Friedrich-Alexander-Universität
Medizinische Fakultät

Universitätsklinikum
Erlangen

IZKF Erlangen 2022








interdisciplinary
Center for
Clinical Research

www.med.fau.de

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EDITORIAL

Dear Friends and Members of the IZKF,
Dear Readers,

Please find on the following pages the Annual Report 2022 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.

The year 2022 has been marked by several developments and activities, but also by change. Such changes concern the composition of various IZKF-Committees: A welcome to Prof. Berking, Prof. Lie and Prof. Zunke as new members of the IZKF Board. At the same time, our thanks go to Prof. Winkler and Prof. Boßerhoff, who left the IZKF Board after many years of membership and important contributions.

We would also like to welcome the new members of the ELAN Committee: Prof. Bosch-Voskens PhD, PD Dr. Brabletz, Prof. Franze, Prof. Kalbitz, Prof. Kinfe, Prof. Reutter, Prof. Rothhammer, Prof. Soba and Prof. Vöhringer. Our warmest thanks go to the retiring members Prof. Behrens, Prof. Engel, Prof. Erim, Prof. Fromm, Prof. Pilarsky, Prof. Steinkasserer and Prof. Winner for their many years of service.

Since the last elections in October, there have also been changes in the make-up of the CSP Committee. In the coming years, the CSP Committee will be chaired by Prof. Berking. She follows Prof. Winkler, who is leaving the committee after molding CSP programme and Committee in their infant years to my deep gratitude. Additionally, Prof. Rothhammer was appointed as a new member.

Prof. Becker continues to run the Junior Scientists Committee. His new colleagues are Prof. Gramberg, Dr. Steffen and Mr. Karius. We would like to thank Prof. Dudziak, Prof. Müller-Deile and Mrs. Jeninga for dedicating their time and completing their term.

In the summer of 2022, the Junior Research Group 2 „Physics and Medicine“ came to an end. Prof. Dulin and his group are now based at the University of Amsterdam. We wish Prof. Dulin all the best for his further research.

Of the many activities of the IZKF, I would like to highlight one event in particular. This is the 8th International IZKF Symposium. I was pleased that after a pandemic-related postponement of one year the symposium could take place again in person in June 2022. On June 9 and 10, 160 scientists met in Kloster Banz to discuss “The Magic M´s in Modern Medicine”. In addition to an attractive conference programme, around 80 posters were presented. All four winners of poster prizes had the opportunity to showcase their research in a short presentation. On this occasion, we also awarded the Publication Prize to Jay Patankar from the Department of Medicine 1 for his publication on “E-type prostanoid receptor 4 drives resolution of intestinal inflammation by blocking epithelial necroptosis”. My gratitude goes to the programme committee, the speakers and sponsors for making this meeting possible. The next symposium will be held from June 20 - 21 in 2024.

Since May 2022, the IZKF has completely taken over the administration of the ELAN programme. The IZKF Board has also decided on important changes in the ELAN funding scheme on the suggestion of the ELAN Committee. ELAN funding is now also available to applicants over the age of 38, provided there is no other project funding in the IZKF. Young scientists and newly appointed researchers continue to enjoy priority in the allocation of funds. Bridging projects will continue within the ELAN programme. In addition to individual projects, synergy projects can also be applied for in the future by consortia consisting of 3-6 applicants from at least three different institutions to provide pilot funding for joint research initiatives. There is no age limit for applicants in synergy projects. Ongoing IZKF funding is permitted.

On November 21 and 22, 2022, the IZKF Erlangen was evaluated by the external scientific advisory board. In addition to the external review of the new IZKF advanced projects (funding start in 2023), the IZKF Erlangen was also evaluated with regard to its funding lines. The advisory board rated the IZKF and its activities as excellent. Specific recommendations will be discussed for implementation in the next board meetings.

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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THE IZKF IN NUMBERS

30 Advanced Projects

17 Immunology and Infection
7 Oncology
3 Neurosciences
3 Renal and Vascular Research

8 tandem projects between departments and institutes
41 project leaders

5 Junior Research Groups

20 Junior Projects

10 Immunology and Infection
3 Oncology
5 Neurosciences
2 Medical Engineering
thereof **6** projects completed in 2022
thereof **2** newly started projects started

6 Appointments of IZKF project leaders to W2/ W3 - positions

41 Institutions with running projects 2022

6,043K€ total expenditures in 2022

511 Members of Life@FAU 2022

36 SFB 1181
2 SFB 1350
34 GRK 2162
8 GRK 1962
27 GRK 2504
9 GRK 1660
22 GRK 2599
3 TRR 130
12 TRR 221
24 TRR 241
21 TRR 225
5 TRR 305
257 IZKF
139 Dr. med.
118 Dr. rer. nat./Dr. rer. biol. hum.
51 participants outside RTG

42 Pilot Projects

19 Newly granted in 2022
20 Projects completed in 2022

41 Ongoing Scientific Theses in 2022

6 Master theses
34 Doctoral theses
1 Habilitations

48 Publications

Cumulative Impact Factor **593.898**
Average Impact Factor per publication **12.372**
Average publications per project **1***
17 publication with an IF more than 10

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

117 Employees of the IZKF

67 Doctoral fellows, Post-Docs and laboratory rotations
50 Non-scientists

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Zens, Christian
Zorob, Alexander
Zundler, Sebastian
Zunke, Friederike

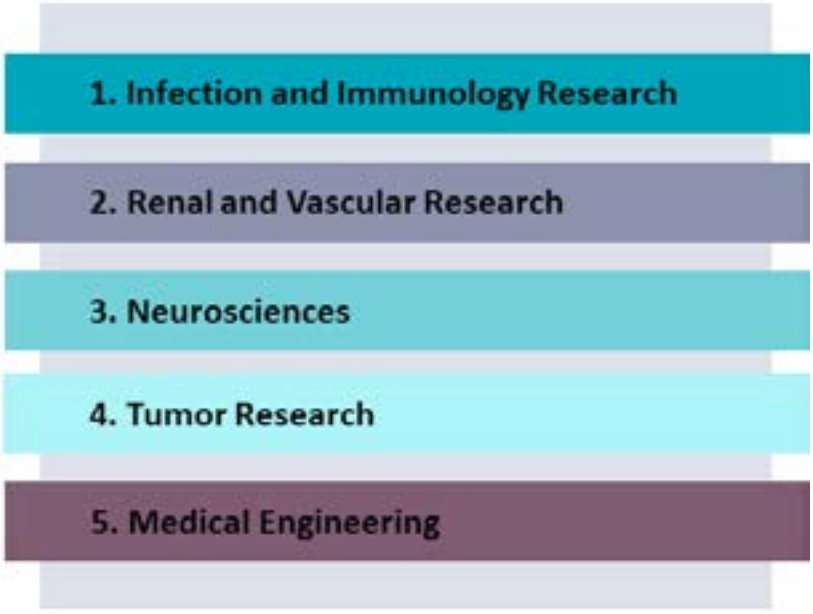
* Project leaders, clinician scientist programme, laboratory rotations and committee members

MD Thesis Scholarships see page 28/29

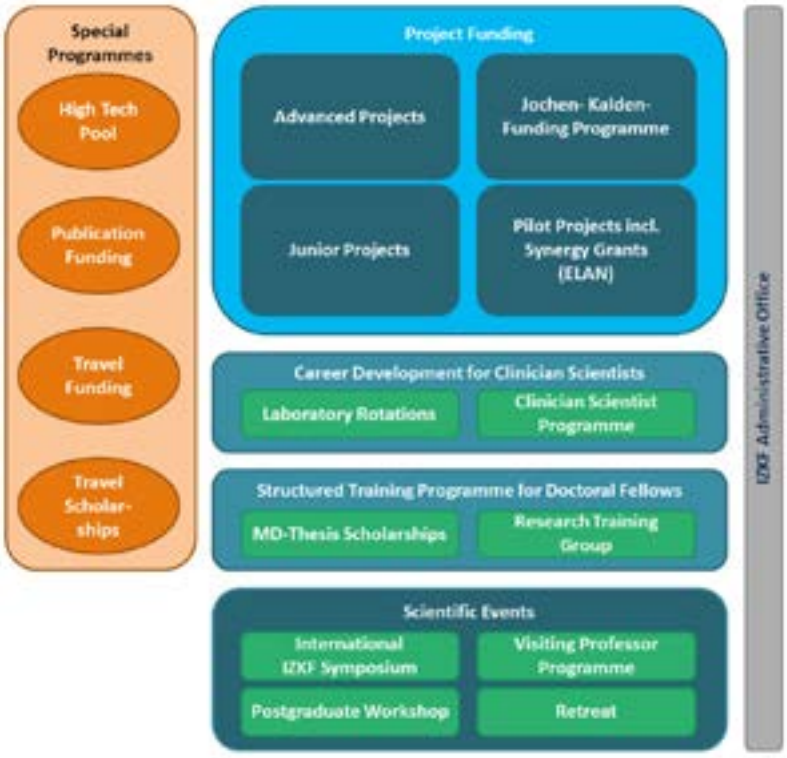
PROGRAMMES

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. Equipped 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 Medicine 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 strengthened cooperation between clinics and institutes, but also between different clinics. The IZKF enables research 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.

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 third-party research 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 doctoral students)
Duration	30 + 6 months

LOM weighted 4-fold

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

LOM weighted 2-fold

- Bayerisches Staatsministerium für Wissenschaft und Kunst
- Bayerische Forschungsstiftung/ Bayerische Landesstiftung
- Wilhelm Sander-Stiftung
- Volkswagen Stiftung
- Deutsche Stiftung für Herzforschung
- Humboldt-Stiftung
- Thyssen-Stiftung
- German-Israelian-Foundation (GIF)
- Mildred-Scheel-Stiftung/ Deutsche Krebshilfe
- Else Kröner Fresenius Stiftung
- José-Carreras-Stiftung
- Bill Gates Stiftung
- DAAD
- Deutsche Kinderkrebsstiftung/ HIT Deutsche Kinderkrebsstiftung
- Hertie-Stiftung
- Herman und Lilly Schilling-Stiftung

Jochen-Kalden-Funding Programme

In honor of the founder and former IZKF chairman the Junior Research Group Programme has been renamed as the Jochen-Kalden-Funding Programme.

Call for proposals	annually
Eligibility	Newly appointed W1 / integrated W2 professors or W3- professors with tenure track or a comparable option of consolidation doctorate 10 years ago (medical doctorate) or 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 doctoral students) Possibility of providing laboratory space for shared use
Duration	24 + 12 months

The junior research groups represent a central funding instrument of the IZKF. As the group of Prof. Dr. Ceppi (Junior Research Group 1) expired in mid-2021 and the group of Prof. Dr. Dulin (Junior Research Group 2) ended in August 2022, the Management Board established a new concept for the junior research groups. Funding volume and application requirements have been redefined. Every year, two new junior research groups have now 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 to a third-party agency that is at least LOM-weighted 2-fold a further project year is granted.

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.

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

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.

ELAN - 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.

ELAN - SYNERGY PROJECTS

In addition to the pilot 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 € 200,000 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	twice a year
Eligibilty	for scientists with a doctoral degree and at least one first author publication no age limit
Funding	max. EUR 200,000
Others	Participation in Travel and Publication Pool
Duration	max. 24 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 Scientists 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 enrolement in the Notice Programme. The admission requirement for the step 2 module is also fulfilled with a post doctoral 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 ben completed or 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.

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 post- graduate 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 including guest speaker seminars, soft skills courses and the continuous supervision by a mentoring committee should continue throughout and until completion of the doctorate. 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 to 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).

IZKF Postgraduate Workshop 2022: Winners of Poster Prizes, Ingrid Zahn and Lena Erkert, 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.

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.

Due to the pandemic, the IZKF temporarily covers the costs of web-based events up to € 500. 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 on the next page.

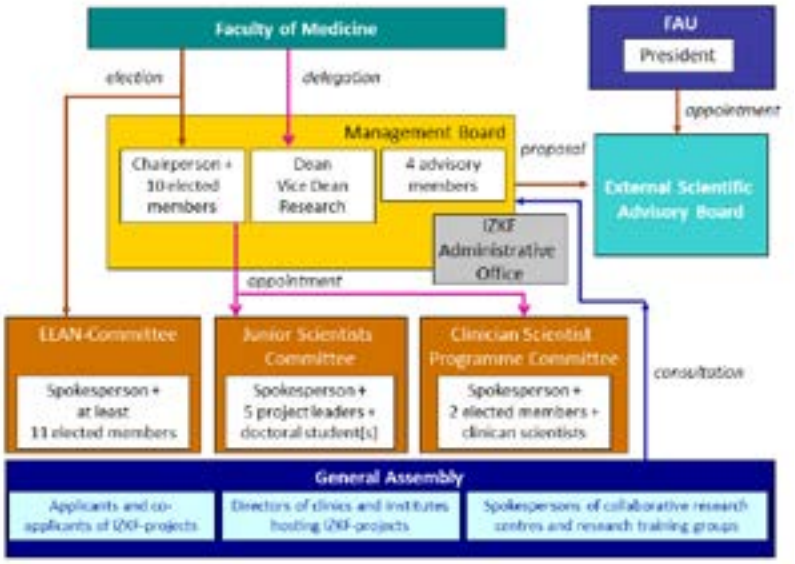
	High Tech Pool	Travel Pool	Publication Pool	Travel Scholarships
Advanced Projects (Project leaders and scientific staff financed by project)	✓	✓	✓	✓ (only for doctoral students)
Junior Projects (Project leaders and scientific staff financed by project)	✓	✓	✓	✓
Pilot Projects incl. Syngery Projects (Project leaders and scientific staff financed by project)	✗	✓	✓	✓ (only for scientists of pilot projects under the age limit)
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

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

Deputy Chairperson

Prof. Dr. Aline Bozec, Department of Medicine 3


Prof. Dr. Wegner


Prof. Dr. Bozec

Members

Prof. Dr. Christoph Becker, Department of Medicine 1
Prof. Dr. Carola Berking, Department of Dermatology (since 10/2022)
Prof. Dr. Christian Bogdan, Institute of Clinical Microbiology, Immunology and Hygiene
Prof. Dr. Anja Bosserhoff, Institute of Biochemistry - Chair of Biochemistry and Molecular Medicine (until 09/2022)
Prof. Dr. Thomas Brabletz, Chair of Experimental Medicine I
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 - Chair of Biochemistry and Molecular Medicine (since 10/2022)
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. Jürgen Winkler, Department of Molecular Neurology (until 09/2022)
Prof. Dr. Friederike Zunke, Department of Molecular Neurology (since 10/2022)

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 2022)

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. 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

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

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. Lydia Sorokin, University of Münster, Institute of Physiological Chemistry and Pathobiochemistry (until 06/2022)

Prof. Dr. Gisa Tiegs, Hamburg-Eppendorf University Medical Center - Institute of Experimental Immunology and Hepatology

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 2022)

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. Jürgen Behrens, Chair of Experimental Medicine II (until 09/2022)
Prof. Dr. Caroline Bosch-Voskens, Department of Dermatology (since 10/2022)
PD Dr. Simone Brabletz, Chair of Experimental Medicine I (since 10/2022)
Prof. Dr. Felix Engel, Department of Nephropathology (until 09/2022)
Prof. Dr. Yesim Erim, Department of Psychosomatic Medicine and Psychotherapy (until 09/2022)
Prof. Dr. Anna Fejtova, Department Psychiatry and Psychotherapy
Prof. Dr. Kristian Franze, Institute of Medical Physics and Microtissue Engineering (since 10/2022)
Prof. Dr. Martin Fromm, Chair of Clinical Pharmacology and Clinical Toxicology (until 09/2022)
Prof. Dr. Claus Hellerbrand, Institute of Biochemistry - Chair of Biochemistry and Molecular Medicine
Prof. Dr. Miriam Kalbitz, Department of Surgery (since 10/2022)
Prof. Dr. Thomas Kinfe, Department of Neurosurgery (since 10/2022)
Prof. Dr. Gerhard Krönke, Department of Medicine 3 (until 03/2023)
Prof. Dr. Christian Pilarsky, Department of Surgery (until 09/2022)
Prof. Dr. Heiko Reutter, Department of Paediatrics and Adolescent Medicine (since 10/2022)
Prof. Dr. Veit Rothhammer, Department of Neurology (since 10/2022)
Prof. Dr. Peter Soba, Institute of Physiology and Pathophysiology (since 10/2022)
Prof. Dr. Alexander Steinkasserer, Department of Immune Modulation (until 09/2022)
Prof. Dr. David Vöhringer, Department of Infection Biology (since 10/2022)
Prof. Dr. Maximilian Waldner, Department of Medicine 1
Prof. Dr. Beate Winner, Department of Stem Cell Biology (until 09/2022)

Prof. Dr. Bäuerle

Prof. Dr. Bosch-Voskens

PD Dr. Brabletz

Prof. Dr. Fejtova

Prof. Dr. Franze

Prof. Dr. Hellerbrand

Prof. Dr. Kalbitz

Prof. Dr. Kinfe

Prof. Dr. Krönke

Prof. Dr. Reutter

Prof. Dr. Rothhammer

Prof. Dr. Soba

Prof. Dr. Vöhringer

Prof. Dr. Waldner

Members of the ELAN-Committee (as of 31st December 2022)

Junior Scientists Committee

Spokesperson for career development programmes

Prof. Dr. Christoph Becker, Department of Medicine 1

Prof. Dr. Becker

Members

Prof. Dr. Diana Dudziak, Department of Dermatology (until 11/2022)

Sebastian Gehlen-Breitbach, Institute of Biochemistry - Chair of Biochemistry and Pathobiochemistry

Prof. Dr. Thomas Gramberg, Institute of Clinical and Molecular Virology (since 12/2022)

Prof. Dr. Claudia Günther, Department of Medicine 1

Myriam Jeninga, Institute of Clinical Microbiology, Immunology and Hygiene (until 07/2022)

André Karius, Department of Radiation Oncology (since 10/2022)

Prof. Dr. Chichung Lie, Institute of Biochemistry - Chair of Biochemistry and Molecular Medicine

Prof. Dr. Janina Müller-Deile, Department of Medicine 4 (until 11/2022)

Dr. Adrian Regensburger, Department of Paediatrics and Adolescent Medicine

Dr. Ulrike Steffen, Department of Medicine 3 (since 12/2022)

Gehlen-Breitbach

Prof. Dr. Gramberg

Karius

Prof. Dr. Günther

Prof. Dr. Lie

Dr. Steffen

Dr. Regensburger

Members of the Junior Scientists Committee (as of 31st December 2022)

Clinician Scientist Programme Committee

Spokesperson for Clinician Scientist Programme

Prof. Dr. Carola Berking, Department of Dermatology

Prof. Dr. Berking

Members

Prof. Dr. Jürgen Winkler, Department of Molecular Neurology (until 09/2022)

Dr. Markus Eckstein, Institute of Pathology

Dr. Eva Maier, Department of Oral and Cranio-Maxillofacial Surgery

Prof. Dr. Veit Rothhammer, Department of Neurology (since 12/2022)

Prof. Dr. Maximilian Waldner, Department of Medicine 1

Dr. Eckstein

Dr. Maier

Prof. Dr. Rothhammer

Prof. Dr. Waldner

Members of the CSP-Committee (as of 31st December 2022)

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 2022 were financed from residual funds of the previous years.

Revenues	
Support of the Medical Faculty	5,378 K€
Support of the University	372 K€
Other revenues	17 K€
Total revenues 2022	**5,767 K€**

Expenditures	
Advanced projects	2,334 K€
Pilot projects	1,045 K€
Career development	2,238 K€
thereof junior research groups	560 K€
thereof junior projects	892 K€
thereof laboratory rotations	541 K€
thereof clinician scientist programme	10 K€
thereof MD-thesis scholarships	197 K€
thereof research training groups	38 K€
Central projects	166 K€
Administration	260 K€
Total expenditures 2022	**6,043 K€**

Revenues and expenditures 2022

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 103 scientific projects were actively running: 30 advanced projects, 18 junior projects, 50 pilot projects and five junior research groups. In addition, six junior projects started their work in 2022 (2) or in the beginning of 2023 (4).

30 advanced, 18 junior projects and five junior research groups published 48 original articles in 2022 resulting in an average of 0,9 publications per project. The cumulative impact factor (IF) was 593.898, averaging 12.372 per publication. 17 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, 34 doctoral theses and one habilitation that were in progress or finalised in 2022. Six professorships to IZKF project leaders were offered. A total of 64 project leaders and 51 employed scientists (PhDs and Post-Docs) are involved in 53 scientific projects (running advanced projects, junior research groups and junior projects 2022) 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.

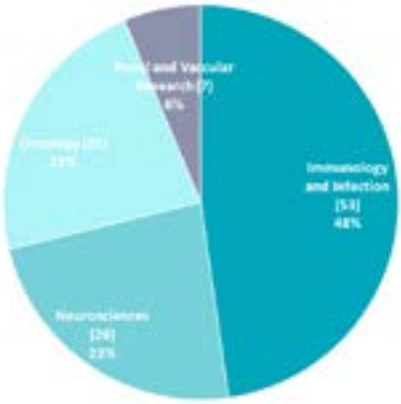
The following table shows all institutions with a running Advanced, Junior or Pilot Project in 2022 and their association to the main research areas of the Faculty. In addition, it can be seen which institution was funded with rotation positions (without assignment to a research area):

Institute	Advanced Projects	Junior Projects	Pilot Projects	Laboratory Rotation
Chair of Anatomy II			S	
Chair of Clinical Pharmacology and Clinical Toxicology			I	
Chair of Experimental Medicine II	O			
Department of Child and Adolescent Mental Health			S	
Department of Dermatology	I			
Department of Immune Modulation	I		I	
Department of Medicine 1	I, O	I, O, N	I, O	
Department of Medicine 3	I, O	I	I	X
Department of Medicine 4	O, R		R	X
Department of Medicine 5	O	I, O	O	X
Department of Molecular Immunology			I	
Department of Molecular Neurology	N	N	N	X
Department of Molecular Pneumology	I			
Department of Nephropathology	I, R	M	M, N	
Department of Neurology			N	X
Department of Neurosurgery				X
Department of Obstetrics and Gynecology	O		O, S	
Department of Operative Dentistry and Periodontology		M		
Department of Oral and Cranio-Maxillofacial Surgery			I	
Department of Orthodontics and Orofacial Orthopedics	N		I	
Department of Paediatric Cardiac Surgery				X
Department of Paediatrics and Adolescent Medicine	O	M	S	X
Department of Plastic and Hand Surgery			S	
Department of Psychiatry and Psychotherapy		N	N	X
Department of Psychosomatic Medicine and Psychotherapy			S	
Department of Radiation Oncology		O		
Department of Stem Cell Biology	N	N	N	X
Department of Surgery	O		I, R	
Institute for Biomedicine of Aging			S	
Institute of Anatomy and Cell Biology			N	
Institute of Biochemistry - Chair of Biochemistry and Molecular Medicine	I, N, 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		S	
Institute of Clinical Microbiology, Immunology and Hygiene	I	I	I	
Institute of Human Genetics	I			
Institute of Neuropathology		N		
Institute of Neuroradiology			M	
Institute of Pathology	O			X
Institute of Physiology and Pathophysiology			N	
Institute of Radiology		O	M	

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

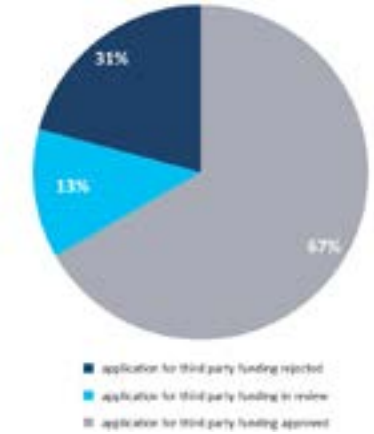
The 41 project leaders of the funding period 2020 - 2023 come from 23 different institutions. 11 (27%) of the project managers are women, 30 (73%) men. Project leaders include 19 (46%) natural scientists and 22 (54%) clinician scientists. In 2022, 25 new projects were approved. Of the 34 project leaders,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



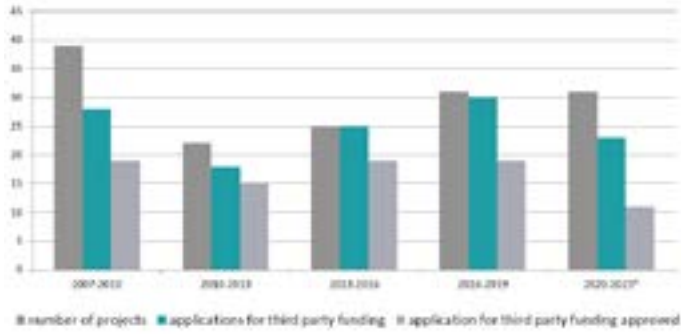
Distribution of advanced projects as per main research area between 2013 and 2022 incl. newly granted advanced projects 2022 - 2025

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 third party funds 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 exten- sions. From the cohort 2020-2023, 23 (74%) of the 31 projects have already 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 third party funding applications. 53 of these projects (73%) were granted extramural funding, 20 (27%) were not funded.

Regarding the projects of the period 2020 - 2023, 11 (48%) of the 23 projects, which applied for external grants, already received funding approvals.

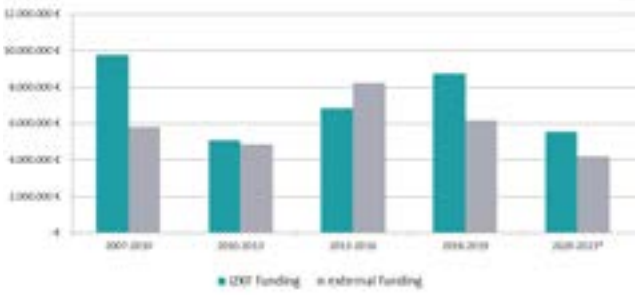


Approved applications for third-party funding of advanced projects between 2010 and 2022



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.
* Current funding period. Further applications to external third-party agencies are planned.

External funding received from advanced projects between 2010 and 2022



External funding received from advanced projects between 2007 and 2022

* Current funding period. Further applications to external third-party agencies are planned.

Jochen-Kalden-Funding Programme

In 2022 there were 5 running junior research groups.

In August 2022, the junior research group of Prof. Dr. Dulin (N2) ran out. The group was located at the South-Campus within the Optical Imaging Center Erlangen (OICE), where the group had modern laboratories and offices with excellent equipment at its disposal. We thank Prof. Dulin for his commitment and we wish him success with his research.

For almost a year now, the programme for the junior research groups has been running under the new name „Jochen-Kalden-Förderprogramm“. In the first round of applications, Prof. Claudia Günther, Prof. Janina Müller-Deile, Prof. Marisa Karow and Prof. Friederike Zunke were selected as group leaders. Three of the groups took over laboratories of the former junior research group of Prof. Ceppi in the Nikolaus Fiebiger Center with its attractive scientific environment.

In 2022, the third call for proposals took place. The procedure is currently ongoing.

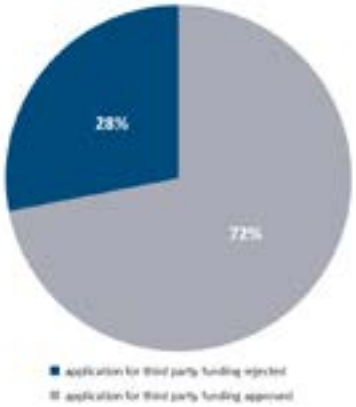
Junior Projects

The first call for junior projects was in 2009. Proposals are accepted every year. Overall 103 junior projects were selected for funding between 2009 and 2022. In this period, 42 (41%) physicians received funding and 61 (59%) scientists. 29 (69%) of the physicians requested a laboratory rotation. Of them, 10 (34%) were women and 19 (66%) men. In general, men and women were almost equally supported when assessed over the entire funding period.

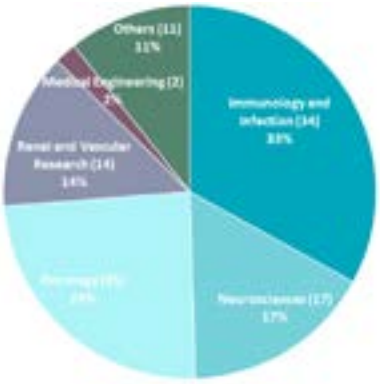
50 successful applicants were women and 53 men. The median age was 32 at the time of application, for both women and men. All main research areas of the Faculty are represented with immunology and infection (33%) and oncology (24%) being the most successful over the years. Overall candidates from 27 different institutions within the Faculty of Medicine were selected.

In 2022, eight proposals were reviewed and six (75%) of them received funding. The approved projects cover the main research areas oncology, neurosciences, renal and vascular research as well as medical engineering. The successful applicants work in six different institutions within the Faculty of Medicine. In total, four (67%) are physicians and two (33%) are other scientists; in this year's call for applications, funding was distributed equally between women and men. The median age was 32 years.

The Junior Projects also perform very well in raising third-party funding. 70% from the projects that started between 2009 and 2019 applied for third-party funding to an external funding agency. This development has been stable over the entire duration of the programme.

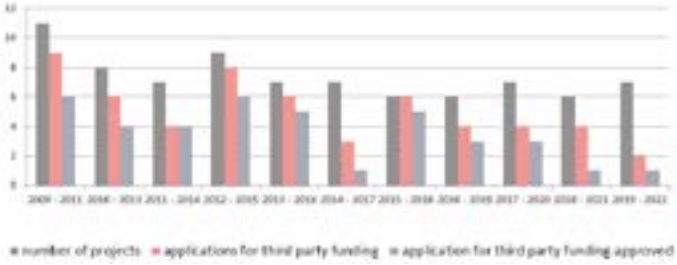


Approved applications for third-party funding of junior projects (projects initiated between 2009 and 2019)

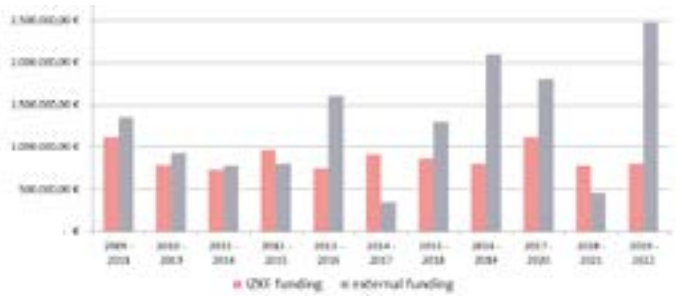


Distribution of junior projects as per main research area of the Faculty of Medicine between 2009 and 2022

External funding received from junior projects started between 2009 and 2019



Success-rate of junior projects initiated between 2009-2019



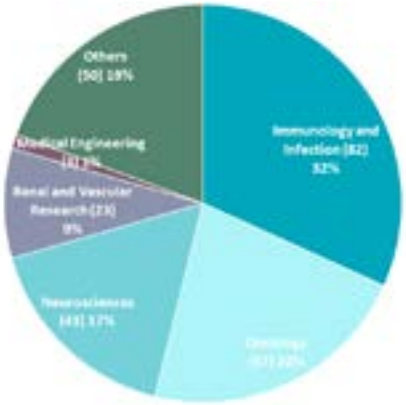
External funding received from junior projects initiated between 2009 and 2019

Pilot Projects (ELAN)

Pilot projects are intended to support scientists at an early stage. Additonally, funds are also available for applicants above the age limit.

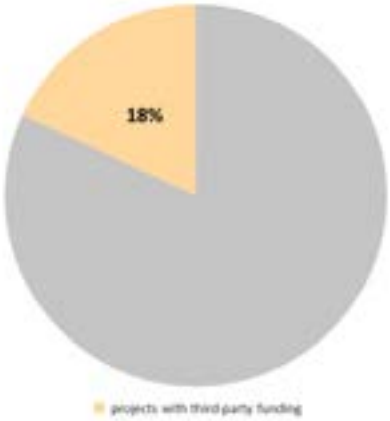
In the reporting period of 2022, 19 proposals were assessed during the meetings of the ELAN-Commission, an internal reviewer was assigned to 20 projects. Of the 19 proposals evaluated in the meetings, 100% received funding. One application was retracted before handling by the commission. The approved projects cover most main research areas of the Faculty of Medicine: immunology and infection (7), neurosciences (4), oncology (2), as well as renal and vascular research (2). The remaining 4 projects were not within one of the main research areas. In 2022, applicants were from 13 different institutions. In total, 5 (26%) of the successful applicants were men and 14 (74%) women. The median age was 34, by gender 39 for men and 34 for women.
Applications for pilot projects can be submitted at any time. Since 2012 an electronic application using the ELAN-Tool is expected. The ELAN-Commitee meets four times a year and selects projects for funding after inclusion of external expertise. Between 2012 and 2022, a total of 351 proposals for pilot projects were reviewed by the ELAN-Committee. Overall, 258 (74%) projects were granted for funding. Between 2012 and 2022 in total 124 women (48%) and 134 men (52%) applied successfully for pilot projects. The median age was 34 years.

All main research areas of the Faculty are represented; with immunology and infection (32%) and oncology (22%) being the most successful over the years.

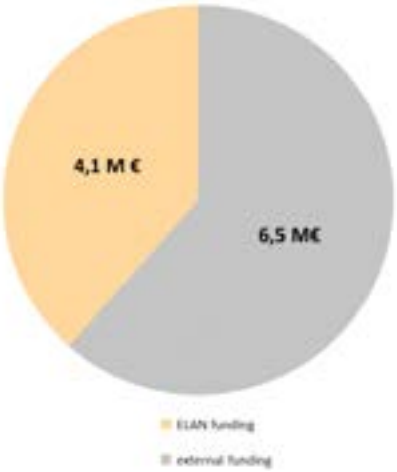


Distribution of pilot projects as per main research area between 2012 and 2022

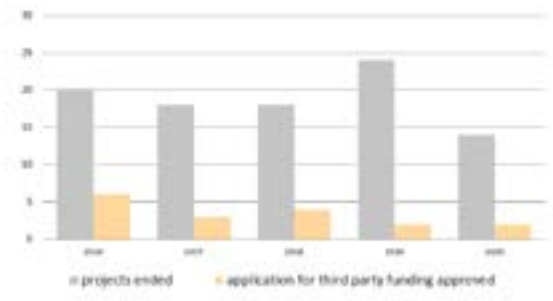
In the following, the success rate of acquiring third-party funding is shown graphically.



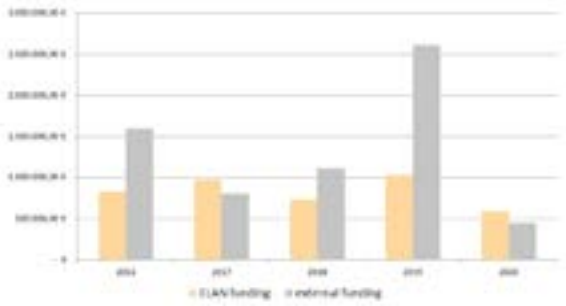
Pilot projects with third-party funding (completed projects with approval years between 2016 and 2020)



External funding received from all completed pilot projects (year of approval between 2016 and 2020)



Success-rate of pilot projects.
Further applications of projects, initiated in 2020, are planned.



External funding from completed pilot projects started between 2016 and 2020

Laboratory Rotations

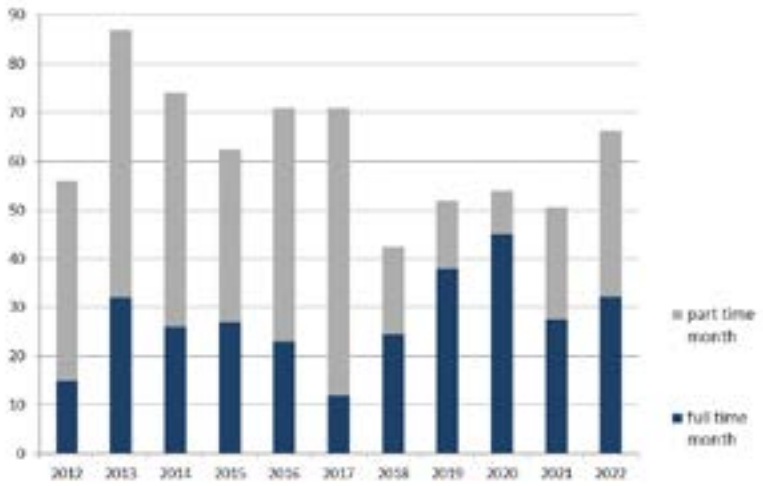
In 2022, 16 physicians were funded with a rotation position. In addition to pure laboratory rotations, positions are also open to junior project leaders and participants in the Module Step 1 of the Clinician Scientist Programme.

Rotations		
Dr. Rebecca Baur	Department of Medicine 5	07/2022 - 07/2023, 50%
Dr. Marius Brazdis	Department of Psychiatry and Psychotherapy	02/2022 - 07/2022, 100%
Dr. Dennis Kannenkeril	Department of Medicine 4	10/2022 - 09/2023, 50%
Dr. Johanna Kurzhagen	Department of Medicine 4	07/2022 - 12/2022, 50%
Dr. Anna Maslarova	Department of Neurosurgery	07/2022 - 12/2022, 100%
Dr. Harriet Morf	Department of Medicine 3	09/2022 - 08/2023, 50%
Dr. Kathrin Rottermann	Department of Paediatric Cardiac Surgery	06/2022 - 05/2023, 50%
Dr. Alexander Schnell	Department of Paediatrics and Adolescent Medicine	04/2022 - 10/2022, 100%
Dr. Stephanie Sembill	Department of Paediatrics and Adolescent Medicine	09/2022 - 02/2023, 100%
Dr. Maximilian Sprügel	Department of Neurology	01/2022 - 06/2022, 100%

Rotations of Junior Project Leaders		
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. Adrian Regensburger	Department of Paediatrics and Adolescent Medicine	01/2021 - 05/2021, 01/2022 - 11/2023, 50%
Dr. Patrick Süß	Department of Molecular Neurology	05/2022 - 10/2022, 100%

Rotations of Clinician Scientists		
Dr. Markus Eckstein	Institute of Pathology	07/2020 - 06/2022, 50%
PD Dr. Martin Regensburger	Department of Stem Cell Biology	08/2020 - 12/2021, 01/2022 - 07/2022, 50%

Laboratory rotations 2022 with name, institute, funding period und scope of position



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 28 physicians took part in the CSP. A rotation position within in the CSP (Module Step 2) can be applied for. The deadline for the submission of applications was March 7, 2022. In 2022 no application was 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 2022:

Module Step 1	
Dr. Razvan Marius Brazdis	Department of Psychiatry and Psychotherapy
Dr. Danilo Hackner	Department of Surgery (S)
Dr. Anna Kanewska	Department of Orthopaedic and Trauma Surgery (S)
Dr. Elias Koch	Department of Dermatology (S)
Dr. Maria Gabriella Raimondo	Department of Medicine 3
Dr. Jan Schaefer	Department of Paediatrics and Adolescent Medicine
Dr. Alexander Schnell	Department of Paediatrics and Adolescent Medicine
Dr. Andrej Stoll	Department of Medicine 5
Dr. Thanos Tsaktanis	Department of Neurology (S)
Dr. Raluca Ursu	Department of Medicine 4 (RECORD)
Dr. Lisette Warkentin	Institute of General Practice
Dr. Alexander Zorob	Department of Medicine 4 (RECORD)

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

(S) started in 2022
(C) completed in 2022

In mid-May, the second retreat of the IZKF Clinician Scientists took place at the Fraunhofer research campus in Waischenfeld. The programme included both - own presentations by the participants and guest presentations. In addition to scientists from Erlangen, the organizers were able to attract two renowned guest speakers from Munich and Mainz. The participants heard a lecture by Professor Noessner (Helmholtz Institute, Munich) on the subject of tumor immunology and by Dr. Foersch (Institute for Pathology of the University Medicine of the Johannes Gutenberg University Mainz) on digital pathology. A team-building event was also included. After 1.5 days of interesting lectures, the participants set out on a canoe trip on the Wiesent.

CSP-Retreat 2022 (Waischenfeld)

CSP Retreat 2022 (Waischenfeld)

Course	Lecturer
Bioinformatics/ data analysis (Basic)	Dr. Fulvia Ferrazzi (Institute of Pathology)
Good Scientific Practice	Dr. Anne Hamker (external)
Grant Proposal Writing	Dr. Sabine Preusse (external)

Courses given in 2022 for participants of the CSP

Life@FAU as structured training programme for doctoral fellows

In 2022, the number of doctoral fellows participating in Life@FAU increased significantly compared to the previous year. In 2021, 405 doctoral fellows took part, in the reporting year there were already 511. The doctoral fellows are distributed between research training groups, research centres etc. as follows:

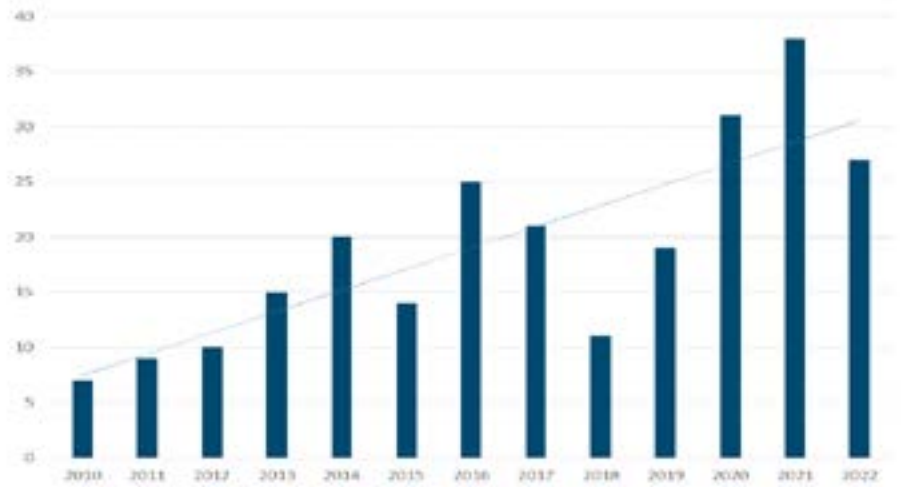
Programme/ Research Training Group	Registered participants	thereof Dr. rer. nat. and others	thereof Dr. med. / dent.
SFB 1181	36	26	10
SFB 1350	2	2	0
GRK 2162	34	23	11
GRK 2504	27	20	7
GRK 2599	22	16	6
TRR 221	12	9	3
TRR 241	24	15	9
TRR 225	21	0	0
TRR 305	5	5	0
IZKF	28	0	0
IZKF associated	90	79	11
IZKF MD	139	0	139
no connection to RTG	51	48	3
Ongoing	491	296	195
GRK 1962	**8**	**8**	**0**
GRK 1660	**9**	**3**	**6**
TRR 130	**3**	**3**	**0**
Expired	**20**	**14**	**6**
total	**511**	**310**	**201**

Research Training Groups participating in Life@FAU, indicating the number of participants as of 31st December 2022

MD-Thesis Scholarships

In 2022, a total of 49 medical doctoral students from 22 institutions were funded. Due to the fact that some scholarships granted in 2021 ended in 2022, the number of funded doctoral students is higher than the number of scholarships available.

Overall, 33 applications for the MD-Thesis scholarship programme have been received in 2022. The Junior Scientists Committee approved 27 applications (81%), 18 (66%) of the successful applicants were females and 9 (33%) males. The median age was 23 years. Since its inception in 2007, the IZKF supported a total of 289 medical students with a scholarship. Medical students often 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 2022, 89 (31%) students had already completed their doctoral thesis. Interestingly, 32 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 2022

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 2022.

Department of Dermatology	
Arnet, Lisa	10/2022 - 05/2023
Azodanlou, Delara	08/2022 - 03/2023
Karimi, Bita	10/2022 - 05/2023

Department of Medicine 3	
Hendel, Anna	11/2021 - 06/2022
Hofmann, Thea	06/2022 - 01/2023
Zagrada, Mrika	02/2023 - 09/2023

Department of Medicine 4	
Lippler, Susanne	08/2021 - 03/2022
Loderbauer, Lisa	12/2022 - 07/2023
Wangerin, Sarah	03/2022 - 10/2022

Department of Molecular Neurology	
Färber, Franziska	12/2021 – 07/2022
Seisenberger, Juliana	12/2021 – 07/2022
Weiß, Alexander	12/2021 – 07/2022

Department of Paediatrics and Adolescent Medicine	
Einhaus, Johanna	12/2022 - 07/2023
Nedoschill, David	06/2022 - 01/2023
Schielein, Sophie	09/2021 - 04/2022
Seiser, Esra	12/2021 - 07/2022
Yankouskaya, Katharina	03/2022 - 10/2022

Department of Plastic and Hand Surgery	
Englich, Moritz	08/2022 - 03/2023
Wattenbach, Christian	06/2022 - 01/2023
Weinhold, Claire	08/2021 - 03/2022

Department of Stem Cell Biology	
Düfel, Leonore	06/2022 - 01/2023
Geißler, Simon	06/2022 - 01/2023
Leupold, Lukas	08/2021 - 03/2022

Department of Surgery	
Eiselt, Jan	12/2022 - 07/2023
Groh, Marie	04/2022 - 11/2022
König, Clara Maria	12/2021 - 07/2022
Krämer, Florian	08/2022 - 03/2023

Others		
Bülow, Nicolas	Institute of Physiology and Pathophysiology	11/2021 - 06/2022
Büttner, Clara	Department of Medicine 5	08/2022 - 03/2023
Dashi, Tobias	Institute of Radiology	06/2022 - 01/2023
Dorner, Heidrun	Department of Medicine 1	08/2021 - 03/2022
Hustadt, Samuel	Institute of Microbiology	10/2021 - 05/2022
Kißler, Alicia	Institute of Cellular and Molecular Physiology	07/2022 - 02/2023
Kösters, Peter	Department of Nephropathology	08/2021 - 03/2022
Lampersberger, Hanna	Institute of Biochemistry - Chair of Biochemistry and Pathobiochemistry	12/2021 - 07/2022
Lötzsch, Chiara	Institute of Biochemistry - Chair of Biochemistry and Molecular Medicine	12/2022 - 07/2023
Lüders, Anina	Institute of Microbiology	03/2022 - 10/2022
Möhwald, Alexander	Institute of Physiology and Pathophysiology	12/2021 - 07/2022
Neurath, Nicole	Department of Psychiatry and Psychotherapy	12/2021 - 07/2022
Pfeuffer, Ann-Kathrin	Institute of Cellular and Molecular Physiology	11/2022 - 06/2023
Roukhami, Sofia	Department of Nephropathology	08/2022 - 03/2023
Sankina, Polina	Department of Anesthesiology	08/2021 - 03/2022
Schomburg, Simon	Chair of Functional and Clinical Anatomy	08/2021 - 03/2022
Sebald, Adrian	Department of Medicine 1	04/2022 - 11/2022
Siegert, Juliane	Department of Radiation Oncology	12/2021 - 07/2022
Speer, Katharina	Department of Molecular Pneumology	04/2022 - 11/2022
Spießl, Kathrina	Department of Medicine 5	04/2022 - 11/2022
Ünüvar, Sumeyya	Institute of Biochemistry - Chair of Biochemistry and Molecular Medicine	09/2022 - 04/2023
Wachter, Matthias	Department of Radiation Oncology	10/2022 - 05/2023
Wicht, Simon	Department of Psychiatry and Psychotherapy	12/2021 - 07/2022

Training courses in the IZKF

The IZKF Research Training Group again offered numerous courses in 2022. The effects of the pandemic can also be seen here. Almost all courses were offered as a virtual workshop.

Course	Course days	Offers 2022	Lecturer
Scientific Writing 1 An introduction to scientific writing	2,5	2	Dr. Deborah Bennett Bennett English Training for Academics
Scientific Writing 2 Writing research articles	2,5	2	Dr. Deborah Bennett Bennett English Training for Academics
Scientific Writing 3 Writing a PhD Thesis: Streamlining the writing process	2,5	2	Dr. Deborah Bennett Bennett English Training for Academics
An introduction to presentation skills	2,5	3	Dr. Deborah Bennett Bennett English Training for Academics
Application related statistics	1,5	1	Dr. Matthias Englbrecht Healthcare Data Scientist & Career Coach
Basic Scientific Imaging	2,5	1	Dr. Ralph Palmisano (OICE)
Good Scientific Practice	1	6	Dr. Anne Hamker Weiterbildung – Wissenschaftsberatung - Projektmanagement
Poster Workshop	1,5	2	Dr. Deborah Bennett Bennett English Training for Academics
Kommunikation und Rhetorik	2	1	Gerhard Kranz WiSo-Führungskräfte-Akademie (WFA)
Fundamentals of bioinformatics analysis of functional genomics data	5	1	Dr. Fulvia Ferrazzi Department of Nephropathology
Grant Writing	5	1	Prof. Dr. Christoph Becker (Department of Medicine 1) Prof. Dr. Katharina Zimmermann (Department of Anesthesiology) Prof. Dr. Felix Engel (Department of Nephropathology)

Soft skill- and statistic courses given in 2022

On October 19, the **IZKF Postgraduate workshop** took place in the lecture halls of the faculty of medicine. Among all participants, the IZKF awarded two poster prizes.

- Ingrid Zahn (Impact of melanocortins on the lipid production of meibocytes investigated by a cell line and a new 3D ex vivo vibratome slice culture) and
- Lena Erkert (The role of Tifa in immune-epithelial communication, intestinal infection and inflammation).

Both doctoral students convinced the reviewers at their posters and in the flash talks. The reviewers emphasized the very good performance of all participants.

In addition to excellent talks of guest speakers, the awards for doctorates of the FAU Faculty of Medicine were presented during the event. Professor Hohenberger (Chairman board of trustees) from the Forschungsstiftung Medizin awarded the prizes to Dr. med. Anna-Lena Mayer and Dr. med. Sören Schnellhardt.

Awarding of doctorates: Laudatio Prof. Hohenberger

The **IZKF Retreat** in 2022 took place at the Fraunhofer Forschungscampus - again for the first time after the pandemic.

The keynote session was led by an external speaker about "Aspects of modern computed tomography" (Bernhardt Schmidt, Siemens). For the first time, the lectures were devided into three types of presentations (progress reports, methods, problems). In addition to presentations, participants had an active role n chairing sessions. A total of 48 doctoral students participated.

IZKF Retreat 2022 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
Isabel Galicia Ernst, Institute of Biomedicine of Aging
Pia Scheufele, Institute of General Practice

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 research orientation, even if in some doctoral projects there are clear references to other fields of sciences 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
Andre Karius, Department of Radiation Oncology
Sascha Daniel, Institute 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
Sebastian-Gehlen Breitbach, Institute of Biochemistry - Chair of Biochemistry and Pathobiochemistry
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 - Chair of Biochemistry and Molecular Medicine

Spokespersons
Sabrina Kojic, Institute of Biochemistry - Chair of Biochemistry and Molecular Medicine
Sandra Lörentz, Institute of Biochemistry - Chair of Biochemistry and Molecular Medicine

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.

IZKF Symposium 2022

After a postponement due to the pandemic, around 160 participants met on June 09 and 10 for the 8th International IZKF Symposium „**The Magic M's in Modern Medicine**" in Kloster Banz in Bad Staffelstein.
In addition to an attractive conference programme, there was also a poster exhibition with around 80 exhibitors.

Poster prize of 250 euros were awarded

- Lisa Mészáros, Department of Molecular Neurology (PI Winkler) Human alpha-synuclein overexpressing MBP29 mice: a model for the cerebellar subtype of multiple system atrophy
- Jan Philipp Dobert, Department of Molecular Neurology (PI Zunke) Targeting beta-glucocerebrosidase in Parkinson disease - structural insights into transport and activation
- Karen Ullrich, Department of Medicine 1 (PI Zundler) IL-3 receptor signalling suppresses chronic intestinal inflammation by controlling mechanobiology and tissue egress of regulatory T cells
- Alice Drobny, Department of Molecular Neurology (PI Zunke) The role of lysosomal cathepsin D (CTSD) in alpha synuclein metabolism and aggregation in Parkinson Disease

Congratulations to all award winners.

Scientific Reports

Funded Advanced projects in 2022:

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
A80	Prof. Dr. Diana Dudziak	Department of Dermatology	Inflammasomes in primary dendritic cells
A81	Prof. Dr. Armin Ensser	Institute of Clinical and Molecular Virology	Receptor and neuropathogenicity of Bornavirus
A82	Prof. Dr. Susetta Neurath-Finotto	Department of Molecular Pneumology	Role of RANTES in the resolution of asthma
A83	Prof. Dr. Thomas Gramberg	Institute of Clinical and Molecular Virology	The role of SAMHD1 in CMV/ HIV coinfections
A84	Prof. Dr. Kai Hildner PD 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
A85	Prof. Dr. Ulrike Hüffmeier	Institute of Human Genetics	The pathophysiology of SAPHO syndrome
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 Chair of Biochemistry and Molecular Medicine	Cyclin interaction with a CDK-like viral kinase
A89	Prof. Dr. Alexander Steinkasserer	Department of Immune Modulation	CD83 regulates homeostasis and inflammation

No.	Name	Institution	Project title
A90	Prof. Dr. Matthias Tenbusch	Institute of Clinical and Molecular Virology	The fate of lung-resident memory T-cells
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
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
A96*	Prof. Dr. Kai Hildner Prof. Dr. Thomas Winkler	Department of Medicine 1 Department Biology - Chair of Genetics	Immune/ IEC crosstalk during intestinal CMV
A97*	Prof. Dr. Clemens Neufert	Department of Medicine 1	STAT3 in IMCs during mucosal healing in IBD
A98*	PD Dr. Kilian Schober	Institute of Microbiology	RA-T
A99*	Dr. Ulrike Steffen	Department of Medicine 3	Mechanisms of cortical bone remodelling
A100*	Prof. Dr. Alexander Steinkasserer	Department of Immune Modulation	sCD83 induces would 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
D30	Prof. Dr. Jürgen Behrens Dr. Dominic Bernkopf	Chair of Experimental II – Molecular Oncology	Axin at microtubuli
D31	Prof. Dr. Anja Bosserhoff	Chair of Biochemistry and Molecular Medicine	Modulation of oncogene-induced senescence
D32	PD 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	PD Dr. Andreas Ramming Prof. Dr. Michael Stürzl	Department of Medicine 3 Department of Surgery	Fibroblast polarization in colorectal carcinoma
D35	PD Dr. Johannes Schödel	Department of Medicine 4	Interactions of DPF3 and hypoxia in renal cancer
D36	Prof. Dr. Reiner Strick Prof. Dr. Arndt Hartmann	Department of Obstetrics and Gynaecology Institute of Pathology	Endogenous retroviruses drive tumor inflammation
D37*	PD Dr. Imke Atreya	Department of Medicine 1	ACLY in IBD-associated cancer
D38*	Prof. Dr. Anja Bosserhoff	Chair of Biochemistry and Molecular Medicine	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	Chair of Biochemistry and Molecular Medicine	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
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	Chair of Biochemistry and Molecular Medicine	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
E32*	Dr. Sven Falk	Chair of Biochemistry and Pathobiochemistry	Molecular nexuses in neurodevelopmental diseases
E33*	Dr. Melanie Küspert	Chair of Biochemistry and Pathobiochemistry	Deubiquitinase Otud7b in CNS myelination
E34*	Prof. Dr. Dieter Chichung Lie Prof. Dr. Kristian Franze	Chair of Biochemistry and Molecular Medicine 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	Chair of Biochemistry and Pathobiochemistry	Temporal patterning of dopaminergic neurons
E37*	Prof. Dr. Michael Wegner Prof. Dr. Anna Fejtova	Chair of Biochemistry and Pathobiochemistry Department of Psychiatry and Psychotherapy	CtBP1, oligodendrocytes & myelination
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

*funding period 2023 - 2025

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 continued to study Gasdermin C, a member of the Gasdermin family of pore forming proteins. We have discovered Gasdermin C, as a protein strongly induced in the gut epithelium by type 2 immunity. We have been continuing to study mice deficient in Gasdermin C using mouse models of inflammation and infection.

Special methods

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

Publications

Gonzalez Acera M., J.V. Patankar, L. Diemand, M.F. Neurath, S. Wirtz, C. Becker. (2021) Comparative transcriptomics of IBD patients indicates induction of type 2 immunity irrespective of the disease ideotype. Frontiers in Medicine. 8:664045.

Patankar JV, Chiriac M, Lehmann M, Kühl AA, Atreya R, Becker C et al. (2020) Severe Acute Respiratory Syndrome Coronavirus 2 Attachment Receptor Angiotensin-Converting Enzyme 2 Is Decreased in Crohn's Disease and Regulated By Microbial and Inflammatory Signaling. Gastroenterology. 160:925-928

HIF expression in B cells regulates bone loss

Prof. Dr. Bozec

A77 12/2020 - 06/2023

Prof. Dr. Aline Bozec, Department of Medicine 3

e-mail: aline.bozec@uk-erlangen.de

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.

Publications

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

Important results

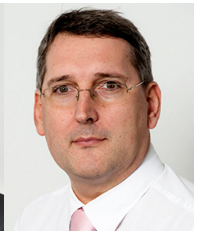
Our data demonstrate that HIF-1a binds to HRE in Rankl promoter, leading to increased RANKL production by B cell and enhanced osteoclastogenesis. Estrogen controls HIF-1a level via HSP70-mediated protein degradation pathway. Pharmacological induction of HSP70 inhibits HIF-1a activation and protects against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

Smurf2-IFN axis in IBD and mucosal healing


Dr. Dr. Chiriac


Prof. Dr. Neurath

A78 01/2021 - 06/2023

Dr. Dr. Mircea Chiriac, Department of Medicine 1
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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.

Publications

no project-specific publications so far

Important results

In various experimental models, Smurf2KO mice were more susceptible whereas Stat2KO and Stat2ΔICE mice (lacking STAT2 only in IECs) were more resistant to the induction of colitis as compared to WT mice. Hence, targeting this Smurf2-dependent regulation of interferon-STAT2 signaling in the gut might emerge as an attractive therapy in IBD patients.

Special methods

1. Generation of Smurf2fl/flxVillinCre mice in which Smurf2 is lacking from intestinal epithelial cells
2. Comprehensive analysis (e.g. RNA-seq & gene ontology, IF) of Smurf2KO mice in experimental colitis models (DSS, oxazolone, TNBS)
3. Characterization of intestinal epithelial cell-derived organoids produced from more than ten IBD patients

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 TGFbeta-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 TGFbeta 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 Galpha12-/ 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

Zhang Y, Shen L, Dreißigacker K, Zhu H, Trinh-Minh T, Meng X, Tran-Manh C, Dees C, Matei AE, Chen CW, Ditschkowski M, Krauss S, Winkler J, Wolff D, Ziemer M, Beilhack A, Karrer S, Herr W, Mackensen A, Schett G, Spriewald BM, Distler JHW (2021) Targeting of canonical WNT signaling ameliorates experimental sclerodermatous chronic graft-versus-host disease. Blood. 137:2403-2416

Inflammasomes in primary dendritic cells

Prof. Dr. Dudziak

A80 01/2020 - 12/2022

Prof. Dr. Diana Dudziak, Department of Dermatology
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Abstract

Inflammasomes play a pivotal role in the immune response against pathogens, but also in the pathogenesis of inflammatory disorders. Our data indicate that inflammasome activation in DCs is leading to full DC stimulation without induction of pyroptosis. We hypothesize that uncontrolled inflammasome stimulation in DCs might be key component in inflammatory disorders. In this study, we want to elucidate the mechanisms in this specific inflammasome activation in primary DC.

Important results

To understand the role of inflammasome activation in primary DCs in human blood we analyzed the expression of inflammasome components in steady state and inflammation. We found a DC subset specific expression pattern of inflammasome subunits with an increased - but DC subset fixed - expression upon stimulation with TLR ligands.

Special methods

Our laboratory has established cell isolation and culturing methods for the analysis of DC subpopulations from peripheral blood but also human lymphoid and non-lymphoid tissues. We use RNAseq and Nanostring analyses to identify transcriptional changes in primary cell populations including DCs, monocytes, macrophages and T cells.

Publications

Hatscher L, Lehmann CHK, Purbojo A, Onderka C, Liang C, Hartmann A, Cesnjevar R, Bruns H, Gross O, Nimmerjahn F, Ivanovic-Burmazovic I, Kunz M, Heger L*, Dudziak D*. (2021) Select hyperactivating NLRP3 ligands enhance the TH1- and TH17-inducing potential of human type 2 conventional dendritic cells. Sci. Signal. 14, eabe1757

Receptor and neuropathogenicity of Bornavirus

Prof. Dr. Ensser

A81 01/2020 - 12/2022

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*The project was interrupted from July-Dec 2020 due to staff diagnostic obligations during the ongoing SARS-CoV2 pandemic.

Abstract

Recently, we detected Borna disease virus (BoDV-1) as the cause of human fatal encephalitis. Previous studies have addressed the immune response and viral replication, but the host cell receptor of BoDV-1 remained unknown. We will use an unique BoDV-1 patient isolate to search for this receptor, and we will address the possible direct, non-immune related neuropathogenic potential of BoDV-1, as well as antiviral (chemo)therapeutic options, in IPSC derived human neuronal 3D organoid cultures.

Publications

Fricke T, Großkopf AK, Ensser A, Backovic M, Hahn AS (2022) Antibodies Targeting KSHV gH/gL Reveal Distinct Neutralization Mechanisms. Viruses 14:541

Großkopf AK, Schlagowski S, Fricke T, Ensser A, Desrosiers RC, Hahn AS (2021) Plxdc family members are novel receptors for the rhesus monkey rhadinovirus (RRV). PLoS Pathog 17(3):e1008979

Important results

Domain swap constructs of BoDV-1 G with VSV glycoprotein failed to incorporate into lentiviral particles. A VSV system allowed pseudotyping of VSV-deltaG-GFP with BoDV-1 G. Production is now optimized by generating stable and inducible BoDV-1 G expressing packaging cell lines in order to get sufficient virus for the CRISPR based entry screen.

Special methods

- Lentiviral pseudotyping and p24 assays; viral infection under BSL2 and BSL3 conditions
- Wide-field fluorescence microscopy in BSL3 and Wide field high content imaging under BSL2 conditions
- Recombinant Vesicular Stomatitis Virus pseudotyping.
- Methods for single cell sequencing of virus-infected cells are beeing established.

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

Publications

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. doi: 10.1016/j.isci.2021.103163. PMID: 34693221; PMCID: PMC8511896.

The role of SAMHD1 in CMV/ HIV coinfections

Prof. Dr. Gramberg

A83 01/2020 - 12/2022

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

HIV patients coinfected with CMV show increased morbidity and mortality, even on therapy. Despite high coinfection rates, surprisingly little is known about molecular interactions of CMV and HIV. We found that CMV blocks the HIV restriction factor SAMHD1 to facilitate its own replication. This finding finally provides a handle to explain how CMV enhances HIV replication in the host. Thus, we will address the working hypothesis that CMV infection boosts HIV replication by inactivating the SAMHD1.

Publications

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

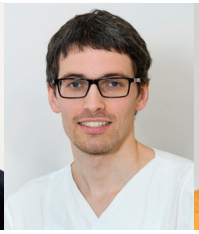
- HCMV coinfection downregulates SAMHD1-mediated restriction of HIV in differentiated THP-1 cells, primary MDMs and MDDCs
- The viral kinase UL97 inhibitor Maribavir potently inhibits HIV infection in CMV-coinfected primary MDM in presence of SAMHD1.
- Maribavir reduces HCMV-dependent phosphorylation SAMHD1.

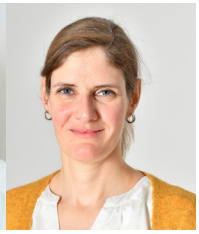
Special methods

- HIV and CMV reporter virus infection of monocyte-derived macrophages and various cell lines
- Kinase activity assays
- Cytokine release assays

Tissue-resident memory T cells in GvHD


Prof. Dr. Hildner


PD Dr. Zundler


Prof. Dr. Büttner-Herold

A84 05/2020 - 05/2023

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Prof. Dr. Maike Büttner-Herold, Department of Nephropathology
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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

Publications

Vonbrunn E, Ries T, Söllner S, Müller-Deile J, Büttner-Herold M, Amann K, Daniel C (2021) Multiplex gene analysis reveals T-cell and antibody-mediated rejection-specific upregulation of complement in renal transplants. Sci Rep.;11(1):15464. doi: 10.1038/s41598-021-94954-3.

Enderle K, Dinkel M, Spath EM, Schmid B, Zundler S, Tripal P, Neurath MF, Hildner K, Neufert C (2021) Dynamic Imaging of IEL-IEC Co-Cultures Allows for Quantification of CD103-Dependent T Cell Migration. Int J Mol Sci.;22(10):5148. doi: 10.3390/ijms22105148.

Müller TM, Becker E, Wiendl M, Schulze LL, Voskens C, Völkl S, Kremer AE, Neurath MF, Zundler S (2021) Circulating Adaptive Immune Cells Expressing the Gut Homing Marker α4β7 Integrin Are Decreased in COVID-19. Front Immunol 12:639329.

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.

The pathophysiology of SAPHO syndrome


Prof. Dr. Hüffmeier

A85 06/2020 - 11/2022

Prof. Dr. Ulrike Hüffmeier, Institute of Human Genetics
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Abstract

SAPHO syndrome is a rare inflammatory disease of the skeleton and skin with unsolved etiology, but suspected causal/ disease-contributing genetic factor(s). We identified several rare *PLXNA1* variants in patients with SAPHO syndrome. We propose to identify the molecular mechanisms by those human variants that lead to disease. Our study will allow to understand the etiology of SAPHO and to pave the way for planned analyses in vertebrates and genetic follow-up studies.

Publications

no project-specific publications so far

Important results

Establishment of a Next Generation Sequencing method to analyze target regions of medium size in intermediate sample sizes (molecular inversion probe-sequencing)

Special methods

- Genotyping of genetic variants in larger patients groups
- Analysis of whole exome sequencing in single patients/ families

Characterization of synovial macrophage subsets

Prof. Dr. Krönke

A86 06/2020 - 06/2023

Prof. Dr. Gerhard Krönke, Department of Medicine 3
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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 - 05/2023

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PD Dr. Ulrike Schleicher, Institute of Microbiology
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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 was identified as main host cell of Leishmania parasites, which we now study in detail. Furthermore, our results help to better define skin mononuclear phagocyte subpopulations. We performed scRNAseq analyses of infected vs non-infected skin cells. Moreover, we showed a 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 nonlymphoid tissues. European journal of immunology. doi: 10.1002/eji.202249819

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. doi: 10.1002/eji.202249925

Cyclin interaction with a CDK-like viral kinase


Prof. Dr. Marschall


Prof. Dr. Sticht

A88 02/2020 - 07/2023

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Prof. Dr. Heinrich Sticht, Institute of Biochemistry - Chair of Biochemistry and Molecular Medicine
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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. Demonstration of primary functional relevance of pUL97-cyclin H interaction using HCMVs carrying deletions in cyclin binding sites, cyclin-KO cells and inhibitory small molecules
2. Generation of drug-resistant HCMVs and cyclin-KO cells
3. Computational assessment of pUL97-cyclin binding interfaces and drug resistance mutations in clinical HCMVs

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, 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

Krämer N, Schütz M, Mato UG, Herhaus L, Marschall M, Zimmermann C (2022) Recombinant Human Cytomegalovirus Expressing an Analog-Sensitive Kinase pUL97 as Novel Tool for Functional Analyses. Viruses 14:2285

Wild M, Hahn F, Brückner N, Schütz M, Wangen C, Wagner S et al. (2022) Cyclin-Dependent Kinases (CDKs) and the Human Cytomegalovirus-Encoded CDK Ortholog pUL97 Represent Highly Attractive Targets for Synergistic Drug Combinations. International journal of molecular sciences 23:2493

CD83 regulates homeostasis and inflammation


Prof. Dr. Steinkasserer

A89 07/2020 - 06/2023

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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.

Important results

A tamoxifen-inducible CX3CR1-CreERT2 system was used to analyze the influence of a microglia-specific CD83 knockout during the course of the neuro-inflammatory disease EAE in mice, showing a drastically aggravated disease severity. Thus, CD83 expression by microglia is absolutely essential for proper resolution of inflammation.

Special methods

- Flow cytometry protocols to analyze microglia and infiltrating monocytes in the CNS
- IHC staining to analyze microglia subpopulations within the CNS
- Tamoxifen-inducible CX3CR1-CreERT2 system to analyze the influence of a microglia-specific CD83 KO during neuro-inflammation
- RNAseq analyses to identify CD83-induced transcriptional changes

Publications

Royzman D, Andreev D, Stich L, Peckert-Maier K, Wild AB, Zinser E et al. (2022) The soluble CD83 protein prevents bone destruction by inhibiting the formation of osteoclasts and inducing resolution of inflammation in arthritis. Frontiers in immunology 13: 936995

Royzman D, Peckert-Maier K, Stich L, König C, Wild AB, Tauchi M et al. (2022) Soluble CD83 improves and accelerates wound healing by the induction of pro-resolving macrophages. Frontiers in immunology 13: 1012647

The fate of lung-resident memory T-cells

Prof. Dr. Tenbusch

A90 01/2020 - 12/2022

Prof. Dr. Matthias Tenbusch, Institute of Clinical and Molecular Virology
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*The project was interrupted from June-Nov 2020 due to staff diagnostic obligations during the ongoing SARS-CoV2 pandemic.

Abstract

In this project, we will analyse the regulatory mechanism for the maintenance of lung-resident memory T-cells. The impact of secondary events of inflammation or infections on the pre-existing immunity will be the major focus. Furthermore, we determine whether the differential induction of the immunity by either a primary infection or a gene-based vaccine might play a role in this context.

Important results

Single-cell RNA sequencing of lung TRM induced either by mucosal adenoviral vector immunization or natural IAV infection revealed differences in the transcriptional profiles and TCR repertoires. In pigs, the quality and quantity of TRM responses depended also highly on the mode of priming confirming our previous data in a large animal model.

Special methods

- Viral respiratory infection models in mice (Influenza, RSV)
- characterization of virus-specific lung T_{RM} by flow cytometry
- In situ pentamer staining in lung tissue

Publications

Irrgang P, Gerling J, Kocher K, Lapuente D, Steininger P, Habenicht K et al. (2022) Class switch towards non-inflammatory, spike-specific IgG4 antibodies after repeated SARS-CoV-2 mRNA vaccination. Science immunology eade2798

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 pre-cursor 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. doi: 10.1371/journal.ppat.1008879.

FRCs and immune tolerance induction

Prof. Dr. Zaiss

A92 09/2020 - 08/2023

Prof. Dr. Mario Zaiss, Department of Medicine 3
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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

Prof. Dr. Jürgen Behrens, Chair of Experimental II – Molecular Oncology
e-mail: juergen.behrens@fau.de

Dr. Dominic Bernkopf, Chair of Experimental II – Molecular Oncology
e-mail: dominic.bernkopf@fau.de

Abstract

Axin is a key negative regulator of the oncogenic Wnt/beta-catenin pathway scaffolding the beta-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 refactory to upstream inhibition by Dvl2 indicating a novell layer of regulation in the Wnt pathway.

Special methods

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

Publications

Miete C, Solis GP, Koval A, Brückner M, Katanaev VL, Behrens J et al. (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

Prof. Dr. Anja Bosserhoff, Institute of Biochemistry - Chair of Biochemistry and Molecular Medicine

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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. Dietrich

D32 03/2020 - 02/2023

PD Dr. Peter Dietrich, Department of Medicine 1

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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

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. Molecular cross-talk between Y5-receptor and neuropeptide Y drives liver cancer. J Clin Invest.2020 May 1;130(5):2509-2526.

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. 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. doi: 10.1016/j.neo.2021.04.001

Fritz V, Malek L, Gaza A, Wormser L, Appel M, Kremer AE, Thasler WE, Siebler J, Neurath MF, Hellerbrand C, Bosserhoff AK, Dietrich P. 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. 2021 Mar 9;13(5):1183.

Immunometabolism in CML


Prof. Dr. Metzler


Prof. Dr. Mougiakakos

D33 05/2020 - 06/2023

Prof. Dr. Markus Metzler, Department of Paediatric and Adolescent Medicine
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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

no project-specific publications so far

Important results

- Combining oxPhos-inhibitors oligomycin and 8-chloro-adenosine or ER-stress-inducer thapsigargin with imatinib increases CML cell death
- Oligomycin and thapsigargin trigger UPR-upregulation which is inhibited by imatinib
- Imatinib combined with oligomycin, thapsigargin or 8-Cl-Ado trigger upregulation of caspases 3/8 and increases cleavage of PARP

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


PD Dr. Ramming


Prof. Dr. Stürzl

D34 05/2020 - 07/2023

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Prof. Dr. Michael Stürzl, Department of Surgery
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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, doi.org/10.1002/path.5860

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

Interactions of DPF3 and hypoxia in renal cancer

PD Dr. Schödel

D35 07/2020 - 12/2022

PD Dr. Johannes Schödel, Department of Medicine 4
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Abstract

The renal cancer risk SNP on chromosome 14q24.2 creates a novel Hypoxia inducible transcription factor (HIF)-binding DNA element in an intronic region of the DPF3 gene, a member of the SWI/SNF chromatin remodelling complex. DPF3 is upregulated in a SNP- and HIF-dependent fashion in renal tubular cells. We investigate the regulation of DPF3 in renal cells and cancer as well as its contribution to global chromatin status and transcription factor binding to critical DNA regions.

Publications

Protze J, Naas S, Krüger R, Stöhr C, Kraus A, Grampp S et al. (2022) The renal cancer risk allele at 14q24.2 activates a novel hypoxia-inducible transcription factor-binding enhancer of DPF3 expression. The Journal of biological chemistry 298: 101699

Important results

In tumor cells as well as in renal tubular cells, in which HIF was stabilized, we determined genotype-specific increases of DPF3 mRNA. The risk SNP creates a novel HIF-binding enhancer. HIF-mediated DPF3 regulation was dependent on the risk allele. DPF3 deletion in tubular cells retarded cell growth, indicating roles for DPF3 in cell proliferation.

Special methods

We used tissue specimens and primary renal cells from a cohort of RCC patients. We have established ATAC-seq experiments which allows for the identification of open chromatin and regulatory DNA-elements on a genome-wide scale. We also use allele-specific assays to interrogate functional effects of polymorphisms on gene regulation.

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.

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

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

Neural Crest Regulators In Orofacial Clefting


Prof. Dr. Gölz


Prof. Dr. Wegner

E28 07/2020 - 07/2023

Prof. Dr. Lina Gölz, Department of Orthodontics and Orofacial Orthopedics
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Prof. Dr. Michael Wegner, Institute of Biochemistry - Chair of Biochemistry and Pathobiochemistry
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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

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 - Chair of Biochemistry and Molecular Medicine
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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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Prof. Dr. Jürgen Winkler, Department of Molecular Neurology
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Abstract

Recent data demonstrate profound immunological alterations 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.

Special methods

- Development of standardized models to generate human IPSC-derived neurons and myeloid cells
- Autologous co-culture system of iPSC derived neurons with immune cells (2D, 3D)
- Analysis of aberrant alternative splicing in human in vitro systems

Important results

We have intensively delineated stimuli, that impact immun-mediated alterations in Parkinson disease (PD) (e.g. Battis et al., 2022) and investigated interactions between the intestinal and the nervous system in the context of degenerative diseases. These strategies will allow to define new compounds for treatment.

Publications

Krach F, Stemick J, Boerstler T, Weiss A, Lingos I, Reischl S et al. (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 et al. (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 et al. (2022) CSF1R-Mediated Myeloid Cell Depletion Prolongs Lifespan But Aggravates Distinct Motor Symptoms in a Model of Multiple System Atrophy. The Journal of neuroscience : the official journal of the Society for Neuroscience 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

no project-specific publications so far

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. 2021 Aug 15;134(16):jcs259013. doi: 10.1242/jcs.259013.

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

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

Publications

no project-specific publications so far

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

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

Cytosolic citrate metabolism in IEC

Prof. Dr. Becker

A93 not started yet

Prof. Dr. Christoph Becker, Department of Medicine 1
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Newly granted

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.

Special methods

- Models of experimental inflammation
- Metabolome analyses
- Methods of cell death research

SARS-CoV-2 host adaptation

Prof. Dr. Ensser

A94 not started yet

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

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.

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 not started yet

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

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.

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 - 06/2025

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

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.

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. Single-cell RNA analysis pipelines for B-cell receptor as well as T-cell receptor analysis

STAT3 in IMCs during mucosal healing in IBD

Prof. Dr. Dr. Neufert

A97 not started yet

Prof. Dr. Dr. Clemens Neufert, Department of Medicine 1
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Newly granted

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.

Special methods

- Live cell imaging of gut cell populations
- Co-culture systems with intestinal mesenchymal cells and intestinal epithelial organoids and/or immune cells
- Experimental models of intestinal mucosal healing

RA-T

PD Dr. Schober

A98 not started yet

PD Dr. Kilian Schober, Institute of Microbiology
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Newly granted

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.

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

Dr. Steffen

A99 not started yet

Dr. Ulrike Steffen, Department of Medicine 3
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Newly granted

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.

Special methods

- Bone formation rate measurement with (lightsheet) microscopy
- Various mouse models of loading, unloading and bone loss
- Bone matrix analysis with scanning electron microscopy

sCD83 induces would healing

Prof. Dr. Steinkasserer

A100 not started yet

Prof. Dr. Alexander Steinkasserer, Department of Immune Modulation
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Newly granted

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.

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 not started yet

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Newly granted

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.

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 not started yet

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Prof. Dr. Jochen Guck, Department of Physics - Chair of Biological Optomechanics
email: jochen.guck@mpl.mpg.de

Newly granted

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.

Special methods

- Real-time deformability cytometry to analyze mechanical properties of immune cells (incl. fluorescence detection and sorting capabilities)
- In vivo evaluation of mechanical cell properties in murine colitis models
- In vitro evaluation of immune cell mechanics in correlation with effector function, migration, transcriptomics etc.

Secretory IgA molecules in intestinal immunity

PD Dr. Weigmann

A103 not started yet

PD Dr. Benno Weigmann, Department of Medicine 1
e-mail: benno.weigmann@uk-erlangen.de

Newly granted

Abstract

Intestinal disorders (IBD) are chronic inflammations of the gastrointestinal tract. Secretory antibodies (SIgA) are produced at the mucosal surface and represent a defence mechanism of the intestine. In one approach, we will look at the secretion of SIgA antibodies in the serum of IBD patients and correlate it with the disease severity. Furthermore, the project aims to elucidate the role of SIgA in the uptake/retrieval process at the endothelium by use of experimental colitis models.

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.

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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Newly granted

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.

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

ACLY in IBD-associated cancer

PD Dr. Atreya

D37 not started yet

PD Dr. Imke Atreya, Department of Medicine 1
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Newly granted

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.

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 not started yet

Prof. Dr. Anja Bosserhoff, Institute of Biochemistry - Chair of Biochemistry and Molecular Medicine
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Newly granted

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.

Special methods

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

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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Newly granted

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.

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 not started yet

PD Dr. Dr. Peter Dietrich, Department of Medicine 1
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Newly granted

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.

Special methods

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

Therapy resistance in urothelial cancer


Prof. Dr.Engel


Dr. Eckstein

D41 not started yet

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Dr. Markus Eckstein, Institute of Pathology
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Newly granted

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.

Special methods

- Biomarker identification
- Zebrafish xenograft/co-injection model
- Lentivirus-mediated knockdown and overexpression

PSAP in liver steatosis-triggered liver cancer


Dr. Hellerbrand

D42 not started yet

Prof. Dr. Claus Hellerbrand, Institute of Biochemistry
Chair of Biochemistry and Molecular Medicine
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Newly granted

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.

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 not started yet

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

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.

Special methods

- scRNA/TCR sequencing
- Analysis of immune cells using high-dimensional flow cytometry
- Cytotoxicity and signaling assays

Molecular nexuses in neurodevelopmental diseases


Dr. Falk

E32 not started yet

Dr. Sven Falk, Institute of Biochemistry - Chair of Biochemistry and Pathobiochemistry
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Newly granted

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.

Special methods

- Human iPSC based brain organoids modeling early brain development
- Combining pooled genetic perturbation with single cell RNAseq
- Patient derived iPSC

Deubiquitinase Otud7b in CNS myelination

Dr. Küspert

E33 not started yet

Dr. Melanie Küspert, Institute of Biochemistry
Chair of Biochemistry and Pathobiochemistry
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Newly granted

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.

Special methods

- Analysis of specific marker expression in Ctrl and Otud7bcko CNS tissue (immunohistochemistry, in situ hybridization)
- Characterization of the Otud7b upstream regulatory network (reporter gene assay, electrophoretic mobility shift assay)
- Characterization of the Otud7b interactome in oligodendrocytes (Co-immunoprecipitation, mass-spectrometry)

Regulation of the adul CNS stem cell niche

Prof. Dr. Lie

Prof. Dr. Franze

E34 not started yet

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Prof. Dr. Kristian Franze, Institute of Medical Physics
email: kristian.franze@fau.de

Newly granted

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.

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 not started yet

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Prof. Dr. Peter Soba, Institute of Physiology and Pathophysiology
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Newly granted

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.

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 not started yet

Dr. Andreas Sagner, Institute of Biochemistry - Chair of Biochemistry and Pathobiochemistry
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Newly granted

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.

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

Newly granted


Prof. Dr. Wegner


Prof. Dr. Fejtova

E37 02/2023 - 07/2025

Prof. Dr. Michael Wegner, Institute of Biochemistry - Chair of Biochemistry and Pathobiochemistry
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Prof. Dr. Anna Fejtova, Department of Psychiatry and Psychotherapy
e-mail: anna.fejtova@uk-erlangen.de

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.

Special methods

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

Funded research groups in 2022:

No.	Name	Institution	Project title
N2	Prof. Dr. David Dulin	IZKF-NW 2	Physics and Medicine
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	Chair of Biochemistry and Pathobiochemistry	Forging neural cell identity
N8	Prof. Dr. Friederike Zunke	Department of Molecular Neurology	Lysosomes & glial cells

Prof. Dr. Dulin

Prof. Dr. David Dulin

N2 09/2016 - 08/2022

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Summary

We develop single-molecule force and fluorescence spectroscopy assays to investigate genome expression, maintenance and replication in cells and RNA viruses. Specifically, we interrogate the mechanism of human mitochondria transcription termination directed by MTERF1, the determinants of RNA polymerase 1 (RNAP1) transcription initiation, i.e. the rate limiting step in rRNA synthesis, and the composition and function of the SARS-CoV-2 replication-transcription complex during viral RNA synthesis.

Important results

- We developed a new assay to monitor the SARS-CoV-2 replication-transcription complex (RTC, the main antiviral drug target against coronaviruses) at near single nucleotide resolution, revealing its nucleotide addition cycle (Bera, Seifert, et al. Cell Rep. 2021).
- We applied this assay to evaluate the mechanism of action of several antiviral nucleotide analogs on SARS-CoV-2 RTC, discovering the real mechanism of action of Remdesivir (Bera, Seifert, et al., eLife 2021) **(Figure 1)**.

Special methods

- Custom high-throughput/resolution magnetic tweezers to investigate protein-nucleic acids interactions, e.g. SARS-CoV-2 replication-transcription complex **(Figure 1)**.
- Correlated high-throughput magnetic tweezers-fluorescence microscope to image and mechanically probe protein-nucleic acid interactions **(Figure 2)**.
- Novel methods to fabricate nucleic acids construct for single-molecule biophysics.

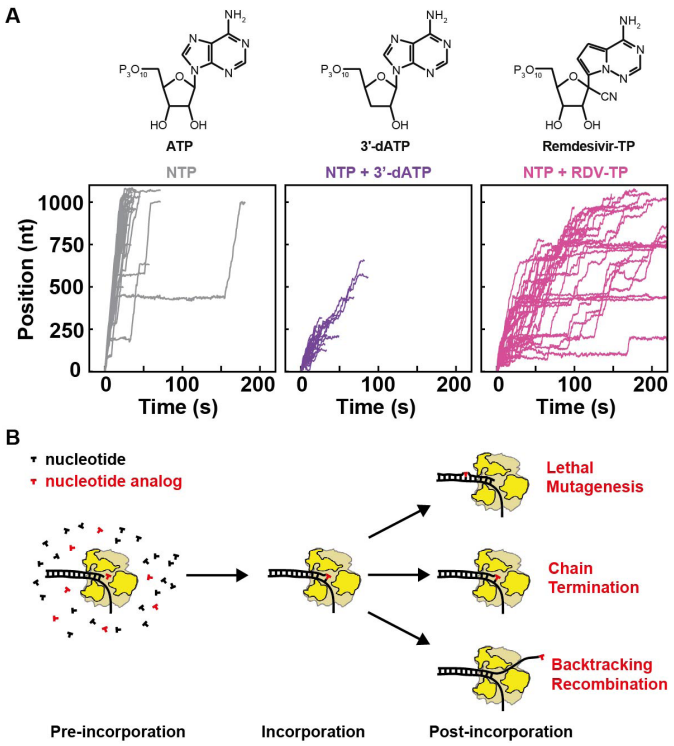

Figure 1: SARS-CoV-2 RTC antiviral nucleotide analog targeting. (A) RNA synthesis dynamics of SARS-CoV-2 RTC in the presence of NTP only, NTP+3'-dATP and NTP+Remdesivir-TP. (B) Antiviral nucleotide analogs mechanism of actions revealed using magnetic tweezers: lethal mutagenesis (e.g. ribavirin, molnupiravir), chain termination (e.g. 3'-dATP), backtracking and recombination (e.g. T-1106, remdesivir).

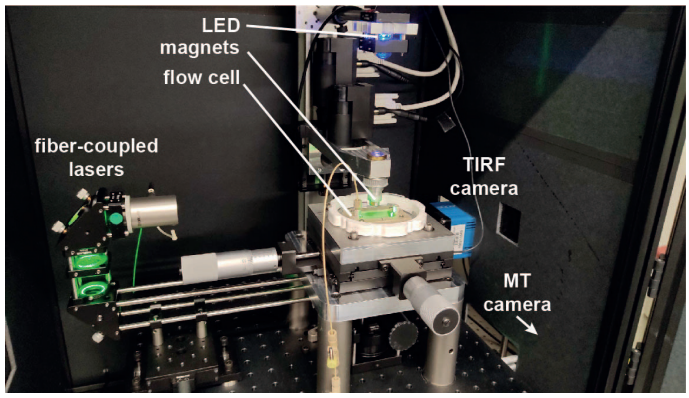

Figure 2: Correlative high-throughput magnetic tweezers-fluorescence microscope.

Publications (selection of)

Bera SC, America PPB, Maatsola S, Seifert M, Ostrofet E, Cnossen J, Spermann M, Papini FS, Depken M, Malinen AM and Dulin D (2022) Quantitative parameters of bacterial RNA polymerase open-complex formation, stabilization and disruption on a consensus promoter. Nucleic Acids Research, 50:13, 7511–7528, gkac560

Seifert M, Bera SC, van Nies P, Kirchdoerfer RN, Shannon A, Le TTN, Meng X, Xia H, Wood JM, Harris LD, Papini FS, Arnold JJ, Almo SC, Grove TL, Shi P-Y, Xiang Y, Canard B, Depken M, Cameron CE, and Dulin D (2021) Inhibition of SARS-CoV-2 polymerase by nucleotide analogs: a single molecule perspective. eLife, 10:e70968

Bera SC, Seifert M, Kirchdoerfer RN, van Nies P, Wubulikasimu Y, Quack S, Papini FS, Arnold JJ, Canard B, Cameron CE, Depken M and Dulin D (2021) The nucleotide addition cycle of the SARS-CoV-2 polymerase. Cell Reports, 36 (10), 109650

Seifert M, van Nies P, Papini FS, Arnold, JJ, Poranen MM, Cameron CE, Depken M, Dulin D (2020) Temperature controlled high-throughput magnetic tweezers show striking difference in activation energies of replicating viral RNA-dependent RNA polymerases. Nucleic Acids Research, 48:10, 5591-5602, gkaa233

Papini FS, Seifert M, Dulin D (2019) High-yield fabrication of DNA and RNA constructs for single molecule force and torque spectroscopy experiments. Nucleic Acids Research, gkz851

Research Focus

The Dulin lab develops high-end microscopes to investigate the fundamental processes involved in the central dogma of molecular biology, i.e. replication, transcription and translation, using single-molecule force and fluorescence spectroscopy techniques. Each step during gene expression involves complex molecular motors, such as polymerases and helicases. Much has been learned related to these motors using standard ensemble biochemical assay, but their detailed kinetic characterization remains elusive. Indeed, these enzymes do not progress linearly along their template, but rather through burst of fast catalytic reactions interrupted by slower events, e.g. co-factors binding, misincorporation, template sequence, which originates from parallel reaction pathways or transient pauses that affect both gene expression and the organism phenotype. By accessing the reactions at the single molecule level, one is capable to interrogate these rare and transient events and reveal their role in gene expression. The single-molecule microscopy techniques our lab develop, such as magnetic tweezers and fluorescence microscopy, enable such observation, and we specifically look into how (1) SARS-CoV-2 replicates its genome and how (2) cells transcribe their genomes.

1- RNA virus replication mechanism

Humankind is currently living through the third and – by far – the largest coronavirus pandemic in the 21st century, i.e. SARS-CoV-2, which has greatly impacted our economy and way of life. While vaccines now exist, we are still in need of high efficacy and specificity drugs to cure infected patients and to act swiftly against future outbreak. Our lab investigates how the multiprotein large SARS-CoV-2 replication transcription complex (RTC) processes and synthesizes the many different viral RNA produced during the cell infection. Using our unique approach, we revealed the nucleotide addition cycle of SARS-CoV-2 RTC, and the mechanism of action of several antiviral drugs targeting the RTC, such as remdesivir (Figure 1). From these foundational successes, we now further explore the RTC dynamic composition and function, and we have been invited to join international consortia to assist the rational design of new antivirals targeting CoV and other RNA viruses.

2- Cellular transcription

Transcription is at the heart of gene expression and maintenance any every organism. Our lab works on three different transcription systems: Escherichia coli (E. coli) bacteria, human mitochondria and yeast RNA polymerase I (Pol I). Bacterial transcription from E. coli is the most studied and therefore a model system of cellular transcription. We specifically investigate the mechanisms of bacterial transcription initiation, the most regulated step in transcription and gene expression. Eukaryotic systems also are of great interest, such as for human mitochondria transcription regulation and the eukaryotic RNAP I (transcribes ribosomal DNA), though their biochemistry is much less studied in vitro. We use single-molecule magnetic tweezers and fluorescence spectroscopy assays to investigate how mitochondria transcription is terminated and how RNAP1 initiates transcription.

Third-party funding

Dutch Research Council (NWO) OCENW.M.21.184 Open Competition Domain Science – M: Revealing how MDA5 interrogates RNA to signal viral infection and trigger innate immunity. €359k, including 1 PhD position, consumables and equipment. 4 years duration, starting in March 2023. Role: Lead Principal Investigator (PI).

NWO OCENW.XL21.XL21.115 Open Competition Domain Science – XL: Know your enemy: deciphering coronavirus biochemical cycles from RNA synthesis to assembly. Consortium of 8 PIs, with a total funding of €3,032k. Dr. Dulin lab receives €800k to fund 1 PhD, 1 Postdoc and 1 technician positions, consumables and equipment. 5 years duration, starting in January 2023. Role: Lead PI.

National Institute of Health (NIH), NIAID U19 AI171421 Antiviral Drug Discovery (AViDD): Rapidly Emerging Antiviral Drug Development Initiative - AViDD Center. US$945k, including two positions and consumables. 5 years duration, started in May 2022. Role: co-applicant.

NIH NIAID U19 AI171292 AViDD: Development of Outpatient Antiviral Cocktails against SARS-CoV-2 and other Potential Pandemic RNA Viruses. US$945k, including two positions and consumables. 5 years duration, started in May 2022. Role: co-applicant.

NIH R01AI161841-01: Coronavirus replication. US$600k, including 1.5 position and consumables. 5 years duration, started in March 2021. Role: Co-applicant.

DFG DU1872/5-1: Determinants and dynamics of RNA polymerase I transcription initiation. €276.3k, including 2.5 years postdoc salary and consumables. 30 months duration, started July 2021. Role: lead PI.

DFG DU1872/4-1: Revealing the mechanism of nucleotide selection, addition and proofreading of the SARS-CoV-1 replication transcription complex at the single molecule level. €221.6k, including 2 years postdoc salary and consumables. 24 months duration, started August 2021. Role: lead PI.

DFG DU1872/3-1: Revealing the mechanism of directional transcription termination at the single-molecule level for the human mitochondrial transcription complex. €276.6k, including 2.5 years postdoc salary and consumables. 30 months duration, started February 2020. Role: lead PI.

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

Current research has attributed the powerful microbial impact on the host organism to bacterial-derived biomolecules transferred to mammalian host cells. We recently uncovered that outer-membrane vesicles (OMVs) released by microbes can serve as a communication tool to maintain and modulate microbe-host interaction in the gut and far beyond.

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

Günther C, Winner B et al. (2022) Organoids in gastrointestinal diseases: from experimental models to clinical translation Gut Sep;71(9):1892-1908.

Bittel M, et al. (2021) Visualizing transfer of microbial biomolecules by outer membrane vesicles in microbe-host-communication in vivo. J Extracell Vesicles. 2021 Oct;10(12):e12159.

Rare glomerular diseases

Prof. Dr. Müller-Deile

N6 04/2021 – 03/2024

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 rare glomerular diseases. Therefore, we use 3D glomerular co-culture, the zebrafish model and mouse model. We speculate that autophagy and exosome secretion are linked by endolysosomal pathways and are dysregulated in membranous glomerulonephritis. We use Raman spectroscopy, mass spectroscopy and our zebrafish model to get a molecular fingerprint in primary 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 in membranous glomerulonephritis.
- Glomerular endothelial cell-derived miRNA-200c impairs glomerular homeostasis by targeting podocyte VEGF-A.
- miRNA-378a increases podocyte autophagy flux by targeting the mTOR-pathway

Special methods

- 3D glomerular co-culture model
- Different transgenic zebrafish models
- Autophagy flux assay

Publications

Ursu R, Sopel N, Ohs A, Tati, R, Buvall, L., Nyström, J, Schiffer, M. Müller-Deile J (2022). Glomerular Endothelial Cell-Derived miR-200c Impairs Glomerular Homeostasis by Targeting Podocyte VEGF-A. Int J Mol Sci. 23(23):15070.

Sopel N, Ohs A, Schiffer M, Müller-Deile J (2022) A tight control of non-canonical TGF-β 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 – 06/2024

Prof. Dr. Marisa Karow, Institute of Biochemistry - Chair of Biochemistry and Pathobiochemistry

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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 therefore dissected the molecular framework underlying successful pericyte-to-iN conversion by performing single cell RNA-sequencing and identified a candidate putatively involved not only in pericyte-to-iN reprogramming but also normal human neurogenesis.

Publications

no project-specific publications so far

Important results

- Cloning of a loss-of-function (LOF) platform allowing Dox-inducible perturbation of genes of interest in human induced pluripotent stem cells (hiPSC)
- Generation of genome-edited hiPSCs stably carrying the LOF platform
- Construction of lentiviral vectors expressing specific gRNAs to manipulate candidate gene expression in the LOF hiPSCs

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

Lysosomes & glial cells

Prof. Dr. Zunke

N8 02/2021 – 02/2024

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 degradation is crucial for glial cell function, this project aims to analyze the reciprocal effects of lysosomal (dys)function under pathological conditions (α-synuclein aggregation). A better understanding of lysosomal turnover in glial cells will help to unravel molecular mechanisms and the search for novel therapeutic strategies in PD.

Important results

1. Establishment and stable differentiation of human iPS cells to oligodendrocytes as well as an oligodendroglial cell line overexpressing PD-associated protein α-synuclein
2. Oligodendrocytes harboring high α-synuclein level show changes in the lysosomal system
3. Lysosomal function was targeted to decrease pathological α-synuclein

Special methods

1. Analyses of lysosomes/autophagy: lysosomal enrichments, enzyme maturation and activities (Cathepsins, b-Glucocerebrosidase etc), pH measurements
2. Induced pluripotent stem cells & differentiation protocols (neurons & oligodendrocytes)
3. Preparation of recombinant protein (lysosomal enzymes, α-synuclein etc.)

Publications

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.

Socher E, Heger L, Paulsen F, Zunke F, Arnold P (2022) Molecular dynamics simulations of the delta and omicron SARS-CoV-2 spike - ACE2 complexes reveal distinct changes between both variants. Comput Struct Biotechnol J. 20:1168-1176.

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.

Funded junior projects in 2022:

No.	Name	Institution		Project title
J76	Dr. Katerina Kachler	Department of Medicine 3	I	The role of itaconate in osteoclasts
J77	Dr. René Pfleifle	Department of Medicine 3	I	Characterization of autoreactive B cells during RA
J78	Dr. Barbara Ruder	Department of Medicine 1	I	Role of ferroptosis during microbial infection
J79	Dr. Christian Schwartz	Clin. Microbiology, Immunology and Hygiene	I	PD-L1 function during obesity and dysbiosis
J81	Prof. Dr. Samir Jabari	Institute of Neuropathology	M	Web based Brain Tumor Image Classifier (WeB-TIC)
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
J86	Dr. Heike Knott	Department of Medicine 1	I	Virome/macrophage interaction in Crohn's disease
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	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	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	Chair of Biochemistry and Pathobiochemistry	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
J98	Dr. Alina Hilger	Department of Pediatrics and Adolescent Medicine	R	Detecting disease genes in urorectal malformations
J99	Dr. Miriam Düll	Department of Medicine 1	N	Reactive carbonyls in metabolic diseases
J100	Dr. Dennis Lapuente	Institute of Clinical and Molecular Virology	O	Mucosal vaccination against lung metastases
J101	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

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

The role of itaconate in osteoclasts

Dr. Kachler

J76 10/2019 - 04/2022

Dr. Katerina Kachler, Department of Medicine 3

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Abstract

The maintenance of healthy bone relies on a balance between bone formation by osteoblasts and bone resorption by osteoclasts. Recent findings indicate that the differentiation and function of osteoclasts can be regulated by certain changes in the cellular metabolism. Accordingly, we demonstrated that the metabolite itaconate inhibits osteoclastogenesis. The major aim of the presented project is the investigation of molecular mechanisms underlying this function of itaconate.

Publications

Andreev D, Liu M, Kachler K, Llerins Perez M, Kirchner P, Kölle J, Gießl A, Rauber S, Song R, Aust O, Grüneboom A, Kleyer A, Cañete JD, Ekici A, Ramming A, Finotto S, Schett G, Bozec A. Regulatory eosinophils induce the resolution of experimental arthritis and appear in remission state of human rheumatoid arthritis. Ann Rheum Dis. 80(4):451-468

Andreev D, Liu M, Weidner D, Kachler K, Faas M, Grüneboom A et al. (2020) Osteocyte necrosis triggers osteoclast-mediated bone loss through macrophage-inducible C-type lectin. The Journal of clinical investigation 130: 4811-4830

Important results

- Rheumatoid arthritis is associated with increased glycolytic activity in osteoclast precursors
- Itaconate suppresses osteoclastogenesis by inhibiting glycolysis in a ROS and Hif1α-dependent manner
- Itaconate-deficiency enhances bone loss in K/BxN serum induced arthritis,while in vivo treatment with an itaconate-derivative ameliorates the disease

Special methods

- In vitro cell differentiation of murine osteoclasts form bone marrow-derived monocytes and human osteoclasts from peripheral blood mononuclear cells
- Analysis of the metabolic state of in vitro cultured osteoclasts using extracellular flux assays (Agilent Seahorse XF Analyzer)
- CRISPR/Cas9-mediated gene editing in in vitro cultured osteoclasts

Characterization of autoreactive B cells during RA

Dr. Pfeifle

J77 11/2019 - 04/2022

Dr. René Pfeifle, Department of Medicine 3
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IMMUNOLOGY AND INFECTION

Abstract

Rheumatoid arthritis is a common autoimmune disease. Anti-citrullinated-protein antibodies (ACPAs) have been identified as key players in RA. But a better understanding of the ACPA-producing B cells and of the transcriptional events in ACPA-specific B cells during the onset of RA is essential. Therefore, we plan to perform an in depth molecular characterization of the dynamic changes occurring inside the ACPA-specific B cell compartment during different phases of RA pathogenesis.

Publications

no project-specific publications so far

Important results

Characterization of autoreactive B cells showed that ACPA+ B cells have a class-switched phenotype in pre-RA & RA patients. In contrast, ACPA+ cells in healthy individuals have a naïve B cell phenotype. Expanded clonotypes were identified and shown to be enriched in ACPA+ B cells.

Special methods

Flow-cytometry-based characterization of antigen-specific B cells. CITE-seq with B cell repertoire sequencing of sorted autoreactive B cells and non-autoreactive B cells from RA patients, asymptomatic ACPA+ (pre-RA) individuals, and healthy controls.

Role of ferroptosis during microbial infection

Dr. Ruder

J78 10/2019 - 02/2022

Dr. Barbara Ruder, Department of Medicine 1

IMMUNOLOGY AND INFECTION

Abstract

In this project, we aim to investigate the role of the Gluthathione peroxidase GPX4 and ferroptosis in macrophages under steady state conditions and during acute Salmonella infection. We hypothesize that GPX4-regulated ferroptotic cell death plays an important role during bacterial infection and might display a new therapeutic target for treatment of acute infections. In this part of the project, we analyzed ferroptosis and GPX4 activity in different experimental settings.

Important results

In this part of the project, we identified inhibitors, which were able to block ferroptosis in macrophages in vitro. Moreover, we observed that reduction of the GPX4 activity during maturation of macrophages influenced the activation profile of these cells. In addition, we established an experimental setting to detect ferroptosis by flow cytometry.

Special methods

Flow cytometry, LDH-assay, mouse infection models

Publications

Ruder B, Günther C, Stürzl M, Neurath MF, Cesarman E, Ballon G et al. (2020) Viral Flip blocks Caspase-8 driven apoptosis in the gut in vivo. PLoS One 15(1): e0228441

Bardenbacher M, Ruder B, Britzen-Laurent N, Naschberger E, Becker C, Palmisano R et al. (2020) Investigating Intestinal Barrier Breakdown in Living Organoids. J Vis Exp 26;(157)

PD-L1 function during obesity and dysbiosis


Dr. Schwartz

J79 09/2019 - 02/2022

IMMUNOLOGY AND INFECTION

Dr. Christian Schwartz, Institute of Clinical Microbiology, Immunology and Hygiene
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Abstract

Obesity has become one of the leading global health concerns. Current research suggests a link between obesity, PD-L1 and the microbiome. This project will investigate the role of the microbiome on the function the regulation of adipose tissue T cell responses mediated by innate expression of PD-L1 in mice and humans. Using state-of-the-art RNA and 16S rRNA sequencing, flow cytometry and co-culture systems, we will reveal important mechanisms for the control of adipose tissue inflammation.

Important results

- Adipose tissue dendritic cells limit T cell-mediated inflammation via PD-L1:PD-1-interaction
- PD-L1-expression in human adipose tissue is increased during obesity
- Obesity promotes skin-barrier breakdown, which leads to increased susceptibility for allergic inflammation

Special methods

- Flow cytometry, cell sorting and ex vivo culture of mouse and human ILC2
- Animal model of diet-induced obesity and analysis of human adipose tissue
- Conditional deletion of PD-L1 on various immune cell populations

Publications

Schwartz C, Schmidt V, Deinzer A, Hawerkamp HC, Hams E, Bayerlein J et al. (2022) Innate PD-L1 limits T cell-mediated adipose tissue inflammation and ameliorates diet-induced obesity. Science translational medicine 14: eabj6879

Saunders SP, Floudas A, Moran T, Byrne CM, Rooney MD, Fahy CMR, Geoghegan JA, Iwakura Y, Fallon PG, Schwartz C (2020) Dysregulated skin barrier function in Tmem79 mutant mice promotes IL-17A-dependent spontaneous skin and lung inflammation. Allergy 75:3216–3227

Web based Brain Tumor Image Classifier (WeB-TIC)


Prof. Dr. Jabari

J81 01/2020 - 06/2022

MEDICAL ENGINEERING

Prof. Dr. Samir Jabari, Institute of Neuropathology
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Abstract

Low-grade epilepsy-associated brain tumours (LEAT) are rare entities with poor interobserver histopathology agreement. The WHO has established an integrated genotype- phenotype classification for most brain tumor entities, but not LEAT. Bioinformatical deep learning algorithms have proven success in extracting such genotype- phenotype information from histopathology slides. Our research proposal evolves around this innovative approach in order to provide diagnostically useful imaging biomarkers.

Important results

DNA methylation-based MCD classification is suitable across major histopathological entities amenable to epilepsy surgery and will help establish an integrated diagnostic classification scheme for epilepsy-associated MCD. CNNs extract neuropathologically relevant information from the WSI and our library facilitated working with slide collections.

Special methods

We present a retrospective, multi-center analysis of genome-wide DNA methylation from human brain specimens obtained from epilepsy surgery using a self written library for EPIC 850 K BeadChip array analysis open to the public. We developed a whole-Slide Image Managing Library Based on Fastai for Deep Learning in the Context of Histopathology.

Publications

Neuner C, Coras R, Blümcke I, Popp A, Schlaffer SM, Wirries A, Buchfelder M, Jabari S (2022) A Whole-Slide Image Managing Library Based on Fastai for Deep Learning in the Context of Histopathology: Two Use-Cases Explained. Appl. Sci. 2022, 12, 13

Jabari S, Kobow K, Pieper T, Hartlieb T, Kudernatsch M, Polster T et al. (2022) DNA methylation-based classification of malformations of cortical development in the human brain. Acta neuropathologica 143:93-104

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

- Successful identification of sensitive tyrosine-based sorting (TBS) motifs that affect indirect antigen presentation of human DBY in two cell lines
- Pharmacologic inhibition of target structures associated with TBS motifs affect indirect antigen presentation of DBY
- Results suggest a role of adaptor protein complexes in 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 - 05/2023

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

no project-specific publications so far

Important results

- Newly generated mice with conditional defective IL36R signaling ($IL36R^{\Delta Fibro}$) in fibroblasts were used in a model of chronic intestinal inflammation and fibrosis
- $IL36R^{\Delta Fibro}$ mice showed reduced inflammation and fibrosis
- We detected diminished accumulation of activated fibroblasts and immune cells e.g. F480+ macrophages and CD4+ T cells

Special methods

- 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
- Characterization of intestinal fibroblasts by scRNAseq from mice and human

Virome/macrophage interaction in Crohn's disease


Dr. Knott

J86 01/2021 - 06/2022

Dr. Heike Knott, Department of Medicine 1
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IMMUNOLOGY AND INFECTION

Abstract

We aim to investigate the composition of the gut virome as a marker for resistance against anti-TNF therapy in Crohn's disease patients. We will functionally characterize the interaction of identified viruses with mucosal CD14+ macrophages. In particular, we will analyze mechanisms of increased mucosal IL23R expression and IL-23 production that mediate molecular resistance to anti-TNF therapy in Crohn's disease, to finally elucidate a signaling pathway that determine non-response to therapy.

Publications

no project-specific publications so far

Important results

1. Different identified viruses are able to induce IL23 expression in CD anti-TNF non-responders
2. The release of IL23 is TLR9 dependent and increases the expression of IL23R on intestinal macrophages from CD anti-TNF non-responders
3. IL23R expression is upregulated during in vitro generation of intestinal macrophages after IL23 stimulation

Special methods

1. Growing and maintaining of 3D human intestinal and colonic organoids
2. Characterization of human intestinal macrophages
3. Viral metagenomics analysis

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

We have found that the cellular architecture of (any) tissue can be represented as a physical network that provides a hardwired signaling grid for interconnected cells. Tissue homeostasis is related to functional network communication and can be temporarily disrupted during inflammation and even chronically damaged during inflammatory injury.

Special methods

- Intravital imaging
- Whole mount tissue imaging
- 3D-reconstruction and quantitative histocytometry

New RNA-binding proteins in sporadic ALS

Dr. Krach

J88 11/2020 - 05/2023

NEUROSCIENCES

Dr. Florian Krach, Department of Stem Cell Biology
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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

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

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

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

MSOT imaging of strictures in Crohn's disease

Dr. Regensburger

J89 01/2021 - 09/2023

MEDICAL ENGINEERING

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

In collaboration with Prof. Bohndiek (Cambridge University), we developed a guided RSOM that allows precise visualization and quantification of murine colitis.

We further investigated the oral application of ICG in humans for non-invasive radiation-free visualization of the gastrointestinal transit by MSOT.

Special methods

- Raster-scanning optoacoustic Mesoscopy (RSOM) allows visualisation of murine vascular networks (axial resolution 10-20µm)
- Multispectral optoacoustic Tomography (MSOT) allows cross-sectional imaging of dedicated chromophores such as hemoglobin (spatial resolution <150µm)

Publications

Tascilar K, Fagni F, Kleyer A, Bayat S, Heidemann R, Steiger F, Krönke G, Bohr D, Ramming A, Hartmann F, Klett D, Federle A, Regensburger AP, Wagner AL, Knieling F, Neurath MF, Schett G, Waldner M, Simon D. (2022) Non-invasive metabolic profiling of inflammation in joints and entheses by multispectral optoacoustic tomography. Rheumatology (Oxford) 14:keac346

Goebel CA, Brown E, Fahlbusch FB, Wagner AL, Buehler A, Raupach T, Hohmann M, Späth M, Burton N, Woelfle J, Schmidt M, Hartner A, Regensburger AP, Knieling F. (2022) High-resolution label-free mapping of murine kidney vasculature by raster-scanning optoacoustic mesoscopy: an ex vivo study. Molecular and cellular pediatrics 9:13

Regensburger AP, Wagner AL, Danko V, Jüngert J, Federle A, Klett D, Schuessler S, Buehler A, Neurath MF, Roos A, Lochmüller H, Woelfle J, Trollmann R, Waldner MJ, Knieling F. (2022) Multispectral optoacoustic tomography for non-invasive disease phenotyping in pediatric spinal muscular atrophy patients. Photoacoustics. 25:100315

The impact of Eos on bone loss

Dr. Andreev

J90 01/2022 - 06/2024

Dr. Darja Andreev, Department of Medicine 3
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IMMUNOLOGY AND INFECTION

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

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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) redistribute pyruvate utilization via increased PDH activity in LPS-activated macrophages
- Patients suffering from rheumatoid arthritis and receiving GCs have significantly higher itaconate serum levels
- Absence of IRG1 abrogates the anti-inflammatory potential of GCs in a model of K/BxN serum transfer arthritis

Special methods

- Primary murine and human macrophage cultures
- Evaluation of the metabolic state of cultured cells using extracellular flux analyses (Seahorse XF Analyzer)
- Murine models of acute lipopolysaccharide-induced lung injury and autoimmune K/BxN serum transfer arthritis

Lipids and Serotonin in drug instrumentalization

Dr. Kalinichenko

J93 01/2022 - 06/2024

NEUROSCIENCES

Dr. Liubov Kalinichenko, Department of Psychiatry and Psychotherapy
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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 NSM in the serotonergic neurons (NSMfl/fl Tph2-iCreER mice) results in pronounced female-specific differences in emotional and drug use phenotype. Female NSMfl/fl Tph2-iCreER mice showed anxiety and depression-like behavior as well as reduced alcohol consumption. Male NSMfl/fl Tph2-iCreER mice had intact behavioral phenotype.

Special methods

The following methods are used in the project: behavioral testing of animals for evaluation of anxiety/depression-like behavior; in-vivo microdialysis allowing to analyze the response of brain monoaminergic systems to drug administration; intracranial administration of substances to certain brain structures with following behavioral testing.

Neuroinflammation and synucleinopathy in IBD

Dr. Süß

J94 12/2021 - 05/2024

NEUROSCIENCES

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

- Mouse models of Crohn's Disease (CD) und Ulcerative Colitis show cellular and transcriptional signs of neuroinflammation.
- Neuroinflammation in a mouse model of CD is accompanied by dopaminergic neuron loss.
- Hexb-based microglia reporter mice show efficient labeling of microglia with only minimal off-target labelling in the gut.

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 and their interaction with synapses
- 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 - Chair of Biochemistry and Pathobiochemistry
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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

Specific polyclonal Tip60 antibodies and a Schwann cell-specific, Cre-mediated knockout mouse model were generated. The histological analyses of Tip60-deficient sciatic nerves are completed and confirmed the strong phenotype of a peripheral neuropathy with hypomyelination due to less Schwann cells that show impaired differentiation capability.

Special methods

- Phenotypic characterization of a Schwann cell- specific Tip60 mouse mutant using i.a. immunohistochemical staining
- Isolation and subsequent cultivation of primary rat Schwann cells under the influence of Tip60-inhibitors to perform RNA-Seq and ChIP-Seq
- Co-immunoprecipitations to validate physical interactions of Tip60

Bace1/Bace2 in colorectal cancer development

ONCOLOGY

Dr. Gamez Belmonte

J96 10/2021 - 03/2024

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

Important results

BACE2 (β-secretase) expression is significantly increased in human colorectal cancer. Human tumor cells deficient in BACE2 exhibit an increased susceptibility to cell death that is partially rescued via apoptosis inhibition. Similarly, knocking out Amyloid precursor protein, a β-secretase substrate, is associated with an excessive apoptosis

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 method

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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recently started

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 them 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.

Special method

- Exome sequencing (for candidate gene identification for birth defects)
- Copy number variations anlyses (for candidate gene identification for birth defects)
- Gene knockdown via microinjections of Morpholino oligonucleotides & mRNA in zebrafish larvae

Reactive carbonyls in metabolic diseases

Dr. Düll

J99 10/2022 - 03/2025

Dr. Miriam Düll, Department of Medicine 1
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NEUROSCIENCES

recently started

Abstract

Reactive carbonyl species (RCS) are linked to development of metabolic syndrome including neuropathic pain and fatty liver disease (MAFLD), but the possibly synergistic role of RCS in both conditions remains to be investigated. This project aims at analyzing RCS as biomarkers in neuropathic pain patients with or without concomitant MAFLD, with parallelncompre-hensive experimental neurophysiological examinations of pa-tients and assessment of functional effects of RCS on sensory neurons in vitro.

Special method

- Single-Cell Calcium-Imaging
- Psychophysik (inkl. Quantitativ-sensorische Testung, QST)
- Mikroneurographie (C-Fasern)

Mucosal vaccination against lung metastases

Dr. Lapuente

J100 01/2023 - 06/2025

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

recently started

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.

Special method

- Mucosal vaccination
- T cell analyses
- Radio- and chemotherapy

AI for GI Histopathology

Dr. Dr. Matek

J101 01/2023 - 06/2025

Dr. Dr. Christian Matek, Institute of Pathology
e-mail: christian.matek@uk-erlangen.de

ONCOLOGY

recently started

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.

Special method

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

cDC1s in abscopal effects and HHP vaccination

Dr. Rückert

J102 12/2022 - 05/2025

Dr. Michael Rückert, Department of Radiation Oncology
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ONCOLOGY

recently started

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.

Special method

- In vitro differentiation of cDC1s from bone marrow
- Investigation of the phagocytosis of the high hydrostatic pressure-generated tumor cell vaccine by cDC1s and their activation by adjuvants
- Establishment of the tumor model to study the impact of the improved tumor vaccine on systemic anti-tumor immune responses

Predicting clinical longevity of dental materials

Dr. Maier

J103 12/2022 - 06/2025

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MEDICAL ENGINEERING

recently started

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.

Special method

- 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)

Funded ELAN projects in 2022:

No.	Name	Institution		Project title
P070	Prof. Dr. Alexey Ponomarenko	Physiology and Pathophysiology	N	Encoding of behaviours in the hypothalamus
P071	Dr. Dennis Lapuente	Clin. and Mol. Virology	S	Tissue-resident memory T cells against lung cancer
P072	Prof. Dr. Moritz Zaiß	Neuroradiology	M	Non-invasive Metabolic MR Fingerprinting
P073	Dr. Maximilian Sprügel	Neurology	N	Role of pericytes in intracerebral hemorrhage
P075	PD Dr. Philipp Arnold	Anatomy II	S	CD109 and cellular functions
P076	PD Dr. Franz Marxreiter	Molecular Neurology	N	MRI based diagnosis of Multiple System Atrophy
P077	Dr. Dmytro Royzman	Immune Modulation	I	Modulation of human osteoclasts by sCD83
P078	Dr. Eva Schäflein	Psychosomatic Medicine a. Psychotherapy	S	Self-perception in trauma-related disorders
P079	PD Dr. Ulrich Rother	Surgery	R	MSOT PAD
P080	Dr. Arne Gessner	Clin. Pharmacology and Clin. Toxicology	I	Tryptophan metabolites and rheumatoid arthritis
P081	Dr. Ines Böhme	Biochemistry	O	SNAT1/SLC38A1 in human melanoma
P082	Dr. Sabine Britting	Institute for Biomedicine of Aging	S	Safer Cycling in Older Age – Impact on Stress
P083	PD Dr. Rocío López Posadas	Medicine 1	I	Epithelial Rho GTPases and type2 immunity
P084	PD Dr. Kilian Schober	Clin. Microbiology, Immunology a. Hygiene	I	TCR repertoires after SARS-CoV-2 vaccination
P085	PD Dr. Fabian Müller	Medicine 5	O	Duotoxins for the treatment of cancer
P086	Dr. Corinna Lesley Seidel	Orthodontics and Orofascial Orthopedics	I	Oral symbiosis and dysbiosis
P087	Dr. Lisa Klotz	Biochemistry	N	Protective function of mGluR7 in the cochlea
P088	Prof. Dr. Miriam Kalbitz	Surgery	I	IL-18 dependent Cx43 translocation after trauma
P089	Dr. Harriet Morf	Medicine 3	I	Effect of Yoga on Spine Flexibility in SpA
P090	Dr. Katharina Gerlach	Medicine 1	I	Analysis of NFATc3 in intestinal inflammation
P091	Dr. Mayte Buchbender	Oral and Cranio-Maxillofacial Surgery	I	Association between P and IBD
P092	Dr. Tanja Müller	Medicine 1	O	Role of GPR15L in colorectal cancer
P093	Dr. Kaveh Roshanbinfar	Nephropathology	M	Vascularization of an ECM-mimicking hydrogel
P094	Dr. Wibke Müller-Seubert	Plastic and Hand Surgery	S	Influence of stem cells on irradiated flaps
P095	Dr. Frederik Stübs	Obstetrics and Gynecology	O	PD-L1 expression in vulvar cancer
P096	Dr. Andrea-Hermina Györfi	Medicine 3	I	DAX-1 mediates fibroblast activation and fibrosis
P097	Dr. Ulrike Steffen	Medicine 3	I	Anti-osteoporotic effects of metoprolol
P098	Dr. Vugar Azizov	Medicine 3	I	Acetate adversely affects T cell migration
P099	Dr. Krystelle Nganou	Clin. and Mol. Virology	I	Interplay between TCR and microbiome
P100	Dr. Simon Lévy	Radiology	M	Dynamic MR pulse design for fat suppression
P101	Prof. Dr. Heiko Reutter	Paediatrics and Adolescent Medicine	S	Exome and zebrafish analyses on VATER/VACTERL
P102	Dr. Hanna Hübner	Department of Obstetrics and Gynecology	O	ADCCresponse
P103	Dr. Robert Becker	Nephropathology	R	Phosphorylation in nuclear envelope MTOC formation
P104	Dr. Christina Bergmann	Medicine 3	I	Interactions Hedgehog-/AP1 signaling in fibrosis
P105	Dr. Katrin Peckert-Maier	Immune Modulation	I	Function of CD83 for human macrophages
P106	Dr. Katharina Pracht	Molecular Immunology	I	Aryl hydrocarbon Receptor (AhR) and vaccinations
P107	Prof. Dr. Lars Fester	Anatomy	N	Neurosteroids and calcium homeostasis
P108	Dr. Nina Sopel	Medicine 4	R	Characterization of exosomes and nanoparticles
P109	Dr. Valeska Stonawski	Child and Adolescent Mental Health	S	Body exposure in adolescents with AN
P110	Dr. Lisa Linck-Paulus	Biochemistry	O	The role of MAGOH in malignant melanoma
P111	Dr. Eva Liebing	Medicine 1	I	Ferroptosis during intestinal inflammation

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

No.	Name	Institution		Project title
P112	Dr. Eva-Maria Weiss	Psychiatry and Psychotherapy	N	Serotonergic psychedelics and presynaptic function
P113	Dr. Anna Dietl	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	Medicine 3	I	The role of Btn2a2 in T cell maturation
P117	PD Dr. Iryna Prots	Operative Dentistry and Periodontology (Stem Cell Biology until 12/2022)	N	T cell migration in neurodegeneration
P118	Prof. Dr. Ralf Enz	Biochemistry	N	GPR179, LRRTM4, GABAcR: new players in night vison
P119	Dr. Iris Stolzer	Medicine 1	O	Tryptophan metabolites in intestinal inflammation
P120	Dr. Jay Patankar	Medicine 1	I	Enteric glial cell-immune cell crosstalk

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

Immune Regulation in the treatment of Depression

P066 09/2020 - 08/2022

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.

Encoding of behaviours in the hypothalamus

P070 06/2021 - 05/2022

Prof. Dr. Alexey Ponomarenko, Institute of Physiology and Pathophysiology
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Abstract
Functional organisation of brain circuits supporting adaptive behaviours has informed development of novel therapeutic interventions. In this interdisciplinary proposal we will combine artificial intelligence approaches with innovative electrophysiological recordings in behaving mice to decipher neural representations of innate behaviours in the hypothalamus. The results will enable new insights into the function of a blueprint circuit for behavioural command.

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

Tissue-resident memory T cells against lung cancer

P071 02/2021 - 01/2022

Dr. Dennis Lapuente, Institute of Clinical and Molecular Virology
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Abstract
Lung cancer is the most prevalent and deadly type of cancer. Although immunotherapy with checkpoint inhibitors can improve the clinical outcome, only a minority of patients responds to this treatment. Recent studies suggest that tissue-resident memory T cells (TRM) in the tumour mass correlate positively with prognosis and are essential for efficacy of immunotherapy. In the present study, a novel mucosal vaccination strategy will be employed to induce lung TRM against defined tumour antigens.

Non-invasive Metabolic MR Fingerprinting

P072 06/2021 - 05/2022

Prof. Dr. Moritz Zaiß, Department of Neuroradiology
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Abstract
The scientific aim of this work is to further develop the metabolic chemical exchange saturation transer MR fingerprinting (CEST MRF) and to translate it from previous animal experiments to human MRI scanners at 3T and 7T. This will enable accelerated quantitative CEST imaging that forms a metabolic MR fingerprinting approach, which can then be evaluated for its potential clinical benefit for tumor diagnosis and stroke prognosis at University Clinic Erlangen.

Role of pericytes in intracerebral hemorrhage

P73 05/2021 - 05/2022

Dr. Maximilian Sprügel, Department of Neurology
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Abstract
Pericytes are small cells around brain capillaries and play a major role in maintenance of the blood brain barrier. In intracerebral hemorrhage (ICH), blood products induce complex processes leading to dysfunction of pericytes, impairment of the blood brain barrier and perihemorrhagic edema (PHE) formation. Aim of this study is to identify the blood metabolites triggering pericyte dysfunction to develop treatment strategies against PHE formation and to improve functional outcome of ICH patients.

CD109 and cellular functions

P075 04/2021 - 04/2022

PD Dr. Philipp Arnold, Chair of Anatomy II
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Abstract
Cluster of Differentiation 109 (CD109) is a cell surface protein that is GPI anchored in the cell membrane. It belongs to the α2-macroglobulin, C3, C4, C5 protein family and is expressed on keratinocytes, platelets, immune stem cells as well as CD4 and CD8 positive T cells. In recent years CD109 was also described as risk factor for several tumour entities. In this project we will elucidate the interactome of CD109 on the cell surface and evaluate resulting cell- type specific changes.

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.

Modulation of human osteoclasts by sCD83

P077 07/2021 - 06/2022

Dr. Dmytro Royzman, Department of Immune Modulation
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Abstract
Osteoclasts are the bone-resorbing cells of the body, which lead to severe damage of the musculoskeletal system under pathological conditions (such as RA). Treatment with soluble CD83 inhibited bone destruction in the murine arthritis model. Aim of this proposal is the translation of the murine data into the human system, which represents the next important step towards future therapeutic applications.

Self-perception in trauma-related disorders

P078 09/2021 - 02/2023

Dr. Eva Schäflein, Department of Psychosomatic Medicine and 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.

MSOT PAD

P079 03/2021 - 02/2022

PD Dr. Ulrich Rother, Department of Surgery
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Abstract
Aim of the proposed study is the definition of an independent parameter for the diagnostic evaluation of the perfusion situation of the calf muscle based on MSOT-method in a cross-sectional collective of healthy volunteers and patients with different stages of PAD (study group 1). The validation of the results will be performed by an independent validation group (study group 2).

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

Tryptophan metabolites and rheumatoid arthritis

P080 06/2021 - 05/2022

Dr. Arne Gessner, Chair of Clinical Pharmacology and Clinical Toxicology
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Abstract
Intestinal barrier integrity is an important checkpoint in translating autoimmunity to inflammation in rheumatoid arthritis (RA). Microbial metabolites of tryptophan were shown to reduce intestinal permeability and inflammation. However, it is unknown if this translates to a favourable impact on RA. Furthermore, it is unknown how the metabolites are intestinally resorbed. These questions should be adressed in cell models of intestinal epithelium and in human serum samples.

SNAT1/SLC38A1 in human melanoma

P081 02/2023 - 01/2024

Dr. Ines Böhme, Institute of Biochemistry, Chair of Biochemistry and Molecular Medicine
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Abstract
SNAT1 mediates the transport of neutral amino acids into the cell. Preliminary data show a significant overexpression of SNAT1 in human melanoma cells compared to melanocytes. Transient downregulation of SNAT1 resulted in significant reduction of the cellular proliferation and cell cycle progression. With this project we aim to analyze the functional importance of SNAT1, an attractive therapeutic target, in human melanoma.

Safer Cycling in Older Age – Impact on Stress

P082 09/2021 - 08/2022

Dr. Sabine Britting, Institute for Biomedicine of Aging
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Abstract
SiFAr-Stress investigates the impact of cycling on stress level in older adults. Uncertainty due to change to motorized bicycle or fear of falling can be perceived as stressors for cyclists. Stress activates different physiological signal cascades and stimulate for their part low-grade inflammation, which – in the long-term – can be associated with negative health outcomes. The aim is to analyse inflammatory processes as well as the activity of stress systems.

Epithelial Rho GTPases and type2 immunity

P083 10/2021 - 09/2022

PD Dr. Rocío López Posadas, Department of Medicine 1
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Abstract
Basic research focusing on Tuft Cells (TCs) differentiation might contribute to the understanding of pleiotropic immune functions of the intestinal epithelium, which can be exploited in the context of immunomodulation. Our preliminary data support an interplay between type2 cytokines and Rac1/RhoA function within Intestinal Epithelial Cells (IECs) playing a role in the differentiation of IECs towards a TCs fate. Our aim is then to decipher the molecular mechanisms operating behind intrinsic/extrinsic control of Tuft cell fate decision.

TCR repertoires after SARS-CoV-2 vaccination

P084 07/2021 - 07/2022

PD Dr. Kilian Schober, Institute of Clinical Microbiology, Immunology and Hygiene
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Abstract
T cells are an integral part of adaptive immunity, which forms the basis of protection from infections after vaccination. While B cell and antibody responses are well understood, little is known about which antigen-reactive T cells are recruited after primary and booster vaccination, as well as into long-lasting resting memory. In this project, we will investigate these questions in SARS-CoV-2 vaccinees by state-of-the-art T cell receptor repertoire profiling and functionality assessments.

Duotoxins for the treatment of cancer

P085 07/2021 - 06/2022

PD Dr. Fabian Müller, Department of Medicine 5
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Abstract
We found immunotoxins - fusion proteins of toxins and antibodies - synergistically enhanced 100-fold by Paclitaxel. We developed Duotoxins combining Paclitaxel-like DM1 and immunotoxins on one antibody. But, conventional immunotoxins cannot be conjugated efficiently. After switching to full-length antibodies, an active Duotoxin was generated. Here, we aim to use novel technology to extend the concept to other targets before applying for an extension of current DFG grant.

Oral symbiosis and dysbiosis

P086 10/2021 - 09/2022

Dr. Corinna Lesley Seidel, Department of Orthodontics and Orofascial Orthopedics
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Abstract
In patients with periodontitis, orofascial clefts and partly also during orthodontic treatment an oral dysbiosis and an increase of inflammation markers have been observed. Here, for the first time a systematic analysis of the oral microbiome and local inflammation in oral niches will be carried out using 16S rDNA sequencing and multiplex immuno assay, which will be correlated with determinants such as gingivitis/periodontitis, age, orofacial clefts, exogeneous factors and orthodontic treatment.

Protective function of mGluR7 in the cochlea

P087 09/2021 - 02/2023

Dr. Lisa Klotz, Institute of Biochemistry, Chair of Biochemistry and Molecular Medicine
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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.

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

IL-18 dependent Cx43 translocation after trauma

P088 10/2021 - 10/2022

Prof. Dr. Miriam Kalbitz, Department of Surgery
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Abstract
Trauma is the leading cause of death in humans aged below 45. Trauma can affect everyone, everywhere at any time. Blunt cardiac injury is associated with increased mortality after trauma. Redistribution of the gap junction protein Connexin43 is associated with cardiac dysfunction. In the present project, important new molecular insights into the regulation of Cx43 in the heart after trauma will be revealed and may identify therapeutic targets for preservation of cellular coupling.

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.

Association between P and IBD

P091 08/2021 - 07/2022

Dr. Mayte Buchbender, Department of Oral and Cranio-Maxillofacial Surgery
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Abstract
Inflammatory bowel diseases (IBD) include two major subtypes: Crohn's disease (CD) and ulcerative colitis (UC) with immunological dysfunction underlying its development. Changes in the oral mucosa and changes in the periodontium can also be observed. Periodontitis (P) is defined as a dysbiotic inflammatory disease, however, the relationship between the incidence and severity of periodontitis and cytokine expression in IBD patients remains unclear.

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.

Vascularization of an ECM-mimicking hydrogel

P093 09/2021 - 12/2022

Dr. Kaveh Roshanbinfar, Department of Nephropathology
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Abstract
We aim at generating multicellular engineered tissues based on hiPSC-derived endothelial cells and cardiomyocytes in a collagen-based hydrogel mimicking the fibrous structure of the native cardiac matrix. We will determine whether such hydrogels provide a proper environment to enhance pre-vascularization utilizing hiPSC-derived endothelial cells and whether cardiomyocyte maturation as well as pre-vascularization is enhanced in 3D engineered multicellular cardiac tissues.

Influence of stem cells on irradiated flaps

P094 05/2022 - 04/2022

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 - 04/2023

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.

I	Infection and Immunology
N	Neurosciences
O	Oncology
R	Renal and Vascular Research
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DAX-1 mediates fibroblast activation and fibrosis

P096 01/2022 - 08/2022

Dr. Andrea-Hermina Györfi, Department of Medicine 3
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Abstract
SSc is the systemic rheumatic disease with the highest disease-related mortality. We identified DAX-1 as a mediator of fibroblast activation. We showed that DAX-1 is upregulated in fibrotic skin and that knockdown of Dax-1 ameliorates skin fibrosis. We plan to further characterize the mechanism of DAX-1 upregulation and study its potential transcriptional role in fibroblast activation as well as its potential antifibrotic role in 3D skin models and precision cut tissue slices from SSc skin.

Anti-osteoporotic effects of metoprolol

P097 04/2022 - 03/2023

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.

Acetate adversely affects T cell migration

P098 04/2022 - 03/2023

Dr. Vugar Azizov, Department of Medicine 3
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Abstract
Epidemiological studies showed that alcohol intake reduces the incidence of RA. We published that alcohol sourced acetate prevents Tfh:B cell conjugates, crucial for antibody secretion. Here, we provide data showing that acetylation of cytoskeletal proteins by acetate reduces T cell motility. We propose to study if increased acetate levels favor cytoskeletal protein acetylation impacting cell motility and migration with direct consequences on the onset of autoimmunity and vaccination efficacies.

Interplay between TCR and microbiome

P099 04/2022 - 11/2023

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.

Dynamic MR pulse design for fat suppression

P100 01/2022 - 06/2022

Dr. Simon Lévy, Institute of Radiology
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Abstract
Chemical Exchange Saturation Transfer (CEST) MRI at 7T can provide high-quality metabolic maps for research in knee osteoarthritis, with a potential to replace the biopsy. Heterogeneity of the main magnetic field and constraints of the Specific Absorption Rate (SAR) make the fat suppression and the metabolite quantification challenging. This project aims to implement a routine for dynamic fat suppression pulse calculation including fields inhomogeneities and SAR limits specific to the subject.

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

Dr. Hanna Hübner, Department of Obstetrics and Gynecology
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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.

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

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.

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 Macrophage activation is associated with transplant rejection or chronic of inflammatory diseases. 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 macrophages 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 establishment 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 determined by RNASeq.

Neurosteroids and calcium homeostasis

P107 03/2022 - 11/2022

Prof. Dr. Lars Fester, Institute of Anatomy
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Abstract
Learning and memory formation are influenced in a sex-specific manner by neurosteroids, such as 17beta-estradiol and dehydrotestosterone. However, the structural mechanisms of how de novo synthesis of local neurosteroids in hippocampal neurons and their regulation by gonadotropin releasing hormone (GnRH) lead to the formation and degradation of spine synapses are still poorly understood. The focus of this work is to investigate its influence on calcium homeostasis in both sexes.

Characterization of exosomes and nanoparticles

P108 05/2022 - 10/2022

Dr. Nina Sopel, Department of Medicine 4
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Abstract
In this project we want to investigate cell-to-communication via exosomes and functionalized nanoparticles in the context of glomerular diseases. Therefore, we will characterize microvesicles secreted from glomerular cells regarding size and surface markers with electron and fluorescence microscopy and flow cytometry. Also, we want to study functionalized nanoparticles in vitro in glomerular cells and in vivo in a zebrafish model. Lastly, we want to establish an autophagy model in zebrafish.

Body exposure in adolescents with AN

P109 09/2022 - 08/2023

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 identified 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 12 month

Dr. Lisa Linck-Paulus, Inst. of Biochemistry - Chair of Biochemistry and Molecular Medicine
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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 melanoma 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.

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

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 12 month

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 - 03/2024

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.

The role of Btn2a2 in T cell maturation

P116 10/2022 - 03/2023

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 - 09/2023

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 - 01/2024

Prof. Dr. Ralf Enz, Inst. of Biochemistry - Chair of Biochemistry and Molecular Medicine
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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 12 month

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 12 month

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.

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

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