian	06/2022 - 01/2023
Wunder, Björn	12/2023 - 07/2024

Institute of Radiology	
Sommerfeld, Lisa Maria	08/2023 - 03/2024
Stepansky, Leonard	03/2023 - 10/2023
Türkan, Kaan	04/2023 - 12/2023

Department of Surgery	
Eiselt, Jan	12/2022 - 07/2023
Krämer, Florian	08/2022 - 03/2023
Roth, David	11/2023 - 06/2024

Others		
Birkmann, Lara	Department of Molecular Immunology	02/2023 - 10/2023
Büttner, Clara	Department of Medicine 5	08/2022 - 03/2023
Dashi, Tobias	Institute of Radiology	06/2022 - 01/2023
Düfel, Leonore	Department of Stem Cell Biology	06/2022 - 01/2023
Gawor, Jule	Institute of Microbiology	11/2023 - 06/2024
Gehrke, Raffaela	Department of Psychiatry and Psychotherapy	10/2023 - 05/2024
Geißler, Simon	Department of Stem Cell Biology	06/2022 - 01/2023
Hofmann, Thea	Department of Medicine 3	06/2022 - 01/2023
Kißler, Alicia	Institute of Cellular and Molecular Physiology	07/2022 - 02/2023
Loderbauer, Lisa	Department of Medicine 4	12/2022 - 07/2023
Mundlos, Hanna	Department of Molecular Neurology	09/2023 - 04/2024
Orthen, Hannah	Department of Medicine 3	12/2023 - 07/2024
Pfeuffer, Ann-Kathrin	Institute of Cellular and Molecular Physiology	11/2022 - 06/2023
Roukhami, Sofia	Department of Nephropathology	08/2022 - 03/2023
Schön, Simon	Institute of Pathology	03/2023 - 10/2023
Sichel, Manuel	Department of Medicine 2	03/2023 - 10/2023
Speiseder, Jonas	Department of Neurology	08/2023 - 03/2024
Tripp, Sonja	Institute of Experimental and Clinical Pharmacology and Toxicology	06/2023 - 01/2024
Wachter, Matthias	Department of Radiation Oncology	10/2022 - 05/2023
Wesselmann, Florian	Department of Nephropathology	02/2023 - 09/2023
Wientjes, Peter	Institute of Clinical and Molecular Virology	09/2023 - 04/2024
Zagrada, Mrika	Department of Molecular Immunology	02/2023 - 10/2023

Training courses in the IZKF

The IZKF Research Training Group again offered numerous courses in 2023. Almost all courses were offered as a virtual workshop.

Course	Course days	Offers 2023	Lecturer
Scientific Writing 1 An introduction to scientific writing	5*0,5	2	Dr. Deborah Bennett Bennett English Training for Academics
Scientific Writing 2 Writing research articles	5*0,5	1	Dr. Deborah Bennett Bennett English Training for Academics
Scientific Writing 3 Writing a PhD Thesis: Streamlining the writing process	5*0,5	1	Dr. Deborah Bennett Bennett English Training for Academics
Presentation skills	2	2	Dr. Deborah Bennett Bennett English Training for Academics
Poster Workshop	1,5	2	Dr. Deborah Bennett Bennett English Training for Academics
Staying on track: optimize your dissertation project management	3	1	Dr. Dunja Mohr Go Academic! Beratung – Coaching - Kompetenzentwicklung
Bioinformatics Analysis of Bulk RNA-seq	2	1	Dr. Pooja Gupta CUBiDA
Good Scientific Practice	1	5 (1x cancellation due to illness)	Dr. Anne Hamker Weiterbildung – Wissenschaftsberatung - Projektmanagement
Fundamentals of bioinformatics analysis of functional genomics data	5*0,5	1	Dr. Fulvia Ferrazzi Department of Nephropathology
Kommunikation und Rhetorik	2	1	Gerhard Kranz Seminare - Personalentwicklung - Trainings

Soft skill- and statistic courses given in 2023

As part of the **IZKF-Postgraduate Workshop** on October 12th, 2023, two doctoral students were awarded a poster prize:

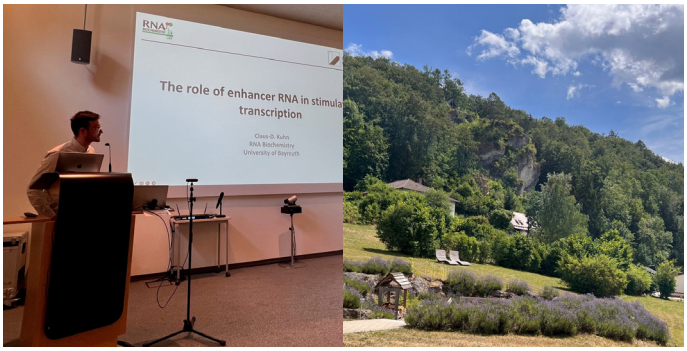
- Chiara Van Passen (Department of Surgery): Integrin ß6 mediates binding of disseminated colorectal cancer cells to endothelial cells
- Diana Matthe (Department of Medicine 1): novel T cell/ organoid culture system allows ex vivo modeling of intestinal graft-versus-host disease

In a two-hour poster session, three scientists reviewed each of the participants' posters. The best six participants were allowed to present their posters to the auditorium in spontaneous flash talks. Ms. Van Passen and Ms. Matthe convinced the reviewers and received the poster prizes worth €250.00. Congratulations to both of them.

The panel of reviewers explicitly emphasized that they had seen many excellent posters on this day and were very impressed by the quality of all the spontaneous presentations.

On 12th July, doctoral students of the IZKF Research Training Group went to the **IZKF Retreat** at Fraunhofer Forschungscampus Waischenfeld. The retreat is prepared by the speakers of the Jour Fixe groups and organised with the support of the administrative office. The programme included contributions from each doctoral student.

The doctoral students shared information about their research projects in several lectures and poster sessions. Two guest speakers were also invited. Dr. Karin Bartel (LMU Munich) gave a lecture on „Modulating endolysosomal cation channels in cancer cells". Prof. Claus Kuhn gave a talk on „The role of enhancer RNA in stimulating transcription." We are pleased that Prof. Kuhn's research group from the University of Bayreuth were our guests on this day. In a panel discussion on the topic of careers, the participants were also able to discuss with Prof. Becker, Prof. Voskens, Prof. Kuhn and Dr. Frey. Mr. Haselmayer from Merck was on board as an industry representative. After a lively round of discussions, the participants rounded off the event with a nice barbecue.



IZKF Retreat 2023 at Fraunhofer Forschungscampus in Waischenfeld

Organisation of the IZKF Research Training Group

All members regularly participate in the Jour Fixe (JF) once a month. Due to the broad thematic range of the doctoral theses at the IZKF, several Jour Fixes are held, which are at the moment

- Digital information technology (DigIT)
- Immunology, infection, kidney and vascular research (Ink)
- Medical and healthcare technology (MedTech)
- Neurology (Neuro) and
- Oncology (Onco)

Each JF is supervised by one to two spokespersons from the doctoral students who are elected by the participants for a period of 2-3 years. Usually, a new election takes place at the end of the doctoral thesis of the respective spokesperson. In addition to the spokespersons, each established JF has an appointed professor as scientific head.

Jour Fixe DigIT

Scientific Head
Prof. Dr. Olaf Gefeller, Institute of Medical Informatics, Biometry and Epidemiology

Spokespersons
Daniel Firmbach, Institute of Pathology
Luisa Brokmeier, Institute of Medical Informatics, Biometry and Epidemiology

The JF DigIT is aimed at doctoral students with a data-analytical methodical approach. All participating institutions are dedicated to life sciences on the basis of their researchorientation, even if in some doctoral projects there are clear references to other fields of science such as mathematics/ statistics, computer science, physics and electrical engineering

Jour Fixe Ink

Scientific Head
Prof. Dr. Christoph Becker, Department of Medicine 1

Spokespersons
Daniela Surrer, Institute of Experimental and Clinical Pharmacology and Toxicology
Lorenz Scherpinski, Institute of Experimental and Clinical Pharmacology and Toxicology

At the Jour Fixe INK, doctoral fellows working in the areas of immunology, infection, renal and vascular research will present the progress and results of their respective doctoral projects. The seminar is held in English and takes place once a month. It promotes both the transfer of knowledge between doctoral fellows in the different fields and the presentation and discussion skills in front of an audience.

Jour Fixe MedTech

Scientific Head
Prof. Dr. Christoph Bert, Department of Radiation Oncology

Spokespersons
Johann Brand, Department of Radiation Oncology
Lisa Sommerfeld, Department of Radiology

The Jour Fixe MedTech is aimed at all doctoral students with a medical-technical/-physical/-biological connection and/or background, but is also open to all other interested parties. The focal points of the Jour Fixes are questions from medical physics (radiation therapy, MR physics, audiology), radiation biology and radiology. Members of the Jour Fixe meet monthly. One project presentation per doctoral student is planned every year.

Jour Fixe Neuro

Scientific Head
Prof. Dr. Dieter Chichung Lie, Institute of Biochemistry - Chair of Biochemistry and Mol. Medicine

Spokespersons
Rebecca Masanetz, Department of Molecular Neurology
Nicole Richter, Department of Anesthesiology

The neuroscientific doctoral fellows of the FAU Erlangen-Nuremberg meet monthly for the Jour Fixe „Neuroscience“, at which the doctoral fellows discuss new methods and techno logies in addition to their respective doctoral projects. The programme of the Jour Fixe is solely organised by the doctoral students.

Jour Fixe Onco

Scientific Head
Prof. Dr. Anja Bosserhoff, Institute of Biochemistry

Spokespersons
Patricia Heinrich, Institute of Biochemistry
David Harris, Institute of Biochemistry

In the Oncology Jour Fixe, doctoral fellows focusing on research in different fields of oncology discuss ongoing work as well as new approaches. Every participant presents her/ his own project once a year in the form of a progress report. The topics of this seminar range from basic research in various cancer entities to clinical studies and targeted therapies.

Scientific Reports

Funded Advanced projects in 2023: Cohort 2020 - 2023

No.	Name	Institution	Project title
A76	Prof. Dr. Christoph Becker	Department of Medicine 1	Role of Gasdermin C in Gut Barrier Defence
A77	Prof. Dr. Aline Bozec	Department of Medicine 3	HIF expression in B cells regulates bone loss
A78	Dr. Dr. Mircea Chiriac Prof. Dr. Markus Neurath	Department of Medicine 1	Smurf2-IFN axis in IBD and mucosal healing
A79	Prof. Dr. Jörg Distler	Department of Medicine 3	TR4 in tissue fibrosis
A82	Prof. Dr. Susetta Neurath-Finotto	Department of Molecular Pneumology	Role of RANTES in the resolution of asthma
A84	Prof. Dr. Kai Hildner Prof. Dr. Dr. Sebastian Zundler Prof. Dr. Maike Büttner-Herold	Department of Medicine 1 Department of Medicine 1 Department of Nephropathology	Tissue-resident memory T cells in GvHD
A86	Prof. Dr. Gerhard Krönke	Department of Medicine 3	Characterization of synovial macrophage subsets
A87	Dr. Christian Lehmann PD Dr. Ulrike Schleicher	Department of Dermatology Institute of Microbiology	DC subsets and natural antibodies in leishmaniasis
A88	Prof. Dr. Manfred Marschall Prof. Dr. Heinrich Sticht	Institute of Clinical and Molecular Virology Institute of Biochemistry	Cyclin interaction with a CDK-like viral kinase
A89	Prof. Dr. Alexander Steinkasserer	Department of Immune Modulation	CD83 regulates homeostasis and inflammation
A91	PD Dr. Dr. Andrea Thoma-Kreß	Institute of Clinical and Molecular Virology	Interfering with HTLV-1 persistence
A92	Prof. Dr. Mario Zaiss	Department of Medicine 3	FRCs and immune tolerance induction
D30	Prof. Dr. Jürgen Behrens Dr. Dominic Bernkopf	Chair of Experimental II – Molecular Oncology	Axin at microtubuli
D31	Prof. Dr. Anja Bosserhoff	Institute of Biochemistry	Modulation of oncogene-induced senescence
D32	PD Dr. Dr. Peter Dietrich	Department of Medicine 1	NPY in chemo-resistance and immune-escape in HCC
D33	Prof. Dr. Markus Metzler Prof. Dr. Dimitrios Mougiakakos	Department of Pediatric and Adolescent Medicine Department of Medicine 5	Immunometabolism in CML
D34	Prof. Dr. Andreas Ramming Prof. Dr. Michael Stürzl	Department of Medicine 3 Department of Surgery	Fibroblast polarization in colorectal carcinoma
D36	Prof. Dr. Reiner Strick Prof. Dr. Arndt Hartmann	Department of Obstetrics and Gynaecology Institute of Pathology	Endogenous retroviruses drive tumor inflammation
E28	Prof. Dr. Lina Gölz Prof. Dr. Michael Wegner	Department of Orthodontics and Orofacial Orthopedics Chair of Biochemistry and Pathobiochemistry	Neural Crest Regulators In Orofacial Clefting
E29	Prof. Dr. Dieter Chichung Lie	Institute of Biochemistry	Lysosome dysfunction in stem cell ageing
E30	Prof. Dr. Beate Winner Prof. Dr. Jürgen Winkler	Department of Stem Cell Biology Department of Molecular Neurology	Impact of the immune system on Parkinson‘s disease
F7	Prof. Dr. Felix Engel	Department of Nephropathology	Gpr126 in kidney development and disease
F8	Prof. Dr. Christoph Korbmacher	Institute of Cell. and Mol. Physiology	Ion channel function of polycystin-2 in ADPKD
F9	Prof. Dr. Janina Müller-Deile Prof. Dr. Mario Schiffer	Department of Medicine 4	Generation of novel glomerular 3D culture systems

Funded Advanced projects in 2023: Cohort 2023 - 2025

No.	Name	Institution	Project title
E32	Dr. Sven Falk	Institute of Biochemistry	Molecular nexuses in neurodevelopmental diseases
E33	Dr. Melanie Küspert	Institute of Biochemistry	Deubiquitinase Otud7b in CNS myelination
E34	Prof. Dr. Dieter Chichung Lie Prof. Dr. Kristian Franze	Institute of Biochemistry Institute of Medical Physics	Regulation of the adult CNS stem cell niche
E35	Prof. Dr. André Reis Prof. Dr. Peter Soba	Institute of Human Genetics Institute of Physiology and Pathophysiology	Deciphering recessive NDDs
E36	Dr. Andreas Sagner	Institute of Biochemistry	Temporal patterning of dopaminergic neurons
E37	Prof. Dr. Michael Wegner Prof. Dr. Anna Fejtova	Institute of Biochemistry Department of Psychiatry and Psychotherapy	CtBP1, oligodendrocytes & myelination
A93	Prof. Dr. Christoph Becker	Department of Medicine 1	Cytosolic citrate metabolism in IEC
A94	Prof. Dr. Armin Ensser	Institute of Clinical and Molecular Virology	SARS-CoV-2 host adaptation
A95	Prof. Dr. Thomas Gramberg	Institute of Clinical and Molecular Virology	Viral RNA methylation inhibits MDA5 sensing
A98	PD Dr. Kilian Schober	Institute of Microbiology	RA-T
A99	PD Dr. Ulrike Steffen	Department of Medicine 3	Mechanisms of cortical bone remodelling
A100	Prof. Dr. Alexander Steinkasserer	Department of Immune Modulation	sCD83 induces wound healing
A101	Prof. Dr. Matthias Tenbusch	Institute of Clinical and Molecular Virology	IgG4 responses after SARS-CoV-2 RNA vaccination
A102	Prof. Dr. Maximilian Waldner Prof. Dr. Jochen Guck	Department of Medicine 1 Dep. of Physics - Chair of Biological Optomechanics	Mechanics of innate immune cells in colitis
A103	PD Dr. Benno Weigmann	Department of Medicine 1	Secretory IgA molecules in intestinal immunity
A104	Dr. Sebastian Zundler Prof. Dr. Stefan Uderhardt	Department of Medicine 1 Department of Medicine 3	Mechanical regulation of intestinal T cell egress
D37	PD Dr. Imke Atreya	Department of Medicine 1	ACLY in IBD-associated cancer
D38	Prof. Dr. Anja Bosserhoff	Institute of Biochemistry	AP2e in malignant melanoma
D39	PD Dr. Simone Brabletz	Chair of Experimental Medicine I	EMT and ferroptosis
D40	PD Dr. Dr. Peter Dietrich	Department of Medicine 1	The role of DDX46 in liver cancer
D41	Prof. Dr. Felix Engel Dr. Markus Eckstein	Department of Nephropathology Institute of Pathology	Therapy resistance in urothelial cancer
D42	Prof. Dr. Claus Hellerbrand	Institute of Biochemistry	PSAP in liver steatosis-triggered liver cancer
D43	PD Dr. Simon Völkl Prof. Dr. Julio Vera Gonzalez	Department of Medicine 5 Department of Dermatology	Regulation of CD19.CAR T-cells

Role of Gasdermin C in Gut Barrier Defence

Prof. Dr. Becker

A76 02/2020 - 01/2023

Prof. Dr. Christoph Becker, Department of Medicine 1

e-mail: christoph.becker@uk-erlangen.de

Abstract

We have discovered Gasdermin C as a protein strongly induced in the gut epithelium by IL-4 and IL-13. We can show that Gasdermin C is released by goblet cells into the mucous layer where it binds to bacteria. Further analyses implicate that Gasdermin C has a pore forming function and promotes anti-microbial defence. We plan to elucidate the regulation of Gasdermin C, its molecular mode of action and its functional impact in vivo.

Important results

We concluded the experimental work.

Special methods

- Intestinal organoid techniques
- Cell death techniques
- Conditional gene targeting in the gut

Publications

Patankar JV, Müller TM, Kantham S, Acera MG, Mascia F, Scheibe K, Mahapatro M, Heichler C, Yu Y, Li W, Ruder B, Günther C, Leppkes M, Mathew MJ, Wirtz S, Neufert C, Kühl AA, Paquette J, Jacobson K, Atreya R, Zundler S, Neurath MF, Young RN, Becker C. (2021) E-type prostanoid receptor 4 drives resolution of intestinal inflammation by blocking epithelial necroptosis. Nat Cell Biol. 23(7):796-807

HIF expression in B cells regulates bone loss

Prof. Dr. Bozec

A77 12/2020 - 12/2023

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Abstract

While the influence of T cells on bone homeostasis has been well characterized, less is known about the role of B cells. Despite that B cells are able to produce RANKL, the major cytokine regulating osteoclast differentiation, its regulation of expression remains unclear. B cells reside in the low oxygen concentrations bone niche, and adapt to the environment through the expression of HIFs. I therefore hypothesize that HIF expression in B cells could influence the development of osteoporosis.

Important results

Our data demonstrate that HIF-1a binds to HRE in Rankl promoter, leading to increased RANKL production by B cell and enhanced osteoclastogenesis. Estrogen controls HIF-1a level via HSP70-mediated protein degradation pathway. Pharmacological induction of HSP70 inhibits HIF-1a activation and protects against ovariectomy-induced bone loss.

Special methods

1. Murine model of Ovariectomy
2. Bone Micro-CT imaging and Bone histomorphometry
3. ChIP sequencing and data analysis

Publications

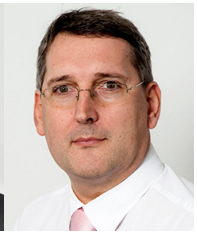
Cao S, Li Y, Song R, Meng X, Fuchs M, Liang C, Kachler K, Meng X, Wen J, Schlötzer-Schrehardt U, Taudte V, Gessner A, Kunz M, Schleicher U, Zaiss MM, Kastbom A, Chen X, Schett G, Bozec A (2024) L-arginine metabolism inhibits arthritis and inflammatory bone loss. Annals of the rheumatic diseases 83:72-87

Wen J, Lyu P, Stolzer I, Xu J, Gießl A, Lin Z, Andreev D, Kachler K, Song R, Meng X, Cao S, Guggino G, Ciccia F, Günther C, Schett G, Bozec A (2022) Epithelial HIF2α expression induces intestinal barrier dysfunction and exacerbation of arthritis. Ann Rheum Dis. annrheumdis-2021-222035

Meng X, Lin Z, Cao S, Janowska I, Sonomoto K, Andreev D, Katharina K, Wen J, Knaup KX, Wiesener MS, Krönke G, Rizzi M, Schett G, Bozec A (2022) Estrogen-mediated downregulation of HIF-1α signaling in B lymphocytes influences postmenopausal bone loss. Bone research 10:15

Smurf2-IFN axis in IBD and mucosal healing


Dr. Dr. Chiriac


Prof. Dr. Neurath

A78 01/2021 - 12/2023

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Abstract

To understand the role played by ubiquitination of type I interferon in the pathogenesis of inflammatory bowel disease we intend to induce DSS colitis in two newly generated conditional mouse strains i.e. Stat2 and Smurf2 in experimental colitis models. CRISPR/Cas, three dimensional organoids coupled with Nanostring and RNA-Seq/GO analysis will be used to understand molecular mechanisms underlying DSS findings. Data will be validated using samples from IBD patients and controls.

Important results

A pro-inflammatory transcriptional activity was observed in Smurf-2KO mice subjected to experimental colitis. In ulcerative colitis, Smurf2 was downregulated whereas IFNAR2-STAT2 and TGFB-TGFBR1 were upregulated. Understanding how Smurf2 controls the balance between these two pathways could provide therapeutic benefits for IBD patients.

Special methods

1. Generation and characterization of Smurf2-conditional KO mice
2. Comprehensive analysis of general and conditional Smurf2KO mice in different models of experimental colitis
3. Generation and characterization of patient-derived and Smurf-2KO-derived organoids

Publications

Chiriac MT, Hracsko Z, Günther C, Gonzalez-Acera M, Atreya R, Stolzer I et al. (2023) IL-20 controls resolution of experimental colitis by regulating epithelial IFN/STAT2 signalling. Gut. 2024 Jan 5;73(2):282-297

Chiriac MT, Hracsko Z, Becker C, Neurath MF (2023) STAT2 Controls Colorectal Tumorigenesis and Resistance to Anti-Cancer Drugs. Cancers (Basel). 15(22):5423

TR4 in tissue fibrosis


Prof. Dr. Distler

A79 01/2021 - 06/2023

Prof. Dr. Jörg Distler, Department of Medicine 3 (until 08/2022)
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Abstract

Fibrotic diseases account for 45% of the deaths in the developed world. We demonstrate that the nuclear receptor TR4 is overexpressed in fibrotic tissues in a TGFβ-dependent manner. TR4 promotes fibroblast-to-myofibroblast transition and collagen release. Knockout of TR4 prevents fibroblast activation and ameliorates experimental fibrosis. In the proposed project, we aim to characterize the molecular mechanisms of fibroblast activation by TR4 and the antifibrotic effects of TR4 inhibition.

Important results

- TR4 expression is deregulated in a TGFβ dependent manner in SSc fibroblasts on the protein level.
- TR4 controls numerous profibrotic transcription programs in human dermal fibroblasts and regulates fibroblast activation in a Gα12-/ Rock-dependent manner.
- Knockout of TR4 ameliorates experimental fibrosis.

Special methods

- Bulk RNA sequencing and ChIP sequencing with subsequent integrated biostatistical evaluation (in cooperation with Meik Kunz; Medical bioinformatics)
- Different mouse models of fibrotic tissue remodeling
- Multicellular cell culture models for human skin

Publications

Zehender A, Li YN, Lin NY, Stefanica A, Nüchel J, Chen CW, Hsu HH, Zhu H, Ding X, Huang J, Shen L, Györfi AH, Soare A, Rauber S, Bergmann C, Ramming A, Plomann M, Eckes B, Schett G, Distler JHW (2021) TGFβ promotes fibrosis by MYST1-dependent epigenetic regulation of autophagy. Nat Commun. 12(1):4404

Györfi AH, Matei AE, Fuchs M, Liang C, Rigau AR, Hong X, Zhu H, Luber M, Bergmann C, Dees C, Ludolph I, Horch RE, Distler O, Wang J, Bengsch B, Schett G, Kunz M, Distler JHW (2021) Engrailed 1 coordinates cytoskeletal reorganization to induce myofibroblast differentiation. J Exp Med. 6;218(9):e20201916

Chakraborty D, Zhu H, Jüngel A, Summa L, Li YN, Matei AE, Zhou X, Huang J, Trinh-Minh T, Chen CW, Lafyatis R, Dees C, Bergmann C, Soare A, Luo H, Ramming A, Schett G, Distler O, Distler JHW (2020) Fibroblast growth factor receptor 3 activates a network of profibrotic signaling pathways to promote fibrosis in systemic sclerosis. Sci Transl Med. 12(563):eaaz5506

Role of RANTES in the resolution of asthma

Prof. Dr. Neurath-Finotto

A82 02/2020 - 01/2023

Prof. Dr. Susetta Neurath-Finotto, Department of Molecular Pneumology
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Abstract

We identified RANTES as a key regulator of the resolution of allergic asthma in human and murine studies. Resolved symptomatic episodes of asthma in children, were found to be associated with elevated serum levels of RANTES indicating the involvement of RANTES in the resolution of allergic asthma. In a murine model after allergen (HDM) challenge, RANTES cured allergic asthma trait. In this project, we want to better understand the mechanism of RANTES mediated resolution of allergic asthma.

Important results

- We observed reduced RANTES levels in PBMCs from asthmatic children with RV infection in their upper airways.
- Mice treated with rRantes resolved allergic asthma.
- CCR3 KO mice show a defect in inflammatory eosinophils (iEos) which contribute to asthma and an induction of asthma resolving resident Eosinophils (rEos).

Special methods

- Whole body plethysmography
- Invasive lung function measurement
- Co-culture of T cells with antigen presenting cells

Publications

Mitländer H, Yang Z, Krammer S, Grund JC, Zirlik S, Finotto S (2023) Poly I:C Pre-Treatment Induced the Anti-Viral Interferon Response in Airway Epithelial Cells. Viruses. 15(12):2328

Krammer S, Yang Z, Mitländer H, Grund JC, Trump S, Mittler S, Zirlik S, Finotto S (2022) Rhinovirus Suppresses TGF-β-GARP Presentation by Peripheral NK Cells. Cells 12(1):129

Li N, Mirzakhani H, Kiefer A, Koelle J, Vuorinen T, Rauh M, Yang Z, Krammer S, Xepapadaki P, Lewandowska-Polak A, Lukkarinen H, Zhang N, Stanic B, Zimmermann T, Kowalski ML, Jartti T, Bachert C, Akdis M, Papadopoulos NG, Raby BA, Weiss ST, Finotto S (2021) Regulated on Activation, NormalT cell Expressed and Secreted (RANTES) drives the resolution of allergic asthma. iScience. 25;24(10):103163

Tissue-resident memory T cells in GvHD

Prof. Dr. Hildner

Prof. Dr. Dr. Zundler

Prof. Dr. Büttner-Herold

A84 05/2020 - 05/2023

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Abstract

T cell mediated intestinal inflammation in acute Graft-versus-Host-Disease (GI-GvHD) represents a life-threatening and therapeutically challenging complication in patients undergoing allogeneic hematopoietic stem cell transplantation (allo-HSCT). Interestingly, the role of tissue-resident memory T cells (Trm) in this context is unknown. Here, we plan studies to assess the development, migration, location and functionality of Trm cells in GI-GvHD both in murine experimental models and in men.

Special methods

1. In vitro T cell/organoid co-culture to study allogeneic T cell functionality and cytotoxicity
2. Live imaging and quantitative methods for analysis of T cell migratory behavior within intestinal organoids
3. Histopathological assessment (IHC, EM) of morphologic alterations of intestinal epithelial cells impacted by allo-reactive T cells

Important results

Our newly developed intestinal epithelial cell/ allogeneic intraepithelial lymphocytes (IEL) co-culture system mimics aspects of intestinal GvHD and allows us to characterize migratory behavior, antigen specificity, cytokine release and mechanisms of cytotoxicity of different allo-reactive T cell pools within intestinal organoids ex vivo.

Publications

Matthe DM, Dinkel M, Schmid B, Vogler T, Neurath MF, Poeck H et al. (2023) Novel T cell/organoid culture system allows ex vivo modeling of intestinal graft-versus-host disease. Frontiers in immunology 14:1253514

Vonbrunn E, Ries T, Söllner S, Müller-Deile J, Büttner-Herold M, Amann K et al. (2021) Multiplex gene analysis reveals T-cell and antibody-mediated rejection-specific upregulation of complement in renal transplants. Scientific reports 11:15464

Enderle K, Dinkel M, Spath EM, Schmid B, Zundler S, Tripal P et al. (2021) Dynamic Imaging of IEL-IEC Co-Cultures Allows for Quantification of CD103-Dependent T Cell Migration. Int J Mol Sci. 22(10):5148

Characterization of synovial macrophage subsets

Prof. Dr. Krönke

A86 06/2020 - 06/2023

Prof. Dr. Gerhard Krönke, Department of Medicine 3 (until 03/2023)
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Abstract

Our preliminary data identified a unique Cx3Cr1-positive macrophage subset that forms a protective barrier around the joint and counteracts inflammation. Accordingly, we will address the developmental origin and differentiation pathways of these specific macrophages and try to understand the molecular basis of their anti-inflammatory properties. Moreover, we will address the relevance of these findings for human diseases such as rheumatoid arthritis.

Publications

no project-specific publications so far

Important results

Using scRNAseq and scATACseq, we performed an in-depth analysis of synovial macrophages in the mouse model of K/BxN serum transfer arthritis. This revealed dynamic changes and an important role of monocyte-derived macrophages during the resolution of arthritis.

Special methods

- ScRNAsequencing
- Preclinical arthritis models
- Light-sheet microscopy

DC subsets and natural antibodies in leishmaniasis

Dr. Lehmann

PD Dr. Schleicher

A87 07/2020 - 11/2023

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Abstract

Dendritic Cells (DCs) are indispensable for the protection from pathogens. Additionally, natural antibodies (nAbs) reacting to evolutionary conserved epitopes foster fast targeted response. Leishmaniasis is an important tropical disease with different manifestations. However, the first events in infection and determination of T/NK cell responses by DCs and nAbs are not fully understood. We now aim to unravel early determining factors for clinical outcome in leishmaniasis on a single cell level.

Important results

A specific skin DC subset, identified as host cell of Leishmania parasites, is crucial for the establishment of chronic cutaneous leishmaniasis. ScRNAseq analyses characterize its effector functions. Our results also help to better define skin mononuclear phagocyte subpopulations. Moreover, we showed binding of natural antibodies to the parasites.

Special methods

- Leishmania infection models in mice (L. major, L. mexicana, L. infantum)
- Characterization of DC subpopulations
- Murine organ preparation
- Multicolor flow cytometry

Publications

Desel C, Murray PJ, Lehmann CHK, Heger L, Christensen D, Andersen P et al. (2022) Monocytes Elicit a Neutrophil-Independent Th1/Th17 Response Upon Immunization With a Mincle-Dependent Glycolipid Adjuvant. Frontiers in immunology 13:880474

Probst HC, Stoitzner P, Amon L, Backer RA, Brand A, Chen J et al. (2022) Guidelines for DC preparation and flow cytometry analysis of mouse non-lymphoid tissues. European journal of immunology. 53(11):e2249819

Clausen BE, Amon L, Backer RA, Berod L, Bopp T, Brand A et al. (2022) Guidelines for mouse and human DC functional assays. European journal of immunology. 53(12):e2249925

Cyclin interaction with a CDK-like viral kinase


Prof. Dr. Marschall


Prof. Dr. Sticht

A88 02/2020 - 07/2023

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Abstract

HCMV replication is characterized by viral CDK-cyclin interaction. The CDK-like viral kinase pUL97 interacts with human cyclins. CycB1 is phosphorylated upon the interaction, dependent on pUL97 activity, whereas cycT1/H interaction stimulates pUL97 activity and substrate phosphorylation. Regions for cyclin interaction and antiviral drug resistance show overlaps in pUL97, so that this correlation will be elucidated in terms of viral fitness for the development of a novel antiviral strategy

Important results

1. Demonstrating the importance of pUL97–cyclin H interaction using HCMV deleted in cyclin binding, cyclin-KO cells, inhibitory small molecules
2. Computational assessment of pUL97–cyclin binding interfaces
3. Structural prediction and experimental verification of pUL97–cyclin H–CDK7 regulatory interplay that codetermines viral replication efficiency

Special methods

1. Molecular characterization of HCMV mutants: qPCR kinetics, confocal imaging, CoIP, cyclin NanoBiT assay, qSOX-IVKA kinase assay
2. Whole genome sequencing of clinical HCMV isolates of HCMV, generation of recombinant HCMVs and cyclin-KO cells
3. Bioinformatics: sequence-based investigation, molecular modeling and molecular dynamics simulations

Publications

Schütz M, Wangen C, Sommerer M, Kögler M, Eickhoff J, Degenhart C et al. (2023) Cytomegalovirus cyclin-dependent kinase ortholog vCDK/pUL97 undergoes regulatory interaction with human cyclin H and CDK7 to codetermine viral replication efficiency. Virus research 335: 199200

Schütz M, Müller R, Socher E, Wangen C, Full F, Wyler E et al. (2022) Highly Conserved Interaction Profiles between Clinically Relevant Mutants of the Cytomegalovirus CDK-like Kinase pUL97 and Human Cyclins: Functional Significance of Cyclin H. International journal of molecular sciences 23:11814

Schütz M, Steingruber M, Socher E, Müller R, Wagner S, Kögel M, Sticht H & Marschall M (2021) Functional relevance of the interaction between human cyclins and the cytomegalovirus-encoded CDK-like protein kinase pUL97. Viruses 13: 1248

CD83 regulates homeostasis and inflammation


Prof. Dr. Steinkasserer

A89 07/2020 - 06/2023

Prof. Dr. Alexander Steinkasserer, Department of Immune Modulation
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Abstract

Inflammation within the CNS can directly affect neuronal structures. Thus, molecules controlling inflammatory responses are of upmost importance. The immune-regulatory CD83 molecule is highly expressed by microglia and tissue-resident macrophages and thus, represents a crucial factor for microglial activation and the neuro-immune crosstalk. Since, its regulation and function in these cells has not been elucidated we will investigate this during immune homeostasis and neuroinflammation.

Special methods

- Flow cytometry analyses of microglia and infiltrating monocytes into the CNS
- Tamoxifen-inducible CX3CR1-CreERT2 system to analyse the influence of a microglia-specific CD83 KO during neuro-inflammation
- RNAseq analyses to identify CD83-induced transcriptional change

Important results

- CD83 expression by microglia is not only associated with cellular activation but also with resolution.
- Deletion of CD83 results in an over-activated immune state during autoimmune neuroinflammation.
- This leads to the recruitment of pathogenic immune cells to the CNS which deteriorate resolving mechanism and exacerbate disease symptoms.

Publications

Langguth P, Peckert-Maier K, Beck P, Kuhnt C, Draßner C, Deinzer A et al. (2023) CD83 acts as immediate early response gene in activated macrophages and exhibits specific intracellular trafficking properties. Biochemical and biophysical research communications 647:37-46

Peckert-Maier K, Langguth P, Strack A, Stich L, Mühl-Zürbes P, Kuhnt C et al. (2023) CD83 expressed by macrophages is an important immune checkpoint molecule for the resolution of inflammation. Frontiers in immunology 14: 1085742

Sinner P, Peckert-Maier K, Mohammadian H, Kuhnt C, Draßner C, Panagiotakopoulou V et al. (2023) Microglial expression of CD83 governs cellular activation and restrains neuroinflammation in experimental autoimmune encephalomyelitis. Nature communications 14:4601

Interfering with HTLV-1 persistence

PD Dr. Dr. Thoma-Kreß

A91 03/2020 - 03/2023

PD Dr. Dr. Andrea Thoma-Kreß, Institute of Clinical and Molecular Virology
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Abstract

The highly oncogenic retrovirus Human T-cell leukemia virus type 1 (HTLV-1) causes incurable neoplastic or inflammatory diseases. The viral accessory protein p8, which is proteolytically cleaved from the precursor p12 and transported to target cells prior to infection, is important for establishing persistent infections in vivo. Here, we aim to identify the protease cleaving p12 into p8, to inhibit this protease, and to assess the impact of blocking of p12/p8 processing on viral persistence.

Important results

We found that the HTLV-1 encoded protein p8 is transferred from T cells to several acceptor cell populations, including various T and B cell lines and primary CD4+ and CD8+ T cells. In stimulated CD4+ T cells, p8 decreases activity of the nuclear factor of activated T-cell (NFAT) signaling pathway, thus, interfering with T cell activation.

Special methods

- Genome Editing (CRISPR/Cas9, shRNA) and retroviral transduction
- Transfection of primary cells
- Spectral flow cytometry

Publications

Schnell AP, Kohrt S, Aristodemou A, Taylor GP, Bangham CRM, Thoma-Kress AK (2022) HDAC inhibitors Panobinostat and Romidepsin enhance tax transcription in HTLV-1-infected cell lines and freshly isolated patients' T-cells. Frontiers in immunology 13:978800

Donhauser N, Socher E, Millen S, Heym S, Sticht H, Thoma-Kress AK (2020). Transfer of HTLV-1 p8 and Gag to target T-cells depends on VASP, a novel interaction partner of p8. PLoS Pathogens, 16(9):e1008879

FRCs and immune tolerance induction

Prof. Dr. Zaiss

A92 09/2020 - 08/2023

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Abstract

As lymphatics in the inflamed joint in rheumatoid Arthritis drain specifically the popliteal lymph node (pLN) where the adaptive immune response is initiated, we investigated a population of stromal cells in the pLN, namely the fibroblastic reticular cells (FRC). Our preliminary data show a significant immunomodulatory potential of pLN FRCs in inflammatory arthritis mouse models. Therefore, we hypothesize that specifically pLN stromal FRCs play a so far neglected role in the early onset of RA.

Publications

no project-specific publications so far

Important results

- Temporary depletion of pLN CCL19+ FRC ameliorates symptoms in collagen-induced arthritis (CIA) .
- FRCs lose their ability to suppress T-cell activation and proliferation during the CIA time course.
- FRCs significantly downregulate NTRK1 before disease onset.
- Inhibition of NTRK1 signalling in FRCs leads to loss of T-cell suppressive capabilities.

Special methods

- Pre-clinical arthitis models
- Bulk mRNA isolated FRCs
- Single cell RNA sequencing of FRC depleted lymph nodes
- Light-sheet microscopy
- Metabolic parameters are determined by Seahorse XF technlogy

Axin at microtubuli


Prof. Dr. Behrens


Dr. Bernkopf

D30 03/2020 - 02/2023

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Abstract

Axin is a key negative regulator of the oncogenic Wnt/β-catenin pathway scaffolding the β-catenin destruction complex. We suggest that the newly found anchoring of axin to microtubules (MTs) is of functional importance for regulating the pathway. We will (i) describe the dynamics of axin association with MTs; (ii) determine the biochemical basis of this interaction and its regulation by phosphorylation; and (iii) define the functional role of axin anchoring to MTs in Wnt signaling.

Important results

We have identified a specific microtubule binding site (MTB) in the Wnt regulator axin. Recombinant MTB bound to microtubules in vitro using pull down assays. Functional experiments suggest that MT bound axin is partially refractory to upstream inhibition by Dvl2 indicating a novel layer of regulation in the Wnt pathway.

Special methods

- Density gradient centrifugation of proteins
- In vitro microtubule binding assay
- FRAP

Publications

Klement K, Brückner M, Bernkopf DB (2023) Axin phosphorylation in condensates counteracts tankyrase-mediated degradation. Journal of cell science. 136(20):jcs261214

Miete C, Solis GP, Koval A, Brückner M, Katanaev VL, Behrens J, Bernkopf DB (2022) Gαi2-induced conductin/axin2 condensates inhibit Wnt/β-catenin signaling and suppress cancer growth. Nature communications 13:674

Modulation of oncogene-induced senescence


Prof. Dr. Bosserhoff

D31 03/2020 - 03/2023

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Abstract

Oncogene-induced senescence (OIS) was recently introduced as a strong tumor suppressive mechanism seen e.g. in development of nevi out of melanocytes after BRAF mutation. Tumor cells like melanoma obviously can overcome these limiting mechanisms by further changes, however the molecular mechanisms leading to and overcoming OIS are just being started to be understood. We aim to understand the role of cell adhesion processes and mechanotransduction in induction and overcoming OIS.

Important results

We could demonstrate that cell matrix adhesion modulates induction of senescence in melanocytes (using BRAFmut expression) via YAP. RNA-Seq was performed to understand the molecular changes and confirmed the result. Further, the bioinformatical analysis supported by experimental data revealed an impact of Wnt signal on senescence in melanoma cells.

Special methods

Analyses of senescence marker, reporter gene assays for analyses of transcription factors, OIS induction via lentiviral transfection

Publications

Zimmermann T, Pommer M, Kluge V, Chiheb C, Muehlich S, Bosserhoff AK (2022) Detection of Cellular Senescence in Human Primary Melanocytes and Malignant Melanoma Cells In Vitro. Cells 11:1489

Pommer M, Kuphal S, Bosserhoff AK (2021) Amphiregulin Regulates Melanocytic Senescence. Cells. 10:326

Böhme I, Bosserhoff A (2020) Extracellular acidosis triggers a senescence-like phenotype in human melanoma cells. Pigment Cell Melanoma Res. 33(1):41-51

NPY in chemo-resistance and immune-escape in HCC

PD Dr. Dr. Dietrich

D32 03/2020 - 02/2023

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Abstract

Neuropeptide Y (NPY) and its receptors represent a highly conserved system which is involved in cancer-related hallmarks. However, the impact of the NPY-system on hepatocellular carcinoma (HCC) remains unclear. The aims of this study are i) to unravel the role of NPY-receptor/NPY-crosstalk in resistance to tyrosine kinase inhibitors such as sorafenib and lenvatinib in HCC, and ii) to analyze the unknown role of the NPY-system as a potential major determinant of immune-escape in HCC.

Important results

We found that NPY exerts a potential novel biomarker to predict response to immune-checkpoint-inhibition and tyrosine-kinase-inhibitors. Moreover, applying RNAi methods, inhibition of liver-derived NPY outlined potential novel therapeutic strategies. These data will be submitted for publication.

Special methods

1. Murine liver cancer models (e.g., orthotopic HCC model, DEN-induced HCC, STAM-induced HCC)
2. RTK-inhibitor-resistant cell lines
3. RNAi-methods, including siRNAs, microRNAs

Publications

Fritz V, Malek L, Gaza A, Wormser L, Appel M, Kremer AE, Thasler WE, Siebler J, Neurath MF, Hellerbrand C, Bosserhoff AK, Dietrich P. (2021) Combined de-repression of chemoresistance associated mitogen-activated protein kinase 14 and activating transcription factor 2 by loss of microRNA-622 in hepatocellular carcinoma. Cancers. 13(5):1183

Gaza A, Fritz V, Malek L, Wormser L, Treiber N, Danner J, Kremer AE, Thasler WE, Siebler J, Meister G, Neurath MF, Hellerbrand C, Bosserhoff AK, Dietrich P. (2021) Identification of novel targets of miR-622 in hepatocellular carcinoma reveals common regulation of cooperating genes and outlines the oncogenic role of zinc finger CCHC-type containing 11. Neoplasia. 23(5):502-514

Dietrich P, Wormser L, Fritz V, Seitz T, De Maria M, Schambony A, Kremer AE, Günther C, Itzel T, Thasler WE, Teufel A, Trebicka J, Hartmann A, Neurath MF, von Hörsten S, Bosserhoff A, Hellerbrand C. (2020) Molecular cross-talk between Y5-receptor and neuropeptide Y drives liver cancer. J Clin Invest.130:2509-2526.

Immunometabolism in CML

Prof. Dr. Metzler

Prof. Dr. Mougiakakos

D33 05/2020 - 06/2023

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Prof. Dr. Dimitrios Mougiakakos, Department of Medicine 5 (until 09/2021)
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Abstract

Despite the improvement through tyrosine kinase inhibitors (TKIs), treatment resistance, relapse and therapy-induced side effects are central problems of CML therapy. Our interdisciplinary project addresses the question whether and how TKIs alter CML cell metabolism and induce synthetic lethality in combination with compounds specifically targeting metabolic pathways. Our approach could help to improve efficacy and reduce side effects of CML treatment in pediatric and adult patients alike.

Publications

Häselbarth L, Karow A, Mentz K, Böttcher M, Roche-Lancaster O, Krumbholz M et al. (2023) Effects of the STAMP-inhibitor asciminib on T cell activation and metabolic fitness compared to tyrosine kinase inhibition by imatinib, dasatinib, and nilotinib. Cancer immunology, immunotherapy. 72:1661-1672

Important results

- Combination therapy prevents the escape mechanisms of CML cells via unfolded protein response and ER-stress.
- Stress-related apoptosis was triggered via cleavage of caspase 3 and inactivation of PARP1.
- Asciminib exhibits milder inhibitory effects on T cell activation, which might be beneficial for the immunological control of residual CML cells.

Special methods

- Measurement of cell death with 7-AAD staining and intracellular cleaved PARP with FACS
- UPR expression analysis by WB (ATF4, CHOP1, XBP1)
- Measurement of caspase-activity by membrane-based sandwich immunoassay and by semi-quantitative caspase 3/8/9 Multiplex Assay

Fibroblast polarization in colorectal carcinoma


Prof. Dr. Ramming


Prof. Dr. Stürzl

D34 05/2020 - 07/2023

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Abstract

We have identified PU.1 as a key regulator of fibroblast polarization. Its role in colorectal carcinoma (CRC) is unknown. We will address the following aims: (1) characterization of cancer-associated fibroblast (CAF) heterogeneity in CRC, (2) analysis of CAF polarization-dependent fibrocrine effects in vitro and (3) in experimental animal models, and (4) validation of the results in CRC tissues. Deciphering the role of fibroblast polarization in CRC may provide a new target for therapy.

Important results

Transcriptome analyses revealed significant differences in gene expression between fibroblasts isolated from CRC with different microenvironments and from healthy colon. These results could be confirmed in tumor and uninvolved colon tissues of CRC patients at the RNA and protein level using immunofluorescence and single cell RNAseq analyses.

Special methods

- RNA-Seq
- ScRNA-Seq
- CRC fibroblast isolation and culture

Publications

Stehr AM, Wang G, Demmler R, Stemmler MP, Straube J, Tripal P, Schmid B, Geppert CI, Hartmann A, Muñoz LE, Schoen J, Völkl S, Merkel S, Becker C, Schett G, Grützmann R, Naschberger E, Herrmann M, Stürzl M (2021) Neutrophil extracellular traps drive epithelial-mesenchymal transition of human colon cancer. Journal of Pathology. 256(4):455-467

Regensburger D, Tenkerian C, Pürzer V, Schmid B, Wohlfahrt T, Stolzer I, López-Posadas R, Günther C, Waldner MJ, Becker C, Sticht H, Petter K, Flierl C, Gass T, Thoenissen T, Geppert CI, Britzen-Laurent N, Méniel VS, Ramming A, Stürzl M, Naschberger E. (2021) Matricellular Protein SPARCL1 Regulates Blood Vessel Integrity and Antagonizes Inflammatory Bowel Disease. Inflamm Bowel Dis., 27(9):1491-1502

Klingler A, Regensburger D, Tenkerian C, Britzen-Laurent N, Hartmann A, Stürzl M, Naschberger E (2020) Species-, organ- and cell-type-dependent expression of SPARCL1 in human and mouse tissues. PLoS One. 15: e0233422

Endogenous retroviruses drive tumor inflammation


Prof. Dr. Strick


Prof. Dr. Hartmann

D36 03/2020 - 02/2023

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Abstract

This proposal will focus on the molecular basis of tumor inflammation of two different advanced cancers; Bladder cancer (MIBC) and Ovarian cancer (OVCA) with poor survival outcomes and high recurrence rates. Endogenous retrovirus (ERV) activations are linked with innate immunity and tumor inflammation. We will correlate patient immune signatures with ERVs and determine the functional role of ERVs, including dsRNA and RNA/DNA intermediates using tumors, cell lines and tumoroids of MIBC and OVCA.

Important results

- MIBC and ovarian cancer samples have distinct ERV expression signatures, which correlate with immune signatures resulting in 5 clusters with different overall survivals.
- dsRNA and RNA:DNA induce specific immune genes as well as cell proliferation or an anti-tumor response, respectively.
- ERV-K pol and LINE1 ORF2 synthesize RNA:DNA hybrids in vitro.

Special methods

- Microarrays with over 1 million repetitive elements including ERVs for analysis of bladder cancer (MIBC) patient RNA
- Synthesis and transfection of dsRNA and RNA:DNA hybrids in MIBC cells with live cell proliferation assays
- Antibody production of ERV-K pol and reverse transcription assays using in vitro transcribed and transfected ERV-pol mRNA

Publications

Köhler SA, Brandl L, Strissel PL, Gloßner L, Ekici AB, Angeloni M, Ferrazzi F, Bahlinger V, Hartmann A, Beckmann MW, Eckstein M, Strick R (2022) Improved Bladder Tumor RNA Isolation from Archived Tissues Using Methylene Blue for Normalization, Multiplex RNA Hybridization, Sequencing and Subtyping. International journal of molecular sciences 23:10267

Neural Crest Regulators In Orofacial Clefting


Prof. Dr. Gölz


Prof. Dr. Wegner

E28 07/2020 - 07/2023

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Abstract

Orofacial clefts are frequent congenital malformations. Etiology is complex, poorly understood and involves environmental and genetic factors. We could identify several cranial neural crest transcription factors and chromatin remodelers as key regulators of palatal development. We now use genome-edited cell lines and mouse mutants to determine the exact function and relationship of these factors in their regulatory network and thus better understand palatal development and orofacial clefting.

Important results

Disruption of Kat5/Tip60 or Ep400 as essential subunits of one chromatin remodeling complex severely affects carbohydrate and amino acid metabolism in cranial neural crest cells. The resulting decrease in protein synthesis, proliferation and survival leads to drastic reduction of cell numbers and near absence of facial structures in mouse embryos.

Special methods

- CRISPR/Cas9-mediated gene knockout
- In vitro neural crest differentiation

Publications

Gehlen-Breitbach S, Schmid T, Fröb F, Rodrian G, Weider M, Wegner M et al. (2023) The Tip60/Ep400 chromatin remodeling complex impacts basic cellular functions in cranial neural crest-derived tissue during early orofacial development. International journal of oral science 15:16

Weider M, Schröder A, Docheva D, Rodrian G, Enderle I, Seidel CL et al. (2020) A Human Periodontal Ligament Fibroblast Cell Line as a New Model to Study Periodontal Stress. International journal of molecular sciences 21:7961

Lysosome dysfunction in stem cell ageing


Prof. Dr. Lie

E29 07/2020 - 07/2023

Prof. Dr. Dieter Chichung Lie, Institute of Biochemistry
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Abstract

Recent data indicates that adult neural stem cell dysfunction and the resulting impairment of adult hippocampal neurogenesis contributes to cognitive deficits in human ageing and neurodegenerative diseases. The mechanisms underlying ageing-associated neural stem cell dysfunction are largely unknown. This project will investigate the hypothesis that dysfunction of lysosome-dependent degradation pathways is a major contributor for hippocampal neural stem cell dysfunction during ageing.

Publications

Schäffner I, Wittmann MT, Vogel T, Lie DC (2023) Differential vulnerability of adult neurogenic niches to dosage of the neurodevelopmental-disorder linked gene Foxg1. Molecular psychiatry 28:497-514

Important results

We now showed that increased lysosomal biogenesis decreases stem cell activation in adult mice and promotes longterm maintenance of the stem cell pool. Our recent data suggest that increased TFEB activity causes a metabolic shift from oxidative phosphorylation towards glycolysis, which may promote stem cell quiescence and longterm maintenance.

Special methods

Measurement of autophagic-lysosomal flux via biochemistry and imaging. Biochemical measurement of lysosome activity. Neural stem cell cultures. Retroviral vectors. Stereotactic injections (mouse).

Impact of the immune system on Parkinson‘s disease


Prof. Dr. Winner


Prof. Dr. Winkler

E30 04/2020 - 03/2023

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Abstract

Recent data demonstrate profound immunological alte rations in Parkinson’s disease (PD). We study the contribution of the peripheral immune system to onset and progression in PD. Specifically, we perform a comprehensive characterization of peripheral immunity in early vs. late onset with rapid vs. slow disease progression PD patients. Subsequently, we will determine neurotoxicity in human autologous co-cultures of stem cell-derived midbrain neurons and specific immune cells.

Important results

- In atypical PD (aPD) post mortem cerebellum from aPD patients, besides Purkinje cell loss, has prototypical GCI pathology and microgliosis.
- Delineated the impact of the microbiome for peripheral immunity in PD and established the concept of the gut brain axis in PD within a DFG funded clinical research unit (CRU5024).

Special methods

- Development of standardized models to generate IPSC-derived dopaminergic midbrain neurons and brain organoids
- Autologous co-culture system of iPSC derived neurons with immune cells
- Biomarker developement based on EV analysis from PD patients

Publications

Krach F, Stemick J, Boerstler T, Weiss A, Lingos I, Reischl S, Meixner H, Ploetz S, Farrell M, Hehr U, Kohl Z, Winner B, Winkler J. (2022) An alternative splicing modulator decreases mutant HTT and improves the molecular fingerprint in Huntington's disease patient neurons. Nature communications 13: 6797

Seebauer L, Schneider Y, Drobny A, Plötz S, Koudelka T, Tholey A, Prots I, Winner B, Zunke F, Winkler J, Xiang W. (2022) Interaction of Alpha Synuclein and Microtubule Organization Is Linked to Impaired Neuritic Integrity in Parkinson's Patient-Derived Neuronal Cells. International journal of molecular sciences 23:1812

Battis K, Florio JB, Mante M, Lana A, Naumann I, Gauer C, Lambrecht V, Müller SJ, Cobo I, Fixsen B, Kim HY, Masliah E, Glass CK, Schlachetzki JCM, Rissman RA, Winkler J, Hoffmann A. (2022) CSF1R-Mediated Myeloid Cell Depletion Prolongs Lifespan But Aggravates Distinct Motor Symptoms in a Model of Multiple System Atrophy. J Neurosci. 42:7673-7688

Gpr126 in kidney development and disease


Prof. Dr. Engel

F7 05/2020 - 04/2023

Prof. Dr. Felix Engel, Department of Nephropathology
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Abstract

Chronic kidney disease represents the fastest growing pathology worldwide. Elucidating new regulators of kidney development and disease will promote the development of strategies for kidney repair. Here we propose to identify how the adhesion G protein-coupling receptor Gpr126 regulates kidney development and which diseases are associated with altered Gpr126 expression in order to design in the future experiments to determine whether Gpr126 inhibition or activation can improve kidney function.

Publications

Cazorla-Vázquez S, Kösters P, Bertz S, Pfister F, Daniel C, Dedden M, Zundler S, Jobst-Schwan T, Amann K, Engel FB (2023) Adhesion GPCR Gpr126 (Adgrg6) Expression Profiling in Zebrafish, Mouse, and Human Kidney. Cells. 12(15):1988

Important results

Gpr126 is expressed in zebrafish, mice, rat, and human kidneys; in adult kidneys in juxtaglomerular cells, collecting duct and parietal epithelial cells, and the urothelium. Gpr126 is required for ureteric bud branching in mice and tubular morphogenesis and segment specification in zebrafish. In diseased kidneys, Gpr126 expression is altered.

Special methods

- RNAscope® in situ hybridization technology
- Zebrafish as a model of kidney disease
- CRISPR/Cas technologies

Ion channel function of polycystin-2 in ADPKD

Prof Dr. Korbmacher

F8 02/2020 - 01/2023

Prof. Dr. Christoph Korbmacher, Institute of Cellular and Molecular Physiology
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Abstract

In about 15 % of affected patients ADPKD (autosomal dominant polycystic kidney disease) is caused by mutations in the PKD2 gene coding polycystin-2 (PC2). Altered ion channel properties of PC2 may contribute to the pathophysiology of ADPKD. This project uses a novel experimental strategy to study the electrophysiological properties of PC2 and mutant PC2 channels in combination with molecular modelling. Its aim is to improve our understanding of PC2 ion channel function in health and disease.

Publications

Grosch M, Brunner K, Ilyaskin AV, Schober M, Staudner T, Schmied D, Stumpp T, Schmidt KN, Madej MG, Pessoa TD, Othmen H, Kubitza M, Osten L, de Vries U, Mair MM, Somlo S, Moser M, Kunzelmann K, Ziegler C, Haerteis S, Korbmacher C, Witzgall R. (2021) A polycystin-2 protein with modified channel properties leads to an increased diameter of renal tubules and to renal cysts. J Cell Sci. 134(16):jcs259013

Important results

Replacing the pore region of PC2 with that of the related channel PC2L1 alters PC2 ion selectivity and leads to cyst formation in mice. Disease-associated pore loop mutations (F629S, C632R, and R638C) alter PC2 ion channel properties. Novel gain-of-function PC2 and PC1 mutants were generated to study properties of PC2/PC1 heteromeric ion channels.

Special methods

Human PC2 channels expressed in Xenopus laevis oocytes are studied with the two-electrode voltage-clamp (TEVC) and patch-clamp technique to record whole-cell and single-channel currents, respectively. Different PC2 mutant channels are generated by site-directed mutagenesis. Electrophysiological studies are complemented by molecular modeling of PC2.

Generation of novel glomerular 3D culture systems

Prof. Dr. Müller-Deile

Prof. Dr. Schiffer

F9 06/2020 - 06/2023

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Abstract

In search for better glomerular ex vivo models, we studied 3D glomerular co-cultures and generated stem cell (iPSC)-derived personalized podocytes from patients with genetic FSGS. These cells were characterized using bulk sequencing, marker expression, actin polymerization, morphology and response to different substances used in the clinic to foresee individual response to treatment. At the moment, CRISPR-Cas9 based rescue experiments of mutated iPSC derived patient podocytes are performed.

Special methods

- 3D spheroidal glomerular cell culture
- Generation of an artificial glomerular filtration barrier with glomerular endothelial cells and podocytes growing on different sides of an artificial basement membrane
- Generation of iPSC derived personalized human podocytes that keep the patients mutation

Important results

- 3D glomerular co-culture leads to differential expression of genes involved in differentiation, cell adhesion and vesicle transportation.
- INF2 mutated iPSC derived podocytes show altered expression in actin associated genes and morphology.
- Generation of personalized podocyte allows characterization and treatment ex vivo.

Publications

Rederer A, Rose V, Krüger R, Schmittutz L, Swierzy I, Fischer L, Thievessen I, Bauer J, Friedrich O, Schiffer M, Müller-Deile J. (2023) Partner, Neighbor, Housekeeper and Dimension: 3D versus 2D Glomerular Co-Cultures Reveal Drawbacks of Currently Used Cell Culture Models. International journal of molecular sciences. 24(12):10384

Kraus A, Rose V, Krüger R, Sarau G, Kling L, Schiffer M, Christiansen S, Müller-Deile J. (2023) Characterizing Intraindividual Podocyte Morphology In Vitro with Different Innovative Microscopic and Spectroscopic Techniques. Cells. 12(9):1245

Müller-Deile J, Sopel N, Ohs A, Rose V, Gröner M, Wrede C, Hegermann J, Daniel C, Amann K, Zahner G, Schiffer M. (2021) Glomerular Endothelial Cell-Derived microRNA-192 Regulates Nephronectin Expression in Idiopathic Membranous Glomerulonephritis. J Am Soc Nephrol JASN 32: 2777-2794

Cytosolic citrate metabolism in IEC

Prof. Dr. Becker

A93 07/2023 - 12/2025

Prof. Dr. Christoph Becker, Department of Medicine 1
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Abstract

We have identified the enzyme ATP Citrate Lyase (ACLY) as a key immunometabolic regulator of intestinal inflammation. We therefore hypothesize that diminished ACLY expression in the intestinal epithelium drives the pathogenesis of Inflammatory Bowel Disease. To evaluate our hypothesis, we plan to elucidate the regulation of Acly, its molecular mode of action and its functional impact for the steady-state gut and for intestinal inflammation using newly generated knockout mice.

Publications

no project-specific publications so far

Important results

We have continued to study the regulation and functions of ACLY and its impact on the cytosolic citrate metabolism. We have consolidated a role for ACLY in regulating intestinal inflammation in mice, have furthermore established a downregulation of ACLY in IBD and have identified inflammatory mediators regulating ACLY expression.

Special methods

- Models of experimental inflammation
- Transcriptomic and metabolomic analyses
- Methods of cell death research

SARS-CoV-2 host adaptation

Prof. Dr. Ensser

A94 07/2023 - 12/2025

Prof. Dr. Armin Ensser, Institute of Clinical and Molecular Virology
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Abstract

The continuous adaptation of the SARS-CoV-2 replicative machinery, as well as the consequences of nonstructural protein (Nsp) mutations to the virus-host interaction need to be considered in emerging variants. SARS-CoV-2 marker viruses will be used to address the role of existing and new variant virus mutations in Nsp's in different culture systems, in viral replication and in their escape from cellular restriction, focusing on the non-spike related phenotype of these variants.

Publications

Cordsmeier A, Jungnickl D, Herrmann A, Korn K, Ensser A (2023) Analysis of SARS-CoV-2 Spike Protein Variants with Recombinant Reporter Viruses Created from a Bacmid System. International journal of molecular sciences 24:8156

Russ A, Wittmann S, Tsukamoto Y, Herrmann A, Deutschmann J, Lagisquet J et al. (2022) Nsp16 shields SARS-CoV-2 from efficient MDA5 sensing and IFIT1-mediated restriction. EMBO reports 23: e55648

Important results

We were able to generate Spike recombinant viruses with the proposed strategy. Bacmids harboring the nonstructural and additional ORFs of Omicron BA.5 genome were cloned and are beeing reconstituted.

Special methods

- Recombinant SARS-CoV-2, viral infection under BSL3 conditions
- Wide-field fluorescence microscopy in BSL3 and Wide field high content imaging under BSL2 conditions
- Methods for single cell sequencing of virus-infected cells are beeing established

Viral RNA methylation inhibits MDA5 sensing

Prof. Dr. Gramberg

A95 01/2023 - 06/2025

Prof. Dr. Thomas Gramberg, Institute of Clinical and Molecular Virology
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Abstract

2'-O-Methylation of mRNA by cellular methyltransferases (MTases) enables discrimination of self and non-self. We found that SARS-CoV-2 lacking the viral MTase Nsp16 triggers an enhanced innate immune response that depends on the RNA receptor MDA5. Thus, we will analyse Nsp16 as a means of SARS-CoV-2 to counteract innate immune sensing and will test the hypothesis that the 2'-O-methylation of viral RNA in general protects from sensing by the pattern recognition receptor MDA5.

Publications

Russ A, Wittmann S, Tsukamoto Y, Herrmann A, Deutschmann J, Lagisquet J, Ensser A, Kato H, Gramberg T. (2022) Nsp16 shields SARS-CoV-2 from efficient MDA5 sensing and IFIT1-mediated restriction. EMBO reports 23: e55648

Important results

SARS-CoV-2 w/o Nsp16 induces a strong type I IFN response, which is absent in MDA5 KO Calu3 cells. We expressed MDA5 proteins in Calu3 MDA5 KO cells and found that wt MDA5 restored the response upon infection, while cells with inactive MDA5 showed reduced IFN secretion, demonstrating the importance of MDA5 signaling for inducing an antiviral state.

Special methods

- SARS-CoV-2 replication and infectivity assay
- Type I IFN bioassay
- Clip-Seq, NGS
- Innate luciferase reporter assays (NfkB, AP-1, IRF-3)
- CoIP experiments

Immune/ IEC crosstalk during intestinal CMV

Prof. Dr. Hildner

Prof. Dr. Winkler

A96 01/2023 - 10/2025

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Prof. Dr. Thomas Winkler, Department Biology - Chair of Genetics
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Abstract

Reactivation of latent Cytomegalovirus (CMV) infections represent a severe, life-threatening intestinal complication in immunocompromised patients. Underlying cellular and molecular mechanisms regulating the immune epithelial cell interaction are only partially understood and targeted treatment options are not available. We seek to decipher the immune / epithelial cell interaction in the context of CMV infection combining novel ex vivo organoid co-culture with innovative genetic model systems.

Publications

no project-specific publications so far

Important results

We have established conditions to co-culture dendritic cells (DCs) in intestinal organoids. Further, we have optimized our protocol to infect intestinal organoids with CMV. Both models will enable us to characterize both molecular properties and migratory behavior of DCs and gene expression pattern of IECs in the context of CMV infections ex vivo.

Special methods

1. MCMV infection of intestinal organoids to study epithelial-immune cell interaction ex vivo
2. New transgenic mouse model system to study the impact of CMV-specific gd T cells on MCMV/ intestinal epithelial cell biology
3. Dendritic cell/ intestinal organoid co-culture model system

STAT3 in IMCs during mucosal healing in IBD

Prof. Dr. Dr. Neufert

A97 07/2023 - 12/2025

Prof. Dr. Dr. Clemens Neufert, Department of Medicine 1
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Abstract

The function of intestinal mesenchymal cells (IMCs) in inflammatory bowel diseases (IBD) has not been clarified yet. The goal of this project is to characterize and to functionally study the role of STAT3 activation in IMCs during mucosal healing in the gut by using established in vivo models and human tissue specimens. Perspectively, these studies aim to pave the way for novel therapeutic options in IBD care.

Important results

STAT3-phosphorylation of IMCs is predominantly found at sites of ongoing mucosal healing in colitis specimens from humans & mice; type VI collagen-expressing IMCs are highly enriched in ulcerated areas of experimental colitis; epithelial proliferation is controlled by the level of STAT3 activation of IMCs in co-culture systems in vitro.

Special methods

Live cell imaging of gut cell populations; co-culture systems with IMCs and intestinal epithelial organoids and/or immune cells; experimental models of intestinal mucosal healing; transcriptional and protein-based molecular characterisation of IMC subsets; modulation of STAT3 activation in gut resident cell populations.

Publications

Lindemann A, Roth D, Koop K, Neufert C, Zundler S, Atreya R, Neurath MF, Leppkes M (2023) Protective effect of the novel calcineurin inhibitor voclosporin in experimental colitis. Frontiers in medicine 10:1177450

Matthe DM, Dinkel M, Schmid B, Vogler T, Neurath MF, Poeck H et al. (2023) Novel T cell/organoid culture system allows ex vivo modeling of intestinal graft-versus-host disease. Frontiers in immunology 14:1253514

Koop K, Enderle K, Hillmann M, Ruspeckhofer L, Vieth M, Sturm G et al. (2023) Interleukin 36 receptor-inducible matrix metalloproteinase 13 mediates intestinal fibrosis. Frontiers in immunology 14:1163198

RA-T

PD Dr. Schober

A98 03/2023 - 09/2025

PD Dr. Kilian Schober, Institute of Microbiology
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Abstract

Autoreactive T cells are thought to play a key role during the pathogenesis of rheumatoid arthritis (RA), but their specificity and their contribution to RA remain elusive. In this project, we will identify autoreactive T cells, their receptors and cognate antigens in RA patients, and study the dynamics of the autoreactive T cell response at different stages of RA. This will yield important information on the pathogenesis of RA and provide the base for a novel generation of immunotherapies.

Publications

no project-specific publications so far

Important results

From the methods outlined (identification of T cell receptors, transgenic re-expression, epitope identification), the first two have been successfully implemented and the third one is ongoing.

Special methods

1. Identification of T cells and T-cell receptors via single-cell RNA sequencing
2. Transgenic re-expression of T-cell receptors via CRISPR/Cas9-mediated orthotopic T-cell receptor replacement
3. T-cell epitope identification via "epitope discovery platform"

Mechanisms of cortical bone remodelling

PD Dr. Steffen

A99 07/2023 - 12/2025

PD Dr. Ulrike Steffen, Department of Medicine 3

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Abstract

Constant bone remodelling is important to prevent fractures. In bones with a thick cortex, we found that remodelling is based on endosteal bone formation and periosteal resorption which stands in contrast to existing models. In this project we will characterize this process and analyse its dependence on age, mechanical load, osteoclast and osteocyte activity. We aim to explain why some bone sites are prone to fracture and to develop new treatment strategies to prevent insufficiency fracture.

Publications

no project-specific publications so far

Important results

- Electron microscopy revealed lamellar structure of bone matrix which fits to permanent endosteal bone formation.
- Endosteal osteocytes express different markers than periosteal osteocytes.

Special methods

- Bone formation rate measurement with (lightsheet) microscopy
- Characterization of osteoblasts, osteoclasts and osteocytes with immunofluorescence microscopy and reporter mice
- Analysis of bone matrix and cellular composition with scanning and transmission electron microscopy

sCD83 induces wound healing

Prof. Dr. Steinkasserer

A100 07/2023 - 06/2026

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Abstract

New medications for the treatment of chronic wounds are urgently needed. Our preliminary data show that sCD83 accelerated wound healing processes in a systemic as well as a topical treatment. Cellular analyses revealed the increase of pro-resolving macrophages, known to improve wound healing processes. These striking regenerative capacities make sCD83 a promising candidate to treat chronic- and hard-to-heal wounds. Within the current project we aim to elucidate the underlying mechanisms.

Publications

no project-specific publications so far

Important results

Within this project, we analyze the therapeutic potential of sCD83 in wound healing in general and especially in aged mice with delayed wound healing properties. Of particular interest is the role of CD83 expressing macrophages during these wound healing processes as well as the identification of sCD83-responder cells in human skin.

Special methods

- sCD83 treated samples will be investigated using FACS in respect to neutrophils, monocytes, macrophages, B cells and T cells.
- Trans-differentiation of macrophages in WT and CD83 cKO-mice
- Analyses of distinct skin cell populations, including keratinocytes, fibroblasts, epithelial stem cells, melanocytes and endothelial cells

IgG4 responses after SARS-CoV-2 RNA vaccination

Prof. Dr. Tenbusch

A101 04/2023 - 09/2025

Prof. Dr. Matthias Tenbusch, Institute of Clinical and Molecular Virology
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Abstract

Recently, we identified atypical, antiviral IgG4 responses after immunizations with a SARS-CoV-2 mRNA vaccine. Since IgG4 responses are considered as anti-infammatory and rather tolerogenic, the impact of this type of antibody response on preventing viral infections or disease will be elucidated. Whether antigen re-exposures in form of infections or boost immunization will further shift the SARS-CoV-2 response towards IgG4 will be analysed as well as potential underlying mechanisms.

Publications

no project-specific publications so far

Important results

The bias towards anti-spike IgG4 were primarily attributed to mRNA vaccinations as first antigen contact. Individuals with prior SARS-CoV-2 infection develop only minor amounts of anti-S IgG4 after subsequent mRNA vaccination. For mechanistic studies, we generated now four different anti-S mAbs with distinct binding and neutralizing properties.

Special methods

- FACS-based antibody assay for the quantification of SARS-CoV-2 specific antibodies and their IgG subclasses
- Cloning of recombinant human anti-spike antibodies and passive immunization experiments in humanized FcgR mice
- Single cell sequencing of spike-specific memory B-cells

Mechanics of innate immune cells in colitis

Prof. Dr. Waldner

Prof. Dr. Guck

A102 07/2023 - 12/2025

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Prof. Dr. Jochen Guck, Department of Physics - Chair of Biological Optomechanics
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Abstract

Immune cell trafficking plays a central role in the pathogenesis of ulcerative colitis (UC). Based on our preliminary data, we propose cell mechanics as an important mechanism in this process. To explore this hypothesis, we will investigate mechanisms regulating mechanics of innate immune cells in colitis models. We will further explore the functional consequences of immune cell deformability in acute colitis and explore therapeutic opportunities for a modulation of cell mechanics in UC.

Publications

no project-specific publications so far

Important results

Using real-time fluorescence and deformability cytometry (RT-fDC), we identified different immune cell populations in human and mouse blood samples. Also, preliminary measurements of whole blood samples from mice exposed to DSS colitis revealed enlarged neutrophils, similar to the phenotypes observed in IBD patients.

Special methods

- Real-time fluorescence and deformability cytometry (RT-fDC) measurements to identify immune cell populations and evaluate their mechanical properties
- Analysis of in vitro stimulated neutrophils isolated from whole blood using RT-fDC
- Evaluation of tissue stiffness in healthy and inflamed mouse tissue using Brillouin microscopy

Secretory IgA molecules in intestinal immunity

PD Dr. Weigmann

A103 07/2023 - 12/2025

PD Dr. Benno Weigmann, Department of Medicine 1
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Abstract

Intestinal diseases (IBD) are chronic inflammations of the gastrointestinal tract. Secretory antibodies (SIgA) are produced by mucosal surfaces and are intestinal defences. The project aims to elucidate the role of SIgA in the uptake/retro process at the endothelium. Furthermore, an analysis of the SIgA-selected bacterial strains in the intestine will be carried out and new targets for a SIgA-mediated therapeutic approach in therapy will be found.

Special methods

- Specific human sIgA/IgA ELISA sandwich of serum concentration
- Transepithelial/endothelial electrical resistance (TEER) to measure the electrical resistance of a barrier tissue model or live cells
- Hapten-mediated experimental colitis model (oxazolone and TNBS-based) which resembles human ulcerative colitis and is mediated by type 2 cytokines.

Publications

no project-specific publications so far

Mechanical regulation of intestinal T cell egress

Prof. Dr. Dr. Zundler

Prof. Dr. Uderhardt

A104 01/2023 - 07/2025

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Prof. Dr. Stefan Uderhardt, Department of Medicine 3
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Abstract

It is still unclear, how the in vivo trafficking of autoreactive T cells in IBD is coordinated. Preliminary data indicate that mechanical properties regulate the motility of gut T cells. Thus, we aim to investigate the interplay of intestinal T cell mechanics and trafficking in a joint effort combining the expertise of two clinician scientist PIs in cell trafficking and bioimaging. We ultimately hope to identify new targets for organ-selective IBD therapy controlling T cell dynamics in the gut.

Important results

1. IL-3 receptor signaling controls the mechanobiology of regulatory T cells resulting in a stiffer actin cytoskeleton and reduced motility.
2. In vivo, this leads to reduced Treg egress from the inflamed colon lamina propria.
3. Such retention of Tregs results in clinical amelioration of experimental chronic colitis.

Special methods

1. Intravital imaging of T cell migration dynamics
2. Single cell transcriptional and bio-mechanical profiling
3. Volumetric tissue imaging, 3D-reconstruction and quantitative histocytometry

Publications

Ullrich KA, Derdau J, Baltes C, Battistella A, Rosso G, Uderhardt S, Schulze LL, Liu LJ, Dedden M, Spocinska M, Kainka L, Kubánková M, Müller TM, Schmidt NM, Becker E, Ben Brahim O, Atreya I, Finotto S, Prots I, Wirtz S, Weigmann B, López-Posadas R, Atreya R, Ekici AB, Lautenschläger F, Guck J, Neurath MF, Zundler S (2023) IL-3 receptor signalling suppresses chronic intestinal inflammation by controlling mechanobiology and tissue egress of regulatory T cells. Gut 72: 2081-2094

ACLY in IBD-associated cancer

PD Dr. Atreya

D37 04/2023 - 09/2025

PD Dr. Imke Atreya, Department of Medicine 1
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Abstract

Our preliminary data indicate a beneficial role of the metabolic enzyme ACLY in T cells in the AOM/DSS-induced CAC (colitis-associated cancer) model, while published data implicate that upregulation of ACLY in colon tumor cells promotes metastasis. Thus, we aim on the development of clinically applicable strategies to trigger ACLY activity selectively in tumor-infiltrating T cells and will focus on the identification of those CAC patients, who could best benefit from an ACLY-targeting therapy.

Publications

no project-specific publications so far

Important results

We described the inflammation-associated downregulation of ACLY in gut T cells in IBD as a regulatory process to dampen their colitogenic capacity. However, in the AOM/DSS-induced CAC model, ACLY levels in LPMC were initially decreased during early colitis induction, but were restored later, implicating modulation of ACLY by the tumor micromilieu.

Special methods

- Experimental in vivo model for colitis-associated cancer (AOM/DSS CAC model)
- Genetic mouse model: Conditional knockout mice carrying a T cell-restricted ACLY (ATP Citrate Lyase) deficiency (Cre-loxP system)
- Purification and flow cytometric characterization of intestinal lamina propria and tumor-infiltrating immune cells

AP2e in malignant melanoma

Prof. Dr. Bosserhoff

D38 03/2023 - 09/2025

Prof. Dr. Anja Bosserhoff, Institute of Biochemistry -
e-mail: anja.bosserhoff@fau.de

Abstract

The transcription factor family AP2 has important functions in development. AP2e was discovered in cooperation with this PI. We newly observed delayed onset of tumorigenesis in a murine Ap2e-deficient melanoma model. This is supported by expression data showing induced AP2e mRNA expression in early tumor development and a correlation of high Ap2e expression with reduced overall survival. In the project, the role of Ap2e in development and progression of melanoma is explored in molecular detail.

Important results

The transcription factor family AP2 has important functions in development. In the project, the role of Ap2e in development and progression of melanoma is explored in molecular detail. Now, we revealed that AP2e is a central regulator of melanoma plasticity, strongly supporting metastasis to distant organs.

Special methods

Analysis of transcriptional regulation (e.g. EMSA, reporter assays, ChIP-Seq), functional analyses of tumor characteristics, bioinformatic analysis of transcriptome data.

Publications

Stüfchen I, Beyer F, Staebler S, Fischer S, Kappelmann M, Beckervordersandforth R, Bosserhoff AK (2023) Sox9 regulates melanocytic fate decision of adult hair follicle stem cells. iScience 26: 106919

EMT and ferroptosis

PD Dr. Brabletz

D39 07/2023 - 12/2025

PD Dr. Simone Brabletz, Chair of Experimental Medicine I - Molecular Pathogenesis Research
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Abstract

We have demonstrated that the EMT-activator ZEB1 provides cancer cells not only with aberrant motility, but also with survival traits enabling tumor progression, metastasis and drug resistance. Our aim is to eliminate these aggressive 'untargetable' EMT-state cancer cells, which strikingly show a high sensitivity to ferroptotic cell death. In this project, we want to elucidate the molecular basis of ZEB1 – associated ferroptosis sensitivity to exploit it as a novel therapeutic target.

Publications

no project-specific publications so far

Important results

- Validation of ZEB1/EMT dependent ferroptosis sensitivity in various tumor cell systems.
- ZEB1 dependent, ESRP1 mediated splice variants of CD44 correlate with ferroptosis sensitivity.
- Establishment of human and murine tumor cell lines with stable shRNA mediated knockdown of ESRP1 and CD44 to characterize their impact on ferroptosis sensitivity.

Special methods

- Ferroptosis induction in cell lines; rescue experiments with ferrostatin1 to distinguish ferroptosis from other types of cell death
- Determine cell viability via MTT-assays or live imaging with the Incucyte device in combination with SYTOX cell death indicator
- Intracellular quantification of lipid peroxidation with C11-BODIPY

The role of DDX46 in liver cancer

PD Dr. Dr. Dietrich

D40 03/2023 - 08/2025

PD Dr. Dr. Peter Dietrich, Department of Medicine 1
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Abstract

The neuropeptide Y (NPY) system was shown by the applicant to be a major driver of HCC. Transcriptome screening revealed that DEAD-box RNA helicase DDX46 is a novel and attractive NPY-regulated target in HCC. The major aims of this study are to characterize NPY-mediated regulation of DDX46 and to decipher the role of DDX46 as a novel and promising diagnostic and therapeutic target in HCC.

Publications

no project-specific publications so far

Important results

Transcriptome screening revealed that DEAD-box RNA helicase DDX46 is a novel and attractive NPY-regulated target in HCC. During the first months of our project, we now further characterize NPY-mediated regulation of DDX46 and decipher the role of DDX46 as a novel and promising diagnostic and therapeutic target in HCC.

Special methods

- HCC models
- RNAi techniques in vivo and in vitro
- Patient-derived samples and biobanking

Therapy resistance in urothelial cancer


Prof. Dr. Engel


PD Dr. Eckstein

D41 07/2023 - 12/2025

Prof. Dr. Felix Engel, Department of Nephropathology
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PD Dr. Markus Eckstein, Institute of Pathology
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Abstract

Urothelial carcinoma (UC) is among the ten most common cancers worldwide and overall therapy systemic response rates are limited (~20%). Molecular insights in processes driving therapy resistance are scarce. Here, we propose to expand our existing patient-derived living UC biobank, develop a novel zebrafish model to study the role of fatty acid metabolism and ferroptosis in UC, and to determine if the zebrafish allows the pre-selection of therapy responsive patients.

Publications

no project-specific publications so far

Important results

Urothelial cancer (UC) cell lines are sensitive to ferroptosis-inducing drugs in vitro and in vivo (zebrafish). Sensitivity depends on cell type and inducing agent type and concentration. SCD inhibition enhances this sensitivity. The patient-derived tumoroid biobank of metastatic UC patients has been expanded by n = 6 patients.

Special methods

- Biomarker identification
- Bioinformatical data mining with DeSEQ2
- Zebrafish xenograft/co-injection model
- Lentivirus-mediated knockdown and overexpression

PSAP in liver steatosis-triggered liver cancer


Prof. Dr. Hellerbrand

D42 04/2023 - 09/2025

Prof. Dr. Claus Hellerbrand, Institute of Biochemistry
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Abstract

Non-alcoholic fatty liver disease (NAFLD) is the leading cause of hepatocellular carcinoma (HCC). Furthermore, NAFLD promotes HCC progression but the mechanism are elusive. Our preliminary work indicates that enhanced expression of prosaposin (PSAP) in NAFLD promotes HCC growth. Therefore, this project aims to characterize the molecular mechanisms by which PSAP affects HCC cells, to test the therapeutic potential of PSAP inhibition and to validate the function of PSAP in clinical HCC samples.

Publications

no project-specific publications so far

Important results

We identified molecular mechanisms leading to an upregulation of prosaposin (PSAP) in steatotic liver and found that PSAP induced pro-tumorigenic signaling pathways in hepatocellular carcinoma (HCC). These data confirm the therapeutic potential of PSAP inhibition in liver steatosis related HCC which will be further analyzed in the ongoing project.

Special methods

- Murine HCC (hepatocellular cacinoma) models
- Diet induced fatty liver models in mice
- Funktional analysis of HCC-cells

Regulation of CD19.CAR T-cells


PD Dr. Völkl


Prof. Dr. Vera Gonzalez

D43 03/2023- 09/2025

PD Dr. Simon Völkl, Department of Medicine 5
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Prof. Dr. Julio Vera Gonzalez, Department of Dermatology
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Abstract

CD19-directed chimeric antigen receptor (CAR) T-cells have shown high efficacy in the treatment of B-cell malignancies and are now emerging as a standard approach for patients with relapsed and refractory disease. Despite this progress, a significant portion of patients still experience resistance to treatment. We aim to understand the intrinsic mechanisms controlling persistence and effector functions of CAR T-cells and therefore identify strategies to overcome treatment failure.

Publications

no project-specific publications so far

Important results

Early CAR T-cell expansion at day 7 post transfusion predicted treatment response in relapsed or refractory large B-cell lymphoma and was associated with survival. This finding offers the possibility to identify treatment failure within the first week after CAR T-cell therapy and thereby laying out the ground for future intervention studies.

Special methods

- Analysis of immune cells using high-dimensional flow cytometry
- Cytotoxicity and signaling assays
- Third-generation Oxford Nanopore sequencing for investigating the vector integration

Molecular nexuses in neurodevelopmental diseases


Dr. Falk

E32 07/2023 - 12/2025

Dr. Sven Falk, Institute of Biochemistry
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Abstract

The development of a functional central nervous system depends on the accurate coordination of the highly dynamic microtubule cytoskeleton. Here we propose to chart the molecular landscape induced by mutations in microtubule cytoskeleton components implicated in neurodevelopmental disorders in human brain organoids to uncover unifying and diverging molecular features in a tissue-like context to design strategies to interfere with disease-phenotype progression.

Publications

Menon R, Petrucci L, Lohrer B, Zhang J, Schulze M, Schichor C, Winner B, Winkler J, Riemenschneider MJ, Kühn R, Falk S, Karow M (2023) Human Induced Pluripotent Stem Cell-Derived Pericytes as Scalable and Editable Source to Study Direct Lineage Reprogramming Into Induced Neurons. Cellular reprogramming 25: 212-223

Important results

- ScRNAseq based deconstruction of the molecular framework resulting in neuronal malformations
- Uncovered shared and specific molecular principles driving similar neuronal malformations triggered by mutations in microtubule associated genes vs transcription factors
- Adaptation of the hiPSC based platform to perform pooled perturbation screens

Special methods

- iPSC based brain organoids modeling early human brain development
- Pooled genetic perturbation screens utilizing single cell RNAseq for phenotyping
- Patient derived iPSC

Deubiquitinase Otud7b in CNS myelination

Dr. Küspert

E33 07/2023 - 12/2025

Dr. Melanie Küspert, Institute of Biochemistry
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Abstract

Specific regulation of protein degradation by the ubiquitin-proteasome system plays important roles in myelination, remyelination and neurodegenerative diseases. I want to analyse the functions of the deubiquitinase Otud7b in oligodendrocytes in vitro and in vivo in an oligodendrocyte-specific Otud7b knockout mouse model and identify functional targets of Otud7b in oligodendrocytes to deepen the understanding of posttranscriptional regulatory events during OL differentiation and CNS myelination.

Publications

no project-specific publications so far

Important results

We identified Otud7b as a novel target of the transcription factors Sox10 and Klf9, both important regulators of oligodendroglial differentiation and myelin gene expression. Initial functional analyses on transduced oligodendroglial cells revealed increased stability of myelin proteins after Cycloheximide treatment if Otud7b was overexpressed.

Special methods

- Analysis of Otud7b cko mouse mutants and primary oligodendrocytes (IHC/ICC, ISH, RNA-Seq)
- Characterization of the Otud7b upstream regulatory network (reporter gene assays)
- Characterization of the oligodendroglial Otud7b interactome and analysis of candidate protein stability upon Otud7b GOF/LOF (Co-IP, mass-spectrometry, Cycloheximide chase)

Regulation of the adul CNS stem cell niche

Prof. Dr. Lie

Prof. Dr. Franze

E34 07/2023 - 03/2026

Prof. Dr. Dieter Chichung Lie, Institute of Biochemistry
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Prof. Dr. Kristian Franze, Institute of Medical Physics
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Abstract

An adverse local environment ("niche") impairs the activity of neural stem cells (NSCs) in the adult brain. We investigate the new hypothesis that NSCs play an active role in generating favorable and adverse niche conditions. Specifically, we will investigate how dysfunctional NSCs generate adverse niche conditions focusing i) on the composition and the biomechanical properties of the extracellular matrix and ii) on NSC-derived exosomes and their composition.

Publications

no project-specific publications so far

Important results

We are establishing protocols to isolate exosomes from adult neural stem cells and to generate tissue culture substrates of defined stiffness for culturing neural stem cells. We found that stem cells produce long-chain fatty acids in a FoxO-dependent manner and that long-chain fatty acids modulate stem cell proliferation.

Special methods

Measurement of autophagic-lysosomal flux via biochemistry and imaging. Biochemical analyses of exosomes. Neural stem cell cultures. Retroviral vectors. Stereotactic injections (mouse). Atomic force microscopy. Traction force microscopy. Custom-built compliant cell culture substrates.

Deciphering recessive NDDs


Prof. Dr. Reis


Prof. Dr. Soba

E35 04/2023 - 09/2025

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Prof. Dr. Peter Soba, Institute of Physiology and Pathophysiology
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Abstract

Autosomal recessive mutations significantly contribute to intellectual disability and neurodevelopmental disorders (NDDs). However, high genetic heterogeneity of NDDs makes it difficult to prove pathogenicity. Using a comprehensive approach, we will combine genome sequencing and transcriptomics in a unique patient cohort of consanguineous Turkish families with at least two affected children, together with in silico analysis of candidates and in vivo screening in the Drosophila model organism.

Publications

no project-specific publications so far

Important results

The genetic analysis of patients with autosomal recessive neurodevelopmental disorders has so far identified 60 novel genetic variants with potential pathogenicity. Assessment of the functional conservation and pathogenicity of 20 candidates with the highest homology is currently ongoing in the fly model.

Special methods

- Genome sequencing
- RNA-Seq transcriptomics
- Drosophila genetics and optogenetics
- Behavioral analyses
- Analysis of neuronal morphology and function

Temporal patterning of dopaminergic neurons


Dr. Sagner

E36 07/2023 - 12/2025

Dr. Andreas Sagner, Institute of Biochemistry
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Abstract

Parkinson's disease is a neurodegenerative movement disorder characterized by the progressive loss of midbrain dopaminergic (mDA) neurons. mDA neurons can be partitioned into numerous molecularly and functionally distinct neuronal subtypes. The molecular mechanisms orchestrating mDA neuron subtype specification are still largely unclear. This project will test the hypothesis that a temporal patterning program I recently uncovered contributes to the establishment of mDA neuron diversity.

Publications

no project-specific publications so far

Important results

- Optimization of antibodies for immunofluorescent staining of dopaminergic neuron (DAN) subtypes and temporal identity markers
- Collection of a developmental timecourse of embryonic mouse midbrain tissue sections.
- Optimization of computational pipelines for segmentation and DAN nuclei in tissue sections

Special methods

- EdU/BrdU birth-dating of mouse midbrain dopaminergic neurons (mDANs)
- Differentiation of human iPSCs into mDANs
- Epigenetic profiling (CUT&RUN; ATACseq) of mDANs

CtBP1, oligodendrocytes & myelination


Prof. Dr. Wegner


Prof. Dr. Fejtova

E37 02/2023 - 12/2025

Prof. Dr. Michael Wegner, Institute of Biochemistry
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Prof. Dr. Anna Fejtova, Department of Psychiatry and Psychotherapy
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Abstract

Mutations in transcriptional corepressor CtBP1 cause the neurodevelopmental disorder HADDTS. Functional CtBP1 studies in the central nervous system so far focused on neurons. We recently found that CtBP1 is also important in oligodendrocytes. Here we will characterize the oligodendroglial functions of CtBP1 and the underlying cellular and molecular mechanisms in mice and a human ES cell-derived cellular disease model to show that defects in oligodendrogenesis and myelination contribute to HADDTS.

Publications

no project-specific publications so far

Important results

- CtBP1 is required to maintain oligodendrocytes (OL) in a spatiotemporally defined manner.
- While early postnatal OL generation remains normal upon its deletion, the maintenance of myelinating OL is impaired in brain but not in spinal cord in adult mice.
- Contact with a HADTTS patient was established and blood cells for iPSC generation were obtained.

Special methods

- Differentiation of human stem cells into glia
- Mouse genetics
- Multiomics

Funded projects Jochen-Kalden-Funding Programme:

No.	Name	Institution	Project title
N5	Prof. Dr. Claudia Günther	Department of Medicine 1	Organ crosstalk in IMIDs
N6	Prof. Dr. Janina Müller-Deile	Department of Medicine 4	Rare glomerular diseases
N7	Prof. Dr. Marisa Karow	Institute of Biochemistry	Forging neural cell identity
N8	Prof. Dr. Friederike Zunke	Department of Molecular Neurology	Lysosomes & glial cells
N9	Prof. Dr. Caroline J. Voskens	Department of Dermatology	Engineered cells in skin diseases
N10	Prof. Dr. Ricardo Grieshaber-Bouyer	Department of Medicine 3	LAMP1+ neutrophils in lupus nephritis
N11	Prof. Dr. Lydia Meder	Department of Experimental Medicine I	ERBB2 in der SCLC Immunantwort

Organ crosstalk in IMIDs

Prof. Dr. Günther

N5 07/2021 – 06/2024

Prof. Dr. Claudia Günther, Department of Medicine 1
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Abstract

A substantial fraction of IMID patients does not sufficiently respond to current therapeutic approaches, whereas others require life-long and cost-intensive treatments. Therefore, both technological as well as scientific progress is urgently needed to allow innovative patient-centred precision medicine. Within the next 5 years, we will establish novel preclinical models to better understand disease mechanisms, to identify novel therapeutic approaches and to allow high throughput drug screening. This will be achieved by combining immunological research with stem cell biology, biophysical approaches and artificial intelligence.

Important results

Our study significantly advances the understanding of PSC-IBD pathogenesis by shedding light on the pivotal role of bacterial membrane vesicles released by gut pathobionts. We further provide compelling translational evidence that OMVs might represent a novel biomarker to identify PBS-IBD patients. These findings may have profound implications for the diagnosis and treatment of this challenging disease.

Special methods

- Human/murine organoid cultures (intestinal, biliary)
- Host-microbe communication via extracellular vesicles (EVs) (bacterial vesicle isolation)
- Mouse models for inter-organ communication

Publications

Wittner L, Wagener L, Wiese JJ, Stolzer I, Krug SM, Naschberger E, Jackstadt R, Beyaert R, Atreya R, Kühl AA, Sturm G, Gonzalez-Acera M, Patankar JV, Becker C, Siegmund B, Trajanoski Z, Winner B, Neurath MF, Schumann M, Günther C (2023) Proteolytic Activity of the Paracaspase MALT1 Is Involved in Epithelial Restitution and Mucosal Healing. Int J Mol Sci. 24(8):7402

Günther C, Winner B, Neurath MF, Stappenbeck TS (2022) Organoids in gastrointestinal diseases: from experimental models to clinical translation. Gut. 71(9):1892-1908

Bittel M, Reichert P, Sarfati I, Dressel A, Leikam S, Uderhardt S, Stolzer I, Phu TA, Ng M, Vu NK, Tenzer S, Distler U, Wirtz S, Rothhammer V, Neurath MF, Raffai RL, Günther C, Momma S (2021) Visualizing transfer of microbial biomolecules by outer membrane vesicles in microbe-host-communication in vivo. J Extracell Vesicles (12):e12159

Prof. Dr. Müller-Deile

N6 04/2021 – 12/2024

Prof. Dr. Janina Müller-Deile, Department of Medicine 4

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Abstract

Cell-cell communication through miR containing exosomes and circulating factors is investigated in 3D glomerular co-culture, zebrafish and mouse model. We speculate that autophagy and exosome secretion are linked by endolysosomal pathways and are dysregulated in membranous glomerulonephritis. Our zebrafish model and exosome reporter enable to live track exosomes. Raman and mass spectroscopy provide a molecular fingerprint for FSGS caused by unknown circulating factors.

Important results

- Podocyte-derived nephronectin is important for proper glomerular function and is regulated by endothelial cell derived miRNA-192 loaded exosomes
- miRNA-378a increases podocyte autophagy flux by targeting mTOR-pathway
- Glomerular endothelial cell-derived miRNA-200c impairs glomerular homeostasis by targeting podocyte VEGF-A.

Special methods

- Exosome reporter plasmids
- 3D glomerular co-culture model
- Different transgenic zebrafish models

Publications

Rederer A, Rose V, Krüger R, Schmittutz L, Swierzy I, Fischer L, Thievessen I, Bauer J, Friedrich O, Schiffer M, Müller-Deile J (2023) Partner, Neighbor, Housekeeper and Dimension: 3D versus 2D Glomerular Co-Cultures Reveal Drawbacks of Currently Used Cell Culture Models. Int J Mol Sci. 24(12):10384

Sopel N, Ohs A, Schiffer M, Müller-Deile J (2022) A Tight Control of Non-Canonical TGF-Pathways and MicroRNAs Downregulates Nephronectin in Podocytes. Cells 11(1):149

Müller-Deile J, Sopel N, Ohs A, Rose V, Gröner M, Wrede C, Hegermann J, Daniel C, Amann K, Zahner G, Schiffer M (2021) Glomerular Endothelial Cell-Derived microRNA-192 Regulates Nephronectin Expression in Idiopathic Membranous Glomerulonephritis. J Am Soc Nephrol 32(11):2777-2794

Forging neural cell identity

Prof. Dr. Karow

N7 07/2021 – 02/2025

Prof. Dr. Marisa Karow, Institute of Biochemistry

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Abstract

Based on our previous work on direct lineage reprogramming of adult human brain pericytes into induced neurons (iNs), we are here following the hypothesis that amongst the genes allowing fate switch of postmitotic pericytes into iNs, novel regulators of human neurogenesis can be identified. We identified candidates putatively involved in pericyte-to-iN reprogramming as well as in normal human neurogenesis. These candidates are currently functionally tested in both paradigms.

Important results

- Successful establishment of a lentivirus-based platform to manipulate candidate gene expression in primary human pericytes
- New results point towards a key role for a metabolic regulator (CHCHD2) during pericyte-to-neuron conversion
- Establishment of an imaging based analysis pipeline to assess mitochondrial dynamics in pericytes

Special methods

- Continuous live-imaging of fluorescently labelled cells for long period of time (up to 2 weeks)
- scATAC-/scRNA-seq using 10xGenomics platform (using the chromium controller) including library construction

Publications

Käseberg S, Bertin M, Menon R, Gabassi E, Todorov H, Frank S, Brennenstuhl H, Lohrer B, Winter J, Krummeich J, Winkler J, Winner B, Weis E, Hartwich D, Diederich S, Luck K, Gerber S, Lunt P, Berninger B, Falk S, Schweiger S, Karow M (2023) Dynamic X-chromosomal reactivation enhances female brain resilience; BioRxiv doi: https://doi.org/10.1101/2023.06.17.545424

Menon R, Petrucci L, Lohrer B, Schichor C, Winner B, Winkler J, Schulze M, Riemenschneider M, Zhnag J, Kühn R, Falk S, Karow M (2022) Using human iPS cell derived pericytes as renewable and editable source to study direct lineage reprogramming into induced neurons. Cell Reprogram. 2023 Oct; 25(5):212-223. doi: 10.1089/cell.2023.0008. Epub 2023 Jun 27

Prof. Dr. Zunke

N8 02/2021 – 11/2024

Prof. Dr. Friederike Zunke, Department of Molecular Neurology

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Abstract

Recent studies suggest that not only neuronal, but also glial dysfunction contribute to neurodegeneration in Parkinson's disease (PD). Since lysosomal homeostasis is crucial for proper function of the central nervous system (CNS), this project aims to analyze effects of lysosomal (dys)function under pathological conditions in neuronal as well as non-neuronal cells, particularly focussing on oligodendrocytes and astrocytes. As a-synuclein aggregation is a hallmark of PD, we study the impact of its lysosomal degradation in neuronal as well as glial cells. A better understanding of lysosomal turnover in glial cells will help to unravel molecular mechanisms and facilitate the search for novel therapeutic strategies in PD still lacking to date.

Important results

1. Oligodendrocytes and astrocytes exposed to a-synuclein show changes in the lysosomal system.
2. Reduction in enzymatic activity of specific lysosomal enzymes in oligodendrocytes results into pathological a-synuclein aggregation.
3. Applying lysosomal activators as therapeutic treatment has positive effects in neurons and oligodendrocytes.

Special methods

1. Analyses of lysosomal and autophagy pathways: lysosomal enrichments, enzyme maturation and activities, pH measurements, analysis of extracellular vesicles
2. Induced pluripotent stem cells & differentiation protocols: neurons and glial cells
3. Structure/function analysis of proteins: recombinant expression of lysosomal enzymes, a-synuclein

Publications

Drobny A, Boros FA, Balta D, Prieto Huarcaya S, Caylioglu D, Qazi N, Vandrey J, Schneider Y, Dobert JP, Pitcairn C, Mazzulli JR, Zunke F. (2023) Reciprocal effects of alpha-synuclein aggregation and lysosomal homeostasis in synucleinopathy models. Transl Neurodegener. 12(1):31. doi: 10.1186/s40035-023-00363-z

Seebauer L, Schneider Y, Drobny A, Plötz S, Koudelka T, Tholey A, Prots I, Winner B, Zunke F, Winkler J, Xiang W. (2022) Interaction of Alpha Synuclein and Microtubule Organization Is Linked to Impaired Neuritic Integrity in Parkinson's Patient-Derived Neuronal Cells. Int J Mol Sci. 23(3):1812. doi: 10.3390/ijms23031812

Prieto Huarcaya S, Drobny A, Marques ARA, Di Spiezio A, Dobert JP, Balta D, Werner C, Rizo T, Gallwitz L, Bub S, Stojkovska I, Belur NR, Fogh J, Mazzulli JR, Xiang W, Fulzele A, Dejung M, Sauer M, Winner B, Rose-John S, Arnold P, Saftig P, Zunke F. (2022) Recombinant pro-CTSD (cathepsin D) enhances SNCA/α-Synuclein degradation in α-Synucleinopathy models. Autophagy. 18(5):1127-1151. doi: 10.1080/15548627.2022.2045534

Engineered cells in skin disease

Prof. Dr. Voskens

N9 10/2023 – 09/2025

Prof. Dr. Caroline J Voskens, Department of Dermatology

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Abstract

We hypothesize that, during inflammation, a highly motile subset of lymphocytes, including T cells, B cells and regulatory T cells migrates from the blood into the skin. The characterization of this highly motile subset would allow us to identify the migration and suppressive molecules selectively employed by these cells to reach the site of inflammation. We propose that we can engineere blood erived immune cells with these molecules. In such a scenario, these engineered immune cells are highly migratory and ready to move to the site of inflammation after adoptive cell transfer.

Special methods

- GMP-compliant expansion of regulatory T cells (Tregs)
- Characterization of immune cell subsets, including Tregs in the skin by robot-automated multi-epitope ligand cartography (MELC)
- Tracking of immune cell subsets in 3-D collagen gels
- Modification of immune cell subsets by mRNA electroporation

Publications

no project-specific publications so far

LAMP1+ neutrophils in lupus nephritis

Prof. Dr. Grieshaber-Bouyer

N10 not started yet

Prof. Dr. Ricardo Grieshaber-Bouyer, Department of Medicine 3

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Abstract

My preliminary data highlight that neutrophil phenotypes define distinct SLE patients and that LAMP-1 is a strongly dysregulated protein in SLE. I hypothesize that LAMP1 expression defines a distinct activation state of neutrophils associated with a clinical subgroup of SLE patients with more severe kidney involvement. Hence, this project aims to study the functional role of LAMP1 in neutrophils and probe associations of LAMP1 expression and serum levels with clinical features in SLE.

Special methods

1. Neutrophil stimulation
2. RNA-seq
3. Functional characterization by imaging flow cytometry and confocal microscopy (phagocytosis, reactive oxygen species, bacterial killing, migratory potential, NET formation, cytokine release)
4. Quantification of LAMP1 in serum, cell-based reporter assays to screen for autoantibodies

Publications

no project-specific publications so far

ERBB2 in SCLC immune response

Prof. Dr. Meder

N11 01.04.2024 - 31.03.2026

Prof. Dr. Lydia Meder, Department of Experimental Medicine I

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Abstract

My group unravels molecular signaling pathways that are involved in metastasis and allow tumor cells to hide from immune surveillance. Our preliminary results suggest that ERBB2 is activated in small cell lung cancer metastasis helping the tumor to escape the host immune system.

We plan to investigate ERBB2 inhibitors, ERBB2 targeting antibodies and antibody-drug conjugates regarding their immunoregulatory properties ex vivo in precision cut tissue slices (PCTS) of the lung and in a SCLC mouse model. We will elucidate the underlying molecular mechanisms downstream of ERBB2 and identify patients who may benefit from an ERBB2 targeted therapy.

Special methods

- Precision-cut tissue slices of the lung
- Confocal time-lapse imaging of cellular interaction in the tumor microenvironment
- Imaging mass cytometry
- Mouse models of small cell lung cancer

Publications

no project-specific publications so far

Funded junior projects in 2023:

No.	Name	Institution		Project title
J84	Dr. Sascha Kretschmann	Department of Medicine 5	I	Direct vs. indirect class II antigen presentation
J85	Dr. Kristina Koop	Department of Medicine 1	I	Cell-type-specific roles of IL36 in the Intestine
J87	Prof. Dr. Stefan Uderhardt	Department of Medicine 3	I	Network Communication in Inflammation
J88	Dr. Florian Krach	Department of Stem Cell Biology	N	New RNA-binding proteins in sporadic ALS
J89	PD Dr. Adrian Regensburger	Department of Pediatrics and Adolescent Medicine	M	MSOT imaging of strictures in Crohn's disease
J90	Dr. Darja Andreev	Department of Medicine 3	I	The impact of Eos on bone loss
J91	Dr. Jean-Philippe Auger	Department of Medicine 3	I	Glucocorticoid-induced macrophage reprogramming
J93	PD Dr. Liubov Kalinichenko	Department of Psychiatry and Psychotherapy	N	Lipids and Serotonin in drug instrumentalization
J94	Dr. Patrick Süß	Department of Molecular Neurology	N	Neuroinflammation and synucleinopathy in IBD
J95	Dr. Franziska Thiele	Institute of Biochemistry	N	Role of Tip60 in the PNS
J96	Dr. Maria de los Reyes Gamez Belmonte	Department of Medicine 1	S	Bace1/Bace2 in colorectal cancer development
J97	Dr. Benedikt Jacobs	Department of Medicine 5	S	Immune-metabolic dysfunction of NK cells
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J101	Dr. Dr. Christian Matek	Institute of Pathology	O	AI for GI Histopathology
J102	Dr. Michael Rückert	Department of Radiation-Oncology	O	cDC1s in abscopal effects and HHP vaccination
J103	Dr. Eva Maier	Department of Operative Dentistry and Periodontology	M	Predicting clinical longevity of dental materials
J104	Dr. Tanja Müller	Department of Medicine 1	I	Stat5 in chronic colitis
J105	Dr. Katharina Pracht	Department of Molecular Immunology	I	GLUT1- metabolism and antibody response
J106	Dr. Maria Gabriella Raimondo	Department of Medicine 3	I	Skin-derived immune cells in psoriatic arthritis
J107	Dr. Simon Rauber	Department of Medicine 3	I	PU.1 in osteoblasts and osteoproliferation
J108	Dr. Alexander Schnell	Department of Paediatrics and Adolescent Medicine	I	Functional role of CFTR in immune cells
J109	Dr. Fanni Annamaria Boros	Department of Molecular Neurology	N	Extracellular vesicles in Parkinson's disease

I - Infection and Immunology, N - Neurosciences, O - Oncology, R - Renal and Vascular Research, M - Medical Engineering, S - Others

Direct vs. indirect class II antigen presentation


Dr. Kretschmann

J84 11/2020 - 04/2023

Dr. Sascha Kretschmann, Department of Medicine 5
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IMMUNOLOGY AND INFECTION

Abstract

Surface presentation of HLA class II-antigens can occur directly by the host cell or after intercellular transfer of the antigen to surrounding antigen presenting cells. We hypothesize that prior to surface presentation endogenously expressed class II-restricted antigens travel in different compartments as compared to exogenous antigens and therefore undergo differential processing. These processing steps which are critical for presentation, are characterized by antigen specific properties.

Publications

no project-specific publications so far

Important results

- 4 of 6 identified tyrosine-based sorting motifs influence indirect DBY-presentation after mutation.
- Targeting intracellular membrane trafficking with 3 distinct inhibitors, indirect DBY-presentation was affected.
- Results reinforce our hypothesis and identify adaptor protein complexes as interesting targets to regulate indirect presentation.

Special methods

- Culture and re-stimulation of primary and antigen-specific CD4+ T-cell clones
- Invention and usage of an accelerated antigen presentation screen assay
- Cloning techniques, e.g. a two-step PCR technique to fuse proteins

Cell-type-specific roles of IL36 in the Intestine


Dr. Koop

J85 11/2020 - 11/2023

Dr. Kristina Koop, Department of Medicine 1
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IMMUNOLOGY AND INFECTION

Abstract

Intestinal fibrosis is a common complication in IBD and has limited therapeutic options. IL36R ligands are upregulated in CD and UC patients as well as CD patients with stenosis. The systemic blockade of IL36R signaling reduces intestinal inflammation and fibrosis in vivo. Deciphering the cell-type-specific roles of IL36 via the newly generated IL36Rfl/f mouse strain will help to understand the mode of action of a neutralizing IL36R antibody in humans.

Publications

Koop K, Enderle K, Hillmann M, Ruspeckhofer L, Vieth M, Sturm G et al. (2023) Interleukin 36 receptor-inducible matrix metalloproteinase 13 mediates intestinal fibrosis. Frontiers in immunology 14: 1163198

Important results

- Mice with defective IL36R signaling in IECs and fibroblasts are more sensitive to DSS in an acute setup compared to littermate controls.
- In chronic DSS, IL36R?IEC and IL36R$^{\Delta Fibro}$ showed a protected phenotype regarding fibrotic remodeling compared to IL36Rfl mice.
- The results fit to former results of universal IL36R-/- animals.

Special methods

- Identification of intestinal fibroblasts by scRNAseq from mice and human
- Characterization of intestinal fibrosis by advanced imaging e.g. LSFM, label-free multiphoton microscopy, tissue CyTOF
- Secretome analysis of primary fibroblasts upon IL36R activation by LC/MS in cooperation with the Chair of Food Chemistry

Network Communication in Inflammation

Prof. Dr. Uderhardt

J87 01/2021 - 06/2023

Prof. Dr. Stefan Uderhardt, Department of Medicine 3
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IMMUNOLOGY AND INFECTION

Abstract

I could previously identify resident tissue macrophages (RTM) as anti-inflammatory protectors of stromal integrity. The molecular mechanisms that regulate this tissue-protective function, however, are unknown. My preliminary work strongly suggests that within stromal tissues exist extensive, heterocellular communication networks. I hypothesize that functional network communication between stromal fibroblasts and RTM coordinate biological behavior of tissues and facilitate RTM functionality.

Publications

Silvin A, Uderhardt S, Piot C, Da Mesquita S, Yang K, Geirsdottir L et al. (2022) Dual ontogeny of disease-associated microglia and disease inflammatory macrophages in aging and neurodegeneration. Immunity 55: 1448-1465.e6

Important results

- Tissues can be represented as multi-level graph networks. Hard-wired interconnections provide the architecture for local communication via gap junctions.
- Functional heterogeneity of tissue cells is a product of network organization.
- Geometrical deep learning allows to establish structure-function relationships in health/diseased tissues.

Special methods

- Intravital and tissue imaging
- 3D-reconstruction and histocytometry
- Network extraction from multiplex imaging data and analysis

New RNA-binding proteins in sporadic ALS

Dr. Krach

J88 11/2020 - 05/2023

Dr. Florian Krach, Department of Stem Cell Biology
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NEUROSCIENCES

Abstract

sALS is a motor neuron disease where pathological insoluble states of TDP-43, an alternative splicing (AS) factor are found. Dysregulated AS is detected, but it is unknown whether TDP-43 aggregation is causative for this. We develped an iPSC-derived model of sALS where AS changes in this system are not dependent on TDP-43. We propose to investigate pathological mechanisms of new AS factors in sALS using proteomics and NGS approaches and subsequent validation in sALS post mortem tissue.

Important results

- RNA missplicing is a common phenotype observed in ALS and Huntington's disease.
- Biochemical and cellular changes of RNA-binding proteins mediate these changes.
- The alternative splicing modulator Branaplam targets the HTT transcript and improves the molecular fingerprint of Huntington's disease.

Special methods

- Culture and differentiation of induced pluripotent stem cells into neuronal derivatives
- CRISPR/Cas9 genome editing
- Computational analyses in functional transcriptomics of RNA-binding proteins

Publications

Lanfer J, Kaindl J, Krumm L, Gonzalez Acera M, Neurath M, Regensburger M, Krach F*, Winner B* (2022) Efficient and Easy Conversion of Human iPSCs into Functional Induced Microglia-like Cells. Int J Mol Sci. 23:4526 * equal contribution

Krach F, Stemick J, Boerstler T, Weiss A, Lingos I, Reischl S, Meixner H, Ploetz S, Farrell M, Hehr U, Kohl Z, Winner B, Winkler J (2022) An alternative splicing modulator decreases mutant HTT and improves the molecular fingerprint in Huntington's disease patient neurons. Nature Communications 13:6797

Krach F, Wheeler EC, Regensburger M, Boerstler T, Wend H, Vu AQ et al. (2022) Aberrant NOVA1 function disrupts alternative splicing in early stages of amyotrophic lateral sclerosis. Acta neuropathologica 144: 413-435

MSOT imaging of strictures in Crohn's disease

PD Dr. Regensburger

J89 01/2021 - 03/2024

MEDICAL ENGINEERING

PD Dr. Adrian Regensburger, Department of Pediatrics and Adolescent Medicine
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Abstract

Intestinal strictures are a major disease burden in Crohn's disease. Conventional cross-sectional imaging modalities are currently not able to differentiate between inflammatory and fibrotic components of strictures. This would be essential for the initiation of the appropriate therapy. In a translational approach we want to investigate whether optoacoustic imaging can be used to quantify hemoglobin as a sign of inflammation and collagen as a sign of fibrosis in murine and human intestine.

Important results

1. A transrectal absorber guide was developed for label-free in vivo assessment of murine colitis by RSOM.
2. MSOT enables assessment of intestinal inflammation in pediatric patients with Crohn's disease and ulcerative colitis.
3. Functional OAI by orally administered Indocyanine green allows monitoring of the gastrointestinal passage.

Special methods

- Raster-scanning optoacoustic Mesoscopy (RSOM) allows raster scanning over a FOV of 12x12x3 mm (axial resolution 10µm) for the visualisation of murine vasculature.
- Multispectral optoacoustic Tomography (MSOT) allows cross-sectional (spatial resolution of <150µm) quantification of OAI parameters (e.g. hemoglobin).

Publications

Paulus LP, Buehler A, Wagner AL, Raming R, Jüngert J, Simon D et al. (2023) Contrast-Enhanced Multispectral Optoacoustic Tomography for Functional Assessment of the Gastrointestinal Tract. Advanced science (Weinheim, Baden-Wurttemberg, Germany) e2302562

Buehler A, Brown E, Paulus LP, Eckstein M, Thoma OM, Oraiopoulou ME et al. (2023) Transrectal Absorber Guide Raster-Scanning Optoacoustic Mesoscopy for Label-Free In Vivo Assessment of Colitis. Advanced science (Weinheim, Baden-Wurttemberg, Germany) 10: e2300564

Paulus LP, Wagner AL, Buehler A, Raming R, Jüngert J, Simon D et al. (2023) Multispectral optoacoustic tomography of the human intestine - temporal precision and the influence of postprandial gastrointestinal blood flow. Photoacoustics 30: 100457

The impact of Eos on bone loss

Dr. Andreev

J90 01/2022 - 06/2024

IMMUNOLOGY AND INFECTION

Dr. Darja Andreev, Department of Medicine 3
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Abstract

A healthy skeleton relies on a balance between bone-forming osteoblasts and bone-resorbing osteoclasts. A shift towards increased osteoclast activity can therefore lead to bone loss. The immune system strongly affects osteoclast biology, usually promoting osteoclast development. Interestingly, we demonstrated that eosinophils negatively regulate osteoclast formation and activity. Thus, it is of high relevance to unveil the molecular mechanisms underlying this regulatory function of eosinophils.

Publications

no project-specific publications so far

Important results

- Eos release EPX, which lowers ROS level in pre-osteoclasts, thereby inhibiting RANKL-mediated signaling.
- Eos deficient mice (lack of EPX expression) have increased osteoclast numbers, leading to more bone loss.
- Treatment with EPX reduces osteoclast numbers and decreases bone loss.
- High number of Eos is linked to increased bone mass in humans.

Special methods

- In vitro cell differentiation of murine osteoclasts from bone marrow-derived monocytes and human osteoclasts from peripheral blood mononuclear cells
- Murine models of postmenopausal osteoporosis and inflammatory arthritis
- Single-cell RNA sequencing with sorted eosinophils and RNA sequencing with in vitro generated osteoclasts

Glucocorticoid-induced macrophage reprogramming


Dr. Auger

J91 01/2022 - 06/2024

Dr. Jean-Philippe Auger, Department of Medicine 3
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IMMUNOLOGY AND INFECTION

Abstract

Glucocorticoids are amongst the most important anti-inflammatory drugs, promoting inflammatory resolution via the functional reprogramming of macrophages, a process that promotes itaconate production. Though itaconate is a metabolite participating in immune-metabolic rewiring, its role and effects, as with the underlying mechanisms involved in its production, on immunometabolism and inflammatory resolution remain unknown, yet could contribute to further optimizing glucocorticoid treatment.

Publications

no project-specific publications so far

Important results

- Glucocorticoids (GC) promote tricarboxylic acid cycle (TCA) activity and itaconate production in murine pro-inflammatory macrophages.
- The anti-inflammatory effects of GCs require TCA integrity in human pro-inflammatory macrophages.
- Absence of IRG1 abrogates the anti-inflammatory potential of GCs in models of acute lung injury.

Special methods

- Primary mouse and human macrophage cultures in vitro and ex vivo
- Evaluation of the metabolic state of primary cells and cell lines using extracellular flux analyses (Seahorse XF Analyzer)
- Murine models of acute lipopolysaccharide-induced lung injury, ovalbumin-induced allergic asthma and autoimmune K/BxN serum transfer arthritis

Lipids and Serotonin in drug instrumentalization


PD Dr. Kalinichenko

J93 01/2022 - 06/2024

PD Dr. Liubov Kalinichenko, Department of Psychiatry and Psychotherapy
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NEUROSCIENCES

Abstract

Alcoholism and depression are highly comorbid disorders. Neutral sphingomyelinase (NSM) is suggested as a missing link between emotional status and alcohol consumption due to the downstream effects on the serotoninergic system. A new line of mice with NSM gene knockout specifically in the brain serotoninergic system was created to investigate if the interaction between NSM and the brain serotoninergic system determines the comorbidity between negative emotional state and alcohol consumption.

Publications

no project-specific publications so far

Important results

Selective knockout of neutral sphingomyelinase in the serotonergic neurons is a crucial sex-specific mechanism of non-social, but not social alcohol drinking of female mice. This might be related to enhanced depression-like behavior, but is not determined by innate differences in the number of serotonergic cells in the dorsal and median raphe.

Special methods

The following methods are used in the project:

- behavioral testing of animals for evaluation of anxiety/depression-like behavior;
- n-vivo microdialysis allowing to analyze the response of brain monoaminergic systems to drug administration;
- immunohistochemistry

Neuroinflammation and synucleinopathy in IBD

NEUROSCIENCES

Dr. Süß

J94 12/2021 - 10/2024

Dr. Patrick Süß, Department of Molecular Neurology

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Abstract

Inflammatory bowel disease (IBD) predisposes for synucleinopathies like Parkinson Disease. This is putatively caused by propagation of chronic inflammation into the brain. The hypothesis of this project is that chronic inflammation in IBD activates microglia in distinct brain regions, thereby mediating neuronal pathology and aggravating synucleinopathy. This hypothesis will be tested in post mortem brain tissue of IBD patients and mice with colitis.

Publications

Masanetz RK, Baum W, Schett G, Winkler J, Süß P (2023) Cellular plasticity and myeloid inflammation in the adult brain are independent of the transcriptional modulator DREAM. Neuroscience letters 137061

Important results

- Chronic DSS-induced colitis induces innate and adaptive immune cell response at CNS border regions.
- Chronic gut inflammation is transmitted across CNS borders, leading to T cell infiltration and microglial activation in the substantia nigra.
- Mouse models of IBD show dopaminergic neuron loss in the substantia nigra.

Special methods

- Tracing and gene targeting of microglia using a novel and highly specific reporter mouse model based on the microglial marker gene Hexb
- Confocal microscopy of CNS immune cells in the parenchyma and CNS border regions
- RNA sequencing of dissected brain regions and FACS-sorted CNS myeloid cells

Role of Tip60 in the PNS

NEUROSCIENCES

Dr. Thiele

J95 01/2022 - 06/2024

Dr. Franziska Thiele, Institute of Biochemistry

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Abstract

Proper Schwann cell development and myelination are essential for a functional peripheral nervous system and regulated by networks of chromatin modifiers and transcription factors. Here I plan to study the role of the acetyltransferase Tip60 as part of the Tip60/Ep400 chromatin remodeling complex in lineage progression and myelination by characterizing its target genes and interaction with transcription factor Sox10. Results may help to better understand peripheral neuropathies.

Publications

no project-specific publications so far

Important results

The histological analyses of Tip60-deficient sciatic nerves confirmed the strong phenotype of a peripheral neuropathy with hypomyelination due to less Schwann cells that show impaired differentiation. RNA-Seq analysis of Tip60-deficient Schwann cells revealed significantly deregulated genes important for signaling and nervous system development.

Special methods

- Phenotypic characterization of a Schwann cell- specific Tip60 mouse mutant using i.a. immunohistochemical staining
- Isolation of sciatic nerves from a Schwann cell- specific Tip60 mouse mutant to perform RNA-Seq
- Co-immunoprecipitations to validate physical interactions of Tip60

Bace1/Bace2 in colorectal cancer development


Dr. Gamez Belmonte

J96 10/2021 - 09/2024

ONCOLOGY

Dr. Maria de los Reyes Gamez Belmonte, Department of Medicine 1
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Abstract

The β-secretases (Bace1 and Bace2) are proteases involved in the pathogenesis of Alzheimer's disease (AD). However, Bace1/2 can be found in tissues other than the brain, suggesting that their role goes well beyond AD. Interestingly, our preliminary data reveal that the expression of Bace1/2 is modulated in response to intestinal inflammation and during cancer development. We hypothesize that the β-secretases might have regulatory functions in the gut and the pathophysiology of colorectal cancer.

Publications

Gamez-Belmonte R, Mahapatro M, Erkert L, Gonzalez-Acera M, Naschberger E, Yu Y et al. (2022) Epithelial presenilin-1 drives colorectal tumour growth by controlling EGFR-COX2 signalling. Gut. 72(6):1155-1166

Important results

Human tumor cells devoid of BACE2 (beta-secretase 2) exhibit heightened vulnerability to cell death. Conversely, the deletion of Bace1(beta-secretase 1) in intestinal epithelial cells does not impact tumor development in a colorectal cancer mouse model. The administration of BACE inhibitors diminishes tumor size in an allograft tumor model

Special methods

- Gene deletion in tumor organoids and cell lines using CRISPR/Casp9 technology
- Gene expression analysis using RNAscope
- Animal models of colorectal cancer (AOM/DSS, Apc min)

Immune-metabolic dysfunction of NK cells


Dr. Jacobs

J97 01/2022 - 06/2024

ONCOLOGY

Dr. Benedikt Jacobs, Department of Medicine 5
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Abstract

The metabolism of reconstituting NK cells upon autologous SCT is altered in lymphoma patients who experience an early relapse upon transplantation. We intend to decipher the underlying cellular and molecular mechanism to identify factors leading to the increased relapse risk and to reveal potential opportunities to modify them. This will lay the foundation for further projects investigating NK cell reconstitution upon allogeneic SCT and CAR-transfected NK cell expansion in tumor patients.

Publications

no project-specific publications so far

Important results

The immune metabolic profile of reconstituted T and NK cells upon autologous SCT differs between refractory/ recurrent (r/r) und non-r/r lymphoma patients within the first year upon SCT. While the ICP receptor PD1 was only temporarily increased on NK cells, r/r patients demonstrated a continues up-regulation of PD1 on their T cells.

Special methods

Our group is specialized in the analysis of phenotypical, immune-metabolic and functional properties of NK cells from healthy donor and patient samples using multicolor flow cytometry techniques. Moreover, in order to optimize staining quality and reduce false antibody pipetting, we apply live- and fixed-cell fluorescent cell barcoding techniques.

Detecting disease genes in urorectal malformations

Dr. Hilger

J98 01/2023 - 06/2025

RENAL AND VASCULAR RESEARCH

Dr. Alina Hilger, Department of Pediatrics and Adolescent Medicine
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Abstract

Congenital urorectal malformations are rare birth defects with serious consequences for those affected. Still, the genetic causes of which have been little researched to date. The aim of this study is to identify candidate genes for these malformations by exome sequencing and copy number analysis, to re-sequence the identified candidate genes by next generation sequencing in a cohort of about 1100 patients and to characterise them in the zebrafish model by Morpholino oligonucleotide knockdown and CRISPR/Cas9 knockout.

Publications

no project-specific publications so far

Important results

CNV analyses identified a significantly higher occurrence of CNVs, which are significantly longer and affect in total more genes compared to healthy controls ($p<0.001$). CNVs identified comprised known genes (*HPSE2* and *LRIG2*) for LUTO, known genes for CAKUT (*FOXC1* and *CHD1L*) and novel candidate genes *MBNL1* (in 2 idependent patients).

Special methods

Identification of candidate genes:

- Exome sequencing and subsequent molecular inversion probe sequencing of candidate genes in a cohort of 580 LUTO patients
- Copy number variations (CNV) anlyses

Functional studies of the identified candidate genes:

- Gene knockdown via microinjections of Morpholino oligonucleotides or CRISPR KO in zebrafish larvae

Reactive carbonyls in metabolic diseases

Dr. Düll

J99 10/2022 - 03/2025

NEUROSCIENCES

Dr. Miriam Düll, Department of Medicine 1
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Abstract

Reactive carbonyl species (RCS) are linked to development of metabolic syndrome including neuropathic pain and steatotic liver disease (MASLD), but the possibly synergistic role of RCS in both conditions remains to be investigated. This project aims at analyzing RCS as biomarkers in patients with neuropathy and neuropathic pain, with parallel comprehensive experimental neurophysiological examinations of patients and assessment of functional effects of RCS on sensory neurons in vitro.

Publications

Becker AK, Babes A, Düll MM, Khalil M, Kender Z, Gröner J, Namer B, Reeh PW, Sauer SK (2023) Spontaneous activity of specific C-nociceptor subtypes from diabetic patients and mice: Involvement of reactive dicarbonyl compounds and (sensitized) transient receptor potential channel A1. J Peripher Nerv Syst. 28(2):202-225

Important results

- High prevalence of neuropathic changes in small nerve fiber function in patients with metabolic syndrome (with no previously diagnosed peripheral neuropathy)
- In skin preparations from western-type diet-induced obese mice, increased basal and stimulated release of HMGB1 (linked to neuropathic pain) in comparison to healthy control mice

Special methods

- Calcium activity measurements
- Psychophysics (Quantitative Sensory Testing, electrical stimulation)
- Microneurography of C-fibers

Mucosal vaccination against lung metastases

Dr. Lapuente

J100 01/2023 - 06/2025

ONCOLOGY

Dr. Dennis Lapuente, Institute of Clinical and Molecular Virology
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Abstract

The presence of tumor-resident memory T cells (TRM) positively correlates with prognosis in many cancers. In our preliminary data, lung TRM induced by a mucosal vaccine efficiently protected against lung metastasis in a preclinical breast cancer model. We want to investigate the vaccine efficacy against lung metastases at different disease stages and the contribution of TRM and their unique features to this efficacy. The efficacy will also be assessed in combination with radio- and chemotherapy.

Publications

no project-specific publications so far

Important results

Mucosal vaccination results in antigen-specific lung TRM.
In a prophylactic setting, vaccine-induced TRM contribute to an improved survival in a breast cancer lung metastasis model.
Therapeutic vaccination promotes infiltration of TRM into metastases and leads, in combination with stereotactic radiotherapy, to an improved survival.

Special methods

- Mucosal vaccination with specific adjuvant strategies
- In-depth analyses of systemic and tissue-resident T cell responses
- Murine breast cancer metastasis models
- Radio- and chemotherapy

AI for GI Histopathology

Dr. Dr. Matek

J101 01/2023 - 06/2025

ONCOLOGY

Dr. Dr. Christian Matek, Institute of Pathology
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Abstract

The proposed projects aims at using methods from AI-based image analysis to evaluate histopathologic samples from the field of gastrointestinal pathology. Specifically, samples from patients with inflammatory bowel diseases and malignancies of the colorectum will be evaluated. It is the aim of the project to develop algorithms that quantify and detect specific morphologic properties of these samples and integrate them with other data modalities.

Important results

We contributed to several multicentric AI-based studies in the field of Computational Pathology, notably for MSI-prediction from H&E Slides using transformer models.
Additionally, we developed and evaluated digital biomarkers for histological sections from chronic inflammatory diseases using both Deep Learning and classical feature extraction.

Special methods

- AI-based data analysis methods (Machine Learning, Deep Learning)
- Complex image data analysis
- Histopathology and correlation with other diagnostic modalities

Publications

Firmbach D, Benz M, Kuritcyn P, Bruns V, Lang-Schwarz C, Stuebs FA, Merkel S, Leikauf LS, Braunschweig AL, Oldenburger A, Gloßner L, Abele N, Eck C, Matek C, Hartmann A, Geppert CI (2023) Tumor-Stroma Ratio in Colorectal Cancer-Comparison between Human Estimation and Automated Assessment. Cancers. 15(10):2675

Wagner SJ, Reisenbüchler D, West NP, Niehues JM, Zhu J, Foersch S, Veldhuizen GP, Quirke P, Grabsch HI, van den Brandt PA, Hutchins GGA, Richman SD, Yuan T, Langer R, Jenniskens JCA, Offermans K, Mueller W, Gray R, Gruber SB, Greenson JK, Rennert G, Bonner JD, Schmolze D, Jonnagaddala J, Hawkins NJ, Ward RL, Morton D, Seymour M, Magill L, Nowak M, Hay J, Koelzer VH, Church DN, null , Matek C, Geppert C, Peng C, Zhi C, Ouyang X, James JA, Loughrey MB, Salto-Tellez M, Brenner H, Hoffmeister M, Truhn D, Schnabel JA, Boxberg M, Peng T, Kather JN (2023) Transformer-based biomarker prediction from colorectal cancer histology: A large-scale multicentric study. Cancer cell 41: 1650-1661.e4

cDC1s in abscopal effects and HHP vaccination

ONCOLOGY

Dr. Rückert

J102 12/2022 - 05/2025

Dr. Michael Rückert, Department of Radiation Oncology
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Abstract

Abscopal effects are rare events of local radiotherapy (RT) inducing systemic anti-tumor immune responses leading to the reduction of tumor masses outside of the irradiation field. We hypothesize that the addition of adjuvants to high hydrostatic pressure generated whole tumor cell vaccines in combination with RT and immune checkpoint inhibition induce abscopal effects in an orthotopic breast cancer model. Further, we hypothesize that cDC1s play a central role in this immune response.

Publications

no project-specific publications so far

Important results

The addition of adjuvants to the HHP vaccine enhances the local and abscopal tumor control in combination with radiotherapy and immune checkpoint inhibition.
Genes associated with a strong T cell response are increased in the abscopal tumors of the group treated with additional adjuvants.

Special methods

- In vitro differentiation of cDC1s from bone marrow to investigate their radiosensitivity
- Studying the impact of adjuvants for the tumor cell vaccine on systemic anti-tumor immune responses using the established tumor model
- Using bulk RNA sequencing to study the modulation of tumor-infiltrating lymphocytes

Predicting clinical longevity of dental materials

MEDICAL ENGINEERING

Dr. Maier

J103 12/2022 - 06/2025

Dr. Eva Maier, Department of Operative Dentistry and Periodontology
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Abstract

With the rapid translation of emerging material processing technologies for tooth restoration, there is an urgent need for reliable laboratory testing systems that accurately predict the clinical longevity of new materials. The current proposal aims to 1) develop a novel in-vitro wear testing model that demonstrates accurate preclinical predictability of longitudinal clinical trial data and 2) explore the suitability of modern 3D-printing processes for dental material application.

Publications

Maier E, Grottschreiber C, Knepper I, Opdam N, Petschelt A, Loomans B et al. (2022) Evaluation of wear behavior of dental restorative materials against zirconia in vitro. Dental materials : official publication of the Academy of Dental Materials 38: 778-788

Taschner M, Stirnweiss A, Frankenberger R, Kramer N, Galler KM, Maier E (2022) Fourteen years clinical evaluation of leucite-reinforced ceramic inlays luted using two different adhesion strategies. Journal of dentistry 123: 104210

Important results

Minimally invasive CAD/CAM resin based composite restorations showed an acceptable clinical survival up to 5.5.years for rehabilitation of severe tooth wear patients.
The novel Rub&Roll wear machine set up enabled the evaluation of wear behaviour of RBCs, which differed significantly to the one of human molars in an acidic environment.

Special methods

- Translational in-vitro wear testing of dental direct and indirect resin-based composite materials
- Microstructural analysis of in-vitro and in-vivo worn surfaces (digital microscopy, scanning electron microscopy)
- Evaluation of potential clinical applications of 3D-printed dental materials (FTIR spectroscopy, fracture toughness testing)

Stat5 in chronic colitis

Dr. Müller

J104 11/2023 - 04/2026

Dr. Tanja Müller, Department of Medicine 1
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IMMUNOLOGY AND INFECTION

recently started

Abstract

T cells play a key role in IBD, but the impact of Stat5 in CD4+ T cells for chronic colitis is unclear so far. Based on preliminary data demonstrating spontaneous chronic colitis in conditional Stat5 KO mice and decreased Stat5 expression in IBD, I hypothesize that Stat5 in CD4+ T cells counteracts colitis. Thus, in this project, I will explore the mechanisms and effects of CD4-specific Stat5 signalling for experimental colitis and IBD, aiming to identify novel approaches for future therapy.

Special methods

- Single cell RNA-Sequencing of LPMCs from Cre+ and Cre- mice
- Flow cytometry of stimulated CD4+ T cells of patients with IBD or healthy controls
- Engineering E. coli nissle to express soluble IL-3

GLUT1- metabolism and antibody response

Dr. Pracht

J105 10/2023 - 03/2026

Dr. Katharina Pracht, Department of Molecular Immunology
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IMMUNOLOGY AND INFECTION

recently started

Abstract

The secretion of correctly glycosylated protective antibodies by long-lived plasma cells is essential for our immune protection. To survive and produce antibodies, long-lived plasma cells require an optimized metabolism. The aim of this study is to determine whether the glucose transporter GLUT1 plays a role in the metabolism of long-lived plasma cells and the functionality of their antibodies. Therefore, we will study a GLUT1-deficient mouse model and patients with GLUT1-deficiency syndrome.

Special methods

- Mouse model to study glucose metabolism in long-lived plasma cells
- *In vitro* model to generate and analyze mature plasma cells
- LC-MS for the study of antibody glycosylation

Skin-derived immune cells in psoriatic arthritis


Dr. Raimondo

J106 09/2023 - 02/2026

Dr. Maria Gabriella Raimondo, Department of Medicine 3
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IMMUNOLOGY AND INFECTION

recently started

Abstract

To date, it is still obscure why in some patients with psoriasis the autoimmune process is restrained to the skin, whereas in other it extends to the joints. We will adopt models resembling psoriasis and psoriatic arthritis, with the aim of studying the joint involvement secondary to skin inflammation. The comprehension and characterization of the underlying mechanisms involved in the "skin-joint axis" is pivotal for a better understanding of the link between physical barriers and autoimmunity.

Special methods

1. Bioinformatic analysis, including RNA-velocity, pseudotime, cell interaction
2. Mouse model, through overexpression of interleukine-23
3. Flow cytometry for subpopulations of monocytes and fibroblasts
4. Antibody testing with immunofluorescence for imaging mass cytometry and metal labelling

PU.1 in osteoblasts and osteoproliferation


Dr. Rauber

J107 01/2024 - 08/2026

Dr. Simon Rauber, Department of Medicine 3
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IMMUNOLOGY AND INFECTION

recently started

Abstract

PU.1 controls the transcriptional network of matrix production in fibrotic fibroblasts. We have now found that PU.1 is also expressed in matrix-producing osteoblasts. In this proposal, we aim to study the PU.1 network in biopsies from patients with osteoproliferative arthritis by imaging mass cytometry, to dissect PU.1-driven transcription in human osteoblastogenic cultures by ATTAC/CHIP/RNA-seq, and to use a novel osteoblast-targeting PU.1 inhibitor in experimental osteoproliferative arthritis.

Special methods

Human biopsies of osteoproliferative lesions are analysed by imaging mass cytometry for osteoblasts and PU.1. The regulatory network of PU.1 is analysed by ChIP-seq in cultured osteoblasts. Zymosan-induced osteoproliferative arthritis in conditional Col1a2-creER x Spi1-flox knock-out mice is used to validate PU.1 in osteoproliferation.

Functional role of CFTR in immune cells

Dr. Schnell

J108 01/2024 - 06/2026

IMMUNOLOGY AND INFECTION

Dr. Alexander Schnell, Department of Paediatrics and Adolescent Medicine
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recently started

Abstract

This project aims at identifying the expression of the CFTR complex and functionally characterising its role in in peripheral blood mononuclear cells in the context of Cystic Fibrosis (CF). Moreover, the effects of a CFTR-modulating therapy with Elexacaftor - Tezacaftor - Ivacaftor (ETI) on immune cell function and regulation will be examined in a CFTR knock-out cell line and a CF pig model as well as primary patient-derived cells.

Special methods

- Flow cytometry
- 3D live cell migration microscopy
- Western Blot

Extracellular vesicles in Parkinson's disease

Dr. Boros

J109 01/2024 - 06/2026

NEUROSCIENCES

Dr. Fanni Annamaria Boros, Department of Molecular Neurology
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recently started

Abstract

The aim of this project is to facilitate the understanding of the role of extracellular vesicles (EVs) in the development and progression of Parkinson's disease (PD). EVs extracted from blood of PD patients and controls will be fractionated according to cellular origin and cargo profiling will be performed focusing on pathogenic forms of aSyn and regulatory RNAs. The results will offer deeper insights in PD-related signatures, and permit exploring the origin and transfer of pathogenic molecules.

Special methods

Among the main techniques are polymer precipitation- and membrane affinity-based EV enrichment from blood samples, and immunoprecipitation of the vesicles with antibodies against surface markers characteristic of the cell type of origin. For the analysis of EV-derived pathological aSyn conformers, aSyn seed amplification assay is implemented.

Funded ELAN projects in 2023:

No.	Name	Institution		Project title
P063	Prof. Dr. Thomas Kinfe	Department of Neurosurgery	N	Assay of neuroinflammation in chronic pain
P066	Dr. Claudia von Zimmermann	Department of Psychiatry and Psychotherapy	I	Immune Regulation in the treatment of Depression.
P076	PD Dr. Franz Marxreiter	Department of Molecular Neurology	N	MRI based diagnosis of Multiple System Atrophy
P078	Dr. Eva Schäflein / PD Dr. Cosima Rhein	Psychosomatic Medicine a. Psychotherapy	S	Self-perception in trauma-related disorders
P087	Dr. Lisa Klotz	Institute of Biochemistry	N	Protective function of mGluR7 in the cochlea
P089	Dr. Harriet Morf	Department of Medicine 3	I	Effect of Yoga on Spine Flexibility in SpA
P090	Dr. Katharina Gerlach	Department of Medicine 1	I	Analysis of NFATc3 in intestinal inflammation
P092	Dr. Tanja Müller	Department of Medicine 1	O	Role of GPR15L in colorectal cancer
P094	Dr. Wibke Müller-Seubert	Department of Plastic and Hand Surgery	S	Influence of stem cells on irradiated flaps
P095	Dr. Frederik Stübs	Department of Obstetrics and Gynecology	O	PD-L1 expression in vulvar cancer
P097	PD Dr. Ulrike Steffen	Department of Medicine 3	I	Anti-osteoporotic effects of metoprolol
P099	PD Dr. Krystelle Nganou	Institute of Clinical and Molecular Virology	I	Interplay between TCR and microbiome
P101	Prof. Dr. Heiko Reutter	Paediatrics and Adolescent Medicine	S	Exome and zebrafish analyses on VATER/VACTERL
P102	PD Dr. Hanna Hübner	Department of Obstetrics and Gynecology	O	ADCCresponse
P103	Dr. Robert Becker	Department of Nephropathology	R	Phosphorylation in nuclear envelope MTOC formation
P104	Dr. Christina Bergmann	Department of Medicine 3	I	Interactions Hedgehog-/AP1 signaling in fibrosis
P105	Dr. Katrin Peckert-Maier	Department of Immune Modulation	I	Function of CD83 for human macrophages
P106	Dr. Katharina Pracht	Department of Molecular Immunology	I	Aryl hydrocarbon Receptor (AhR) and vaccinations
P109	Dr. Valeska Stonawski	Child and Adolescent Mental Health	S	Body exposure in adolescents with AN
P110	Dr. Lisa Linck-Paulus	Institute of Biochemistry	O	The role of MAGOH in malignant melanoma
P111	Dr. Eva Liebing	Department of Medicine 1	I	Ferroptosis during intestinal inflammation
P112	Dr. Eva-Maria Weiss	Department of Psychiatry and Psychotherapy	N	Serotonergic psychedelics and presynaptic function
P113	Dr. Anna Dietl	Department of Obstetrics and Gynecology	S	3D-Imaging of ovarian follicles in scaffold
P114	Dr. Irmgard Toni	Paediatrics and Adolescent Medicine	S	Data set of drug-related paed. hospitalisations
P116	Dr. Michael Frech	Department of Medicine 3	I	The role of Btn2a2 in T cell maturation
P117	PD Dr. Iryna Prots	Department of Operative Dentistry and Periodontology (Department Stem Cell Biology until 12/2022)	N	T cell migration in neurodegeneration
P118	Prof. Dr. Ralf Enz	Institute of Biochemistry	N	GPR179, LRRTM4, GABAcR: new players in night vison
P119	Dr. Iris Stolzer	Department of Medicine 1	O	Tryptophan metabolites in intestinal inflammation
P120	PD Dr. Jay Patankar	Department of Medicine 1	I	Enteric glial cell-immune cell crosstalk
P121	Dr. Aparna Mahajan	Department of Medicine 3	I	Resolution of ocular surface inflammation
P122	Dr. Theresa Promny	Department of Plastic and Hand Surgery	O	Establishment of a novel breast tumor model
P123	Dr. Lara Berger	Department of Prosthodontics	M	Current chairside materials in dental practice
P124	Dr. Tania Gabriela Rizo Garza	Department of Stem Cell Biology	N	Modulation of SOCE using Davunetide

I - Infection and Immunology, N - Neurosciences, O - Oncology, R - Renal and Vascular Research, M - Medical Engineering, S - Others

No.	Name	Institution		Project title
P125	Dr. Jannis Hanspach	Institute of Radiology	M	Deep learning QSM in the presence of fat
P126	Dr. Kerstin Hübner	Institute of Pathology	O	Mesentery model for peritoneal metastasis
P127	Dr. Annika Weigelt	Department of Paediatric Cardiology	R	Myocarditis in relation to sports in children
P128*	Prof. Dr. Wei Xiang	Department of Molecular Neurology	N	FICD-mediated AMPylation in Parkinson's disease
P129	Dr. Rafael Schmid	Department of Plastic and Hand Surgery	O	Biofabricated breast cancer in a perfusion reactor
P130	Dr. Christine Schauer	Department of Medicine 3	I	Nuclear envelope breakdown during NETosis
P132	Dr. Carina Scherbel	Department of Medicine 3	I	Osteoclast metabolism
P133*	Dr. Harald Schuhwerk	KMFZ - Chair of Experimental Medicine I (Molecular Pathogenesis Research)	O	Cancer cells and CAFs as joint therapeutic target
P134	Dr. Nora Vogg	Institute of Experimental and Clinical Pharmacology and Toxicology	O	Untargeted metabolomics in adrenal tumors
P135	Dr. Ines Willershausen	Department of Orthodontics and Orofacial Orthopedics	S	Examination of craniofacial sutures
P136	Dr. Stephanie Sembill	Department of Paediatrics and Adolescent Medicine	O	Exploring growth retardation under TKI therapy
P137	Dr. Jule Taubmann	Department of Medicine 3	I	Spatial interactions of T-cell clones in RA
P138	Dr. Arwin Groenewoud	Institute of Pathology	O	Lineage tracing of metastases
P139	Dr. Isabell Wank	Chair of Pharmacology and Toxicology	N	Influence of 3-indolepropionic acid on arthritis
P140*	Dr. Matthias Weider	Department of Orthodontics and Orofacial Orthopedics	N	iPSC-derived neural crest cells & palate formation
P141	Dr. Daniel Radtke	Department of Infection Biology	I	Basophils in skin-derived sensitization
P142	Dr. Kristina Koop	Department of Medicine 1	I	IL36 in intestinal inflammation and fibrosis
P143*	Dr. Marios Marcou	Department of Urology	S	The role of miRNAs in Lichen sclerosus
P144	Dr. Kerstin Dürholz	Department of Medicine 3	I	Histamin induces resolution of arthritis
P145	Dr. Leah Trumet	Department of Operative Dentistry and Periodontology	I	Th17/Treg immune response in periodontitis
P146	Dr. Annkathrin Hornung-Eichler	Department of Dermatology	O	Melanoma organoids as platform for testing
P147	Dr. Alexandra Birzer	Institute of Clinical and Molecular Virology	I	Intestinal barrier models in HTLV-1 transmission
P148	Dr. Tilman Jobst-Schwan	Department of Medicine 4	R	Wnt/beta-catenin signaling in kidney disease

I - Infection and Immunology, N - Neurosciences, O - Oncology, R - Renal and Vascular Research, M - Medical Engineering, S - Others

* Project leaders beyond age limit

Assay of neuroinflammation in chronic pain

P063 09/2020 - 07/2024

Prof. Dr. Thomas Kinfe, Department of Neurosurgery
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Abstract
Clinical and animal studies implicate neuroinflammatory features (interleukines, chemokines, adipokines, oxytocin, alarmins) as part of the pathophysiology. BurstDR-SCS and DRG-SCS stimulation present a paradigm shift in current neurostimulation to address the treatment of CPSP-associated pain. Such molecular analysis may underpin the emerging role of CPSP-related molecular patterns as potential biomarkers to reliably reproduce spinal stimulation effects.

Immune Regulation in the treatment of Depression

P066 09/2020 - 09/2024

Dr. Claudia von Zimmermann, Department of Psychiatry and Psychotherapy
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Abstract
One third of the depressed patients do not respond adequately to conventional treatment. This seems to be associated with increased production of proinflammatory cytokines such as TNF-a and IL-1, as well as dysregulation of cortisol levels. This project aims to investigate the impact of the new psychotherapeutic method TaKeTiNa on serum lipids, cortisol Levels, and the production of proinflammatory cytokines.

MRI based diagnosis of Multiple System Atrophy

P076 06/2021 - 11/2023

PD Dr. Franz Marxreiter, Department of Molecular Neurology
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Abstract
Diagnosis of the rare neurodegenerative disease multisystem atrophy (MSA) is hampered by a lack of biomarkers. We could show that in an MSA mouse model, a myelin deficit can be visualized by quant. susceptibility mapping (QSM)on MRI. Our preliminary clinical data show similar results. The aim is now to comprehensively assess QSM imaging as a biomarker for the differential diagnosis of neurodegenerative diseases.

Self-perception in trauma-related disorders

P078 09/2021 - 02/2024

Dr. Eva Schäflein (until 10/2023), PD Dr. Cosima Rhein (from 11/2023), Department of Psychosomatic Medicine a. Psychotherapy
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Abstract
Severe dissociative disorders are characterized by distinct self-perception-related stress accompanied by autonomic blunting. The aim of the current study is to investigate self-reported, psychophysiological and biological stress reactions upon an experimental self-perception paradigm in patients suffering from diverse post-traumatic conditions with different levels of dissociation, to elucidate potential associations between dissociation intensity and the aversiveness of self-perception.

I	Infection and Immunology
N	Neurosciences
O	Oncology
R	Renal and Vascular Research
M	Medical Engineering
S	Others

Protective function of mGluR7 in the cochlea

P087 09/2021 - 02/2023

Dr. Lisa Klotz, Institute of Biochemistry
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Abstract
MGluR7 has been correlated with hearing deficits and low glutamate affinity. Dimeric mGluRs can build inhibitory feedback loops thereby protecting the pre-synapse from toxic stimuli. Besides pre-synaptic localization of mGluR7 also mGluR4 & 8 were described pre-synaptically at IHC ribbon synapses. Heterodimeric mGluRs have unique properties, therefore it is essential to analyse if mGluR7 is present as homo- or heterodimer to analyse the function using electrophysiological techniques.

Effect of Yoga on Spine Flexibility in SpA

P089 10/2022 - 09/2023

Dr. Harriet Morf, Department of Medicine 3
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Abstract
Spondylarthritis can lead to stiffness of the spine and consequently to impaired function. Therefore, it is important to promote daily exercises in Spondylarthritis (SpA) patients. The objective of this study is to assess the feasibility of Yoga to affect spine mobility and disease activity in SpA patients. By measuring the mobility and improving spine flexibility, patients feel better with their disease and learn how important daily exercising is.

Analysis of NFATc3 in intestinal inflammation

P090 02/2022 - 07/2023

Dr. Katharina Gerlach, Department of Medicine 1
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Abstract
The transcription factor NFATc3 is important for regulating T cells. Patients with inflammatory bowel disease had high numbers of NFATc3+ cells in the lamina propria indicating an involvement of NFATc3 in mucosal inflammation. To investigate NFATc3 and colitis we will use specific knockout mice in experimental colitis models and analyse its molecular function. The results should clarify the role of NFATc3 in intestinal inflammation and provide a basis for NFATc3 as a new therapeutic concept.

Role of GPR15L in colorectal cancer

P092 10/2021 - 03/2023

Dr. Tanja Müller, Department of Medicine 1
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Abstract
In this project, the role of GPR15L in the formation and development of colorectal carcinoma will be investigated. For GPR15L anti-proliferative effects on tumor cell growth have already been shown *in vitro* and our aim is to also confirm these effects in a mouse model *in vivo*. In addition, we want to investigate the influence of GPR15L on the intestinal microbiome in relation to the development and progression of colorectal carcinoma *in vitro* and *in vivo*.

I	Infection and Immunology
N	Neurosciences
O	Oncology
R	Renal and Vascular Research
M	Medical Engineering
S	Others

Influence of stem cells on irradiated flaps

P094 05/2022 - 05/2023

Dr. Wibke Müller-Seubert, Department of Plastic and Hand Surgery
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Abstract
Defect reconstruction in plastic surgery using tissue transfer, so called flaps, is a standard procedure, for example after Tumor resection. The proposed study evaluates the effect of topically stem cell or growth factor application on the size of the necrotic area of irradiated and post-ischemic random pattern flaps in an in-vivo model.

PD-L1 expression in vulvar cancer

P095 04/2022 - 10/2023

Dr. Frederik Stübs, Department of Obstetrics and Gynecology
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Abstract
Vulvar cancer is a rare gynecologic tumor with increasing incidence. New therapeutic strategies include the use of checkpointinhibitors, but clinical data is limited and contradictory. In this project we aim to assess the expression of PD-L1 in vulvar cancer. The expression will be assessed independently in primary, recurrent and lymph node metastasis. The expression will be compared to the clinical status such as TNM, L-,V-,Pn-infiltration.

Anti-osteoporotic effects of metoprolol

P097 04/2022 - 03/2023

PD Dr. Ulrike Steffen, Department of Medicine 3
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Abstract
Aberrant activation of bone resorbing osteoclasts causes osteoporosis. We found that the β-blocker metoprolol inhibits osteoclast development and resorption activity and increases bone mass in mice. In this project, we aim to investigate the mechanisms how metoprolol inhibits osteoclasts, focusing on its dependency on β-adrenergic receptor signaling and its effects on osteoclast fusion, motility and resorption. The long-term goal is to find new treatment strategies against osteoporosis.

Interplay between TCR and microbiome

P099 04/2022 - 01/2024

PD Dr. Krystelle Nganou, Institute of Clinical and Molecular Virology
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Abstract
Changes in the T cell receptor (TCR) repertoire can directly impact on the breath and magnitude of antigen-specific T cell responses. During treated HIV infection, dysfunctional T cell responses associate with inflammation that is at least in part driven by microbial translocation. Therefore, we aim to investigate the relationship between the translocated microbiome, the TCR repertoire and T cell functionality, with emphasis on vaccine-induced antigen-specific responses.

Exome and zebrafish analyses on VATER/VACTERL

P101 01/2022 - 04/2023

Prof. Dr. Heiko Reutter, Department of Paediatrics and Adolescent Medicine
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Abstract
The VATER/VACTERL association describes the co-occurrence of malformations of the vertebral bodies, anorectum, heart, esophagus, kidneys, and limbs. The proposed study aims to identify new candidate genes and characterize the candidate gene FZD7 by morpholino knockdown and expression analysis in developing zebrafish larvae. In doing so, we hope to better understand the molecular mechanisms leading to this multisystem malformation.

ADCCresponse

P102 08/2022 - 08/2023

PD Dr. Hanna Hübner, Department of Obstetrics and Gynaecology
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Abstract
The standard of care treatment for HER2-positive breast cancer patients includes an anti-HER2-targeted antibody treatment. The antibody dependent cellular cytotoxicity (ADCC) is a key player associated with treatment response. Thus, the aim of the presented project is to conduct an ADCC biomarker assay in order to evaluate the association of ADCC capacity of peripheral blood mononuclear cells (PBMCs) with therapy response after neoadjuvant treatment with the trastuzumab-biosimilar ontruzant.

Phosphorylation in nuclear envelope MTOC formation

P103 04/2022 - 03/2023

Dr. Robert Becker, Department of Nephropathology
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Abstract
Phosphorylation is a well-known regulatory mechanism of MTOC activity at the centrosome. In contrast, it is unknown, whether non-centrosomal MTOCs are also regulated by phosphorylation. We aim at determining how phosphorylation is utilized to regulate MTOC formation at the nuclear envelope. For this, we will examine a potential role of candidate enzymes derived from preliminary data as well as utilize screening approaches to identify novel regulators of nuclear envelope MTOC formation.

Interactions Hedgehog-/AP1 signaling in fibrosis

P104 08/2022 - 07/2023

Dr. Christina Bergmann, Department of Medicine 3
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Abstract
Systemic Sclerosis (SSc) is a fibrosing disorder with a high lethality. We demonstrate that Hedgehog-Signaling and AP1-signals mutually amplify in fibrosing disorders. We plan to analyze the effects of the combined inhibition of both signaling pathways on the evolvement of fibrosis and the mechanisms of mutual amplification. We will investigate the association of combined upregulation of both pathways with clinical patient data and investigate potential prognostic implications.

I	Infection and Immunology
N	Neurosciences
O	Oncology
R	Renal and Vascular Research
M	Medical Engineering
S	Others

Function of CD83 for human macrophages

P105 07/2022 - 06/2023

Dr. Katrin Peckert-Maier, Department of Immune Modulation
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Abstract
Regulatory macrophages are crucial to induce resolution of inflammation. Excessive ma¬cro-phage activation is associated with transplant rejection or chronic inflammatory di¬seases. Our preliminary murine data revealed that sCD83 induces regulatory macrophages, whilst mCD83 deletion drives macrophages towards a pro-inflammatory phenotype. This project aims to translate these interesting findings into the human macrophage system.

Aryl hydrocarbon Receptor (AhR) and vaccinations

P106 09/2022 - 08/2023

Dr. Katharina Pracht, Department of Molecular Immunology
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Abstract
In this project we want to investigate the role of the transcription factor AhR in the es-tablishment of an antigen-specific humoral immune response. Therefore, B cell-specific AhR-deficient mice and control animals will be 1. analyzed after an immunisation with a T-dependent antigen while fed a diet containing AhR ligands and 2. their B cells will be activated *in vitro* and analyzed in detail. In addition, AhR target genes in B cells will be de-termined by RNASeq.

Body exposure in adolescents with AN

P109 09/2022 - 12/2023

Dr. Valeska Stonawski, Department of Child and Adolescent Mental Health
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Abstract
A computer based body exposure to reduce body dissatisfaction in adolescents suffering from Anorexia nervosa (AN) will be evaluated. Within an RCT, intervention effects will be compared to treatment-as-usual; furthermore, AN-specific characteristics should be identi-fied in a comparison with a highly body-dissatisfied control group. In a multi-level approach, potentially underlying mechanisms in terms of the subjective and objective stress reactivity as well as gaze patterns will be analyzed.

The role of MAGOH in malignant melanoma

P110 03/2024 - 12/2024

Dr. Lisa Linck-Paulus, Institute of Biochemistry
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Abstract
MAGOH is part of the exon junction complex that binds to mRNA and regulates alternative splicing or mRNA degradation via "nonsense mediated decay". This project investigates the role of MAGOH in malignant melanoma. Preliminary data showed that a loss of MAGOH leads to cell death in melanoma cells, which will be further investigated in different mela-noma cell lines, as well as healthy cells. Furthermore, the molecular mechanisms leading to the reduced viability will be analyzed.

Ferroptosis during intestinal inflammation

P111 11/2022 - 10/2023

Dr. Eva Liebing, Department of Medicine 1
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Abstract
A strict cell death regulation is indispensable for the maintenance of intestinal homeostasis, since increased cell death is able to trigger intestinal inflammation. Our newly planned experiments can help to discover the impact of the gluthathione peroxidase GPX4 on the regulation of ferroptotic cell death, as well as the induction and maintenance of intestinal inflammation. GPX4 might display a potential target for new therapeutic strategies.

Serotonergic psychedelics and presynaptic function

P112 09/2022 - 09/2023

Dr. Eva-Maria Weiss, Department of Psychiatry and Psychotherapy
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Abstract
Serotonergic psychedelics represent a potential breakthrough in therapy of several neuropsychiatric disorders. Here we focus on the molecular mechanisms underlying their action on neuronal level, specifically aiming to elucidate their effects on presynaptic function that governs neurotransmitter release, and how these relate to neuronal activity and neuroplasticity. Our results will provide important mechanistic insight into the action of these putative rapid-acting antidepressants.

3D-Imaging of ovarian follicles in scaffold

P113 02/2023 - 10/2024

Dr. Anna Dietl, Department of Obstetrics and Gynecology
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Abstract
Increasing survival of young cancer patients require fertility-preservation like ovarian-cryopreservation pretherapeutically with retransplantation post-therapy. However, this is not appropriate for all patients due to the risk of relapse. A promising alternative is the artificial ovary: follicles are separated from malignant cells. In the research proposed follicle survival, maturation and growth in 3D-scaffold will be observed by live cell imaging with confocal spinning disc microscopy.

Data set of drug-related paed. hospitalisations

P114 04/2023 - 09/2024

Dr. Irmgard Toni, Department of Paediatrics and Adolescent Medicine
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Abstract
Drug therapy in children and adolescents is often associated with uncertainties. Causes and characteristics of adverse drug reactions and medication errors are poorly understood. The main objective of the project is to establish and descriptively describe a data set with medication data and systematically collected drug-related hospital admissions of children in Germany.

I	Infection and Immunology
N	Neurosciences
O	Oncology
R	Renal and Vascular Research
M	Medical Engineering
S	Others

The role of Btn2a2 in T cell maturation

P116 10/2022 - 09/2023

Dr. Michael Frech, Department of Medicine 3
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Abstract
Btn2a2 inhibits T cell activation in vitro and Btn2a2-/- mice show exacerbated experimental autoimmune encephalomyelitis, suggesting a T cell inhibitory role. Strikingly, Btn2a2-/- mice exhibit elevated autoantibody titers, suggesting a defect in tolerance mechanisms. We hypothesize that Btn2a2 affects thymocytes during thymocyte selection, resulting in an altered autoaggressive T cell repertoire.

T cell migration in neurodegeneration

P117 01/2023 - 04/2024

PD Dr. Iryna Prots, Op. Dentistry and Periodontology (Stem Cell Biology until 12/2022)
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Abstract
T cells migrate to and impact the central nervous system (CNS) during disease. We show that diseased CNS allows stronger T cell migration by yet unknown mechanisms. Here, T cell-attracting mechanisms of neurodegenerative CNS tissue and T cell-driven neurodegenerative pathomechanisms will be investigated in a human stem cell-based 3D CNS model using RNA sequencing and biochemical methods. Data will provide mechanistic insights how T cell migration is facilitated by CNS during neurodegeneration.

GPR179, LRRTM4, GABAcR: new players in night vison

P118 02/2023 - 07/2024

Prof. Dr. Ralf Enz, Institute of Biochemistry
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Abstract
We will analyse two new players of the rod pathway in the mammalian retina that are associated with night blindness - GPR179 and LRRTM4. GPR179 and LRRTM4 bind directly to GABAc receptors (GABAcR). Rod bipolar cells express high levels of GABAcR and deletion of LRRTM4 perturbed clustering of GABAcR at their axon terminals. We will analyse these protein complexes in the retina, map binding sites and elucidate functions of the interactions by cell biology, calcium imaging and electrophysiology.

Tryptophan metabolites in intestinal inflammation

P119 08/2023 - 07/2024

Dr. Iris Stolzer, Department of Medicine 1
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Abstract
Extraintestinal manifestations (EIM) are frequent in IBD patients. Our initial data revealed an osteoporosis-& PSC-like phenotype in a murine IBD model. Intestinal inflammation was linked to altered tryptophan metabolism and AHR-signalling, which are assumed to be mediators of EIM. While previous data demonstrate an impact on this pathway, mechanistic knowledge is limited. Within this project we will take advantage of 3D organ cultures to better understand the tryptophan-AHR axis in IBD and EIM.

Enteric glial cell-immune cell crosstalk

P120 07/2023 - 06/2024

PD Dr. Jay Patankar, Department of Medicine 1
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Abstract
The role of the enteric glial cells (EGCs) in regulating mucosal immune homeostasis is largely unknown. We propose that EGC activation is tunable by cytokines and activated EGCs can shape gut immunity. Isolation, ex vivo activation, and submucosal transplantation of EGC will reveal their immunomodulatory capacity. Insights gained will reveal new avenues to curb chronic inflammation in disorders such as IBD.

Resolution of ocular surface inflammation

P121 07/2023 - 06/2024

Dr. Aparna Mahajan, Department of Medicine 3
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Abstract
Eye rheum is a physiological ocular surface discharge contains aggregated neutrophil extracellular traps (aggNETs), indicating that neutrophils are involved in ocular surface homeostasis. In the murine model of allergic eye disease, aggNETs occlude meibomian glands causing meibomian gland dysfunction after ocular surface inflammation. Here we plan to investigate therapeutic potential of eye drops containing DNase-1 or NOX2-inhibitor to alleviate aggNETs driven ocular surface inflammation.

Establishment of a novel breast tumor model

P122 05/2023 - 04/2024

Dr. Theresa Promny, Department of Plastic and Hand Surgery
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Abstract
The aim of the proposed study is to establish a novel and reliable in vivo tumor model by engineering a breast tumor in the arteriovenous rat model. This model could provide the possibility to investigate tumor development, angiogenesis and tumor-stroma interactions in a controlled manner. Selecting appropriate scaffolds for the tumor cells is essential for the success of the model. Therefore, the study includes 3 parts to provide a structured detection of suitable matrices in vitro and in vivo.

Current chairside materials in dental practice

P123 07/2023 - 06/2024

Dr. Lara Berger, Department of Prosthodontics
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Abstract
In this research project, the accuracy of fit of current CAD/CAM crown restorations is to be investigated using a 3D industrial scanner in order to collect scientific data on the success, durability and function of the materials for their clinical application. The fit will be determined material-dependently and also depending on the luting system used. Furthermore, the wear and thus the longevity of the restorations will be tested by means of a chewing simulator and subsequently measured in 3D.

I	Infection and Immunology
N	Neurosciences
O	Oncology
R	Renal and Vascular Research
M	Medical Engineering
S	Others

Modulation of SOCE using Davunetide

P124 04/2023 - 06/2023

Dr. Tania Gabriela Rizo Garza, Department of Stem Cell Biology
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Abstract
Pathogenic variants in SPAST, which encodes spastin, a microtubule-severing enzyme, are the most common cause of Hereditary spastic paraplegia, a motor neuron disorder affecting the axons of corticospinal motor neurons. To date, therapeutic strategies focus on ameliorating the symptoms without treating the underlying cause. Here we investigate the effects of microtubule modifying drugs on SPAST induced pluripotent stem cell derived neurons.

Deep learning QSM in the presence of fat

P125 01/2024 - 12/2024

Dr. Jannis Hanspach, Institute of Radiology
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Abstract
Using advanced deep learning techniques based on synthetic training data, MRI reconstruction methods for quantitative susceptibility mapping (QSM) will be designed and optimized for anatomical regions outside the brain. The neural networks will be generalized for different parameters, such as magnetic field strength, and tested in the prostate, knee, and breast in volunteers and compared against conventional methods.

Mesentery model for peritoneal metastasis

P126 05/2023 - 08/2024

Dr. Kerstin Hübner, Institute of Pathology
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Abstract
Although peritoneal metastasis correlates with poor survival in colorectal cancer (CRC), knowledge on its molecular mechanisms is rather limited. Thus, there is a crucial need for developing novel in vitro models that recapitulate peritoneal seeding and identify putative markers for therapeutic approaches. Our study aims to implement a new ex vivo mesentery model for co-culture with CRC spheroids and organoids to study gene-specific effects on tumor cell adhesion and invasion in the peritoneum.

Myocarditis in relation to sports in children

P127 09/2023 - 08/2024

Dr. Annika Weigelt, Department of Paediatric Cardiology
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Abstract
The current recommendations concerning physical activity after myocarditis in the young and/or PIMS-TS are based on low evidence and are limited to the adult population. Consequently, physical activity is partly heavily restricted in a generation with an increasing sedentary live-style. We aim to evaluate in a prospective study the relationship between sport and myocarditis/PIMS-TS and the safety of the ensuing recommendations.

FICD-mediated AMPylation in Parkinson's disease

P128 09/2023 - 08/2024

Prof. Dr. Wei Xiang, Department of Molecular Neurology
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Abstract
Protein AMPylation, which can be catalyzed by FICD, has emerged as a modulator of neurogenesis. The role of FICD-mediated AMPylation in neurodegeneration, however, has been less understood. Our preliminary data suggest a promoting function of FICD in the aggregation of alpha synuclein (aSyn), which is linked to the pathogenesis of Parkinson's diseases. This project aims to investigate the pathological relevance of FICD-mediated AMPylation in aSyn aggregation-associated neurodegeneration.

Biofabricated breast cancer in a perfusion reactor

P129 08/2023 - 07/2024

Dr. Rafael Schmid, Department of Plastic and Hand Surgery
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Abstract
Aim is the development of biofabricated 3D breast cancer models, which will act as standardized tumor angiogenesis and therapy models mimicking the in vivo situation by using multiple cell types including endothelial cells as well as the supply via a perfusion bioreactor. Evaluation will be based on metabolic activity, proteomic analysis, microscopy and histology. Assessment as therapeutic model will be done using paclitaxel. Goal is the use in basic research and the improvement of therapies.

Nuclear envelope breakdown during NETosis

P130 07/2023 - 06/2024

Dr. Christine Schauer, Department of Medicine 3
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Abstract
During the course of neutrophil extracellular trap (NET) formation, intracellular calcium plays essential role in activation of enzymes like PAD-4 and calpain which are involved in chromatin decondensation. The preliminary data showed the involvement of calpain in degradation of the nuclear envelope protein nesprin. Here we will delineate the exact role of calpain in degradation of nuclear envelope protein nesprin and unfold the mechanism of nuclear membrane breakdown during NET formation.

Osteoclast metabolism

P132 03/2024 - 02/2025

Dr. Carina Scherbel, Department of Medicine 3
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Abstract
Osteoclasts (OCs) play key roles in the regulation of bone mass and excessive osteoclastogenesis is involved in joint destruction in autoimmune arthritis or osteoporosis. The current knowledge on cellular metabolism and its impact on OC function and bone homeostasis remain unclear. In this project, we aim to characterize metabolic dynamics during osteoclastogenesis and to identify novel regulators of bone turnover.

I	Infection and Immunology
N	Neurosciences
O	Oncology
R	Renal and Vascular Research
M	Medical Engineering
S	Others

Cancer cells and CAFs as joint therapeutic target

P133 01/2024 - 09/2024

Dr. Harald Schuhwerk, Chair of Experimental Medicine I
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Abstract
ZEB1 is expressed in chemoresistant tumor cells (TCs) and cancer-associated fibroblasts (CAFs). According to our recent data, it induces replication stress (RS) which can be selectively targeted in TCs for chemo-sensitization. Furthermore, we discovered ZEB1-dependent immunosuppression in CAFs, precluding immune checkpoint therapies. As CAFs also display the ZEB1-driven RS, we now seek to target both unfavorable cell types together in an immunocompetent model to enhance therapeutic efficacy.

Untargeted metabolomics in adrenal tumors

P134 08/2023 - 07/2024

Dr. Nora Vogg, Institute of Experimental and Clinical Pharmacology and Toxicology
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Abstract
The diagnostic workup of frequent adrenocortical adenomas and rare, aggressive adrenocortical carcinomas is challenging and lacks specificity. Determination of deconjugated steroids in urine is an emerging and promising tool in this field, however, the currently best available diagnostic biomarkers provide no benefit to a third of the patients. We plan to screen the urinary metabolome by untargeted metabolomics looking for more suitable diagnostic biomarkers such as intact steroid conjugates.

Examination of craniofacial sutures

P135 01/2024 - 12/2024

Dr. Ines Willershausen, Department of Orthodontics and Orofacial Orthopedics
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Abstract
In orthodontics, craniofacial sutures play a central role. In the present radiological study, we would like to examine to what extent 7T-MRI images of the midface are comparable to the gold standard (CT/CBCT images). To gain a better understanding of sutural remodelling at the cellular level, cyclic pressure loads will be applied to co-cultures of fibroblasts, chondrocytes and osteoblasts in a controlled in vitro system and their gene expression will be investigated.

Exploring growth retardation under TKI therapy

P136 12 months

Dr. Stephanie Sembill, Department of Paediatrics and Adolescent Medicine
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Abstract
As a result of non-specific inhibition, tyrosine kinase inhibitors (TKIs) also affect bone and cartilage development. Children and adolescents therefore suffer from significant growth retardation during therapy. Alternative therapy concepts are therefore urgently needed. In the proposed project, the influences of different TKIs on bone metabolism and cartilage differentiation will be investigated.

Spatial interactions of T-cell clones in RA

P137 12 months

Dr. Jule Taubmann, Department of Medicine 3
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Abstract
RA is a chronic inflammatory autoimmune disease that results in hyperplasia of synovial membrane of joints. However, little is known about the molecular profile and heterogeneity of infiltrating immune cells as well as about the molecular features of their cell-cell interactions. The aim of this project is to generate combined datasets on the molecular features and spatial distribution of resident and infiltrating immune cells via spatial transcriptomics of synovial tissue biopsies.

Lineage tracing of metastases

P138 11/2023 - 11/2024

Dr. Arwin Groenewoud, Institute of Pathology
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Abstract
Despite the clinical importance of bone metastasis, the mechanisms of its formation remain poorly understood. The interaction between cancer and immune cells plays an important role. We propose to use transparent zebrafish larvae to model immune cell interaction during metastatic colonization. Combining immune cell ablation models with a methylation-based transcriptional tracing system, we will measure the effect of individual immune cell populations on the process of metastatic colonization.

Influence of 3-indolepropionic acid on arthritis

P139 12 months

Dr. Isabell Wank, Chair of Pharmacology and Toxicology
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Abstract
Our preliminary study demonstrated protective effects of 3-indolepropionic acid (IPA) on the severity of CIA arthritis in mice. Our project will now I) provide insight into general IPA effects on overall brain function at rest and II) use (thermal) fMRI to evaluate central nociception as a functional readout parameter for RA severity. III) We will assess whether long-term IPA treatment up to day 35 may have additional benefits on disease progression.

iPSC-derived neural crest cells & palate formation

P140 10/2023 - 06/2024

Dr. Matthias Weider, Department of Orthodontics and Orofacial Orthopedics
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Abstract
Orofacial clefts are the second-most congenital malformation. Palate development depends on cranial neural crest cells (CNCCs). CNCCs undergo diverse differentiation programs accompanied by vast changes in gene expression, to which the chromatin remodeling complexes BAF and EP400/TIP60 contribute. We will analyze the function of both complexes in iPSC-derived CNCCs in proliferation and in differentiation to tissues relevant for palatogenesis by CRISPR/Cas9-guided knockout of each central ATPase.

I	Infection and Immunology
N	Neurosciences
O	Oncology
R	Renal and Vascular Research
M	Medical Engineering
S	Others

Basophils in skin-derived sensitization

P141 10/2023 - 06/2024

Dr. Daniel Radtke, Department of Infection Biology
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Abstract
A disturbed skin barrier allows for sensitization to skin-encountered allergen. Upon lung challenge with the same allergen stronger lung inflammation occurs. Preliminary data shows that basophils drive skin-mediated, allergen-specific antibody formation and we want to analyze their impact on barrier integrity and aspects of the antibody repertoire. We further plan lung-challenge of sensitized basophil deficient mice to determine functional relevance potentially critical for asthma development.

IL36 in intestinal inflammation and fibrosis

P142 11/2023 - 11/2024

Dr. Kristina Koop, Department of Medicine 1
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Abstract
Intestinal fibrosis is a common complication in IBD with an unmet need to develop therapy options. Recent studies turned fibroblasts into the spotlight of IBD research as they are associated with fibrosis, control of inflammation and personalized therapy. Published own work showed a major role of IL36R signaling during the perpetuation of intestinal inflammation/fibrosis. This project aims to understand the role of stromal IL36R signaling for the resolution of intestinal inflammation/fibrosis.

The role of miRNAs in Lichen sclerosus

P143 03/2024 - 02/2025

Dr. Marios Marcou, Department of Urology
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Abstract
Lichen sclerosus (LS) is a chronic, inflammatory, scarring disease of the skin, manifesting mostly in the genital region, that can occur at any age and in both sexes. The etiology and pathophysiology of LS remain unknown. The aim of our study is to investigate the expression of miRNAs in the tissue of patients with histologically confirmed LS in all ages and in both sexes. Histological samples from patients without evidence of LS will serve as a control group.

Histamin induces resolution of arthritis

P144 12 months

Dr. Kerstin Dürholz, Department of Medicine 3
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Abstract
Propionate is produced by the gut microbiota and has anti-inflammatory properties. Our preliminary data shows that bacterial histamine production is increased upon propionate treatment. Histamine is able to induce rapid resolution of peripheral inflammation in arthritic mice via the activation of H3 receptor, which is mainly expressed on cells of the central nervous system (CNS). In this project we aim to unravel the role of the CNS in mediating histamine-induced resolution of inflammation.

Th17/Treg immune response in periodontitis

P145 12 months

Dr. Leah Trumet, Department of Operative Dentistry and Periodontology
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Abstract
Periodontitis (PA) is a highly prevalent disease that has bidirectional associations with Diabetes and Alzheimer's disease. PA is leading to irreversible destruction of tooth-surrounding tissues and tooth loss. The pathogenesis of PA is poorly understood. Aim is the analysis of possible Th17/Treg disbalance in PA, association with pro- and anti-inflammatory cytokines, and whether these alterations are local or systemic. The goal is to identify biomarkers and potential targets for immunotherapy.

Melanoma organoids as platform for testing

P146 12 months

Dr. Annkathrin Hornung-Eichler, Department of Dermatology
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Abstract
Despite good overall response rates, there are also high rates of resistance under immu¬notherapy and targeted therapy in the treatment of melanoma. Thus, new therapeutic op¬tions are necessary and we need laboratory test systems to allow a better prediction of therapy response. 3D organoids can be a promising tool in this regard. The aim of this project is to cultivate melanoma-derived organoids as a test platform for the prediction of response to tumour therapies.

Intestinal barrier models in HTLV-1 transmission

P147 12 months

Dr. Alexandra Birzer, Institute of Clinical and Molecular Virology
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Abstract
The focus of the present project is the effect of the human T cell leukemia virus (HTLV-1) on dendritic cells (DCs) in two models. The project focuses on the transmission of HTLV-1 to DCs across an intestinal barrier, analyzing the phenotype of DCs and the mechanism of transmission. For this purpose, two models, a 2D transwell and a 3D organs-on-a-chip model will be established. Finally, both models will be compared regarding their advantages, disadvantages and differences in the DC phenotype.

Wnt/beta-catenin signaling in kidney disease

P148 03/2024 - 12/2024

Dr. Tilman Jobst-Schwan, Department of Medicine 4
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Abstract
We identified a new configuration of the Wnt signaling mechanism at the luminal membrane of the kidney tubule. Thus, tubular cell culture and zebrafish models are used to further investigate how Wnt ligands activate b-catenin in the tubule, and in particular how this affects the intercalated cells of the collecting duct, a cell type important for acid-base regulation. The findings resulting from these efforts could help to identify tubular targets in the therapy of nephrotic syndrome.

I	Infection and Immunology
N	Neurosciences
O	Oncology
R	Renal and Vascular Research
M	Medical Engineering
S	Others

Funded Synergy projects in 2023:

No.	Name	Institution	Project title
S1	**Prof. Dr. D. Chichung Lie,** Prof. Dr. Katharina Breininger, Prof. Dr. Marisa Karow, Dr. Andreas Sagner, Prof. Dr. Peter Soba, Prof. Dr. Julio Vera-González and Prof. Dr. Andreas Möglich (Institute of Biochemistry, University of Bayreuth, external cooperation)	Institute of Biochemistry	TRAIN: Towards Rationalizing Neurodevelopment
S2	**Prof. Dr. Sebastian Zundler,** Prof. Katharina Breininger, Prof. Stefan Uderhardt, Prof. Caroline Voskens and Prof. Jochen Guck (MPI Science of Light, external cooperation)	Department of Medicine 1	TAME THE FLAME

TRAIN: Towards Rationalizing Neurodevelopment

S1 01/2024 - 12/2025

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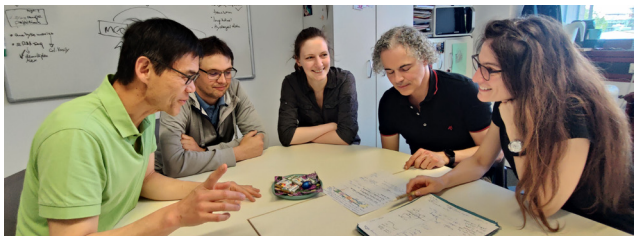
Prof. Dr. Katharina Breininger, Department of Computer Science - Chair for Computer Science 5
Prof. Dr. Marisa Karow, Institute of Biochemistry
Dr. Andreas Sagner, Institute of Biochemistry
Prof. Dr. Peter Soba, Institute of Physiology and Pathophysiology
Prof. Dr. Julio Vera-González, Department of Dermatology
Prof. Dr. Andreas Möglich, University of Bayreuth, Institute of Biochemistry

Abstract

During central nervous system development cells undergo a series of decisions to ultimately form highly specialized networks - the structural basis for behavior and cognition. This developmental decision-making process is poorly understood, yet of high clinical relevance as its disruption can result in neurodevelopmental disorders and loss of resilience to disease in later life. The Synergy Project “TRAIN: Towards Rationalizing Neurodevelopment” pursues a novel concept that key decisions in neurodevelopment are controlled by biological ratios. In TRAIN, experts in neurodevelopment, artificial intelligence, bioinformatics, and optogenetic engineering join forces to generate tools for prediction, genetic manipulation, and high-content analyses of ratios driving neurodevelopmental decisions. Hence, TRAIN will create a truly interdisciplinary research environment allowing to drill deep into the mechanisms of central nervous system development.



TAME THE FLAME

S2 01/2024 - 12/2025

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Prof. Dr. Caroline Voskens, Department of Dermatology
Prof. Dr. Katharina Breininger, Department of Computer Science - Chair for Computer Science 5
Prof. Dr. Stefan Uderhardt, Department of Medicine 3
Prof. Dr. Jochen Guck, Max Planck Institute for the Science of Light

Abstract

Cell trafficking is crucially involved in the pathogenesis of immune-mediated inflammatory diseases such as rheumatoid arthritis or inflammatory bowel disease. While the contribution of cell surface receptors to such trafficking has been explored in detail and has already lead to therapeutic applications, cell-intrinsic properties affecting the cellular migratory behavior have largely been overlooked. Here, we hypothesize that cell mechanical properties and cell trafficking are inextricably linked. Thus, in an interdisciplinary and synergistic effort, this project addresses the role of cellular mechanobiology for homing to the inflamed gut and synovia as well as the mechanical features of therapeutic regulatory T cells and pharmacological opportunities to manipulate cell mechanics. In the long-term perspective, we hope that our insights might provide novel and specific targets for mitigating chronic inflammation.

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