Let Life *Sciences* meet you

Biochemie I Biowissenschaften I Chemie I Molekulare Biotechnologie

ScieGuide

Heidelberg 2022/23

Die Life Sciences Lehrstuhlbroschüre der btS

btS-eV.de/Heidelberg
btS Heidelberg
@bts_heidelberg

btS
Die Life Sciences
Studierendeninitiative


Ab jetzt auf eigenen Beinen!
Die Techniker versichert Sie ab dem 25. Lebensjahr.
Das Thema Krankenversicherung ist jetzt Ihre Sache. Denn mit dem 25. Lebensjahr sind Sie nicht mehr über die Familie mitversichert. Wir beraten Sie gerne zu unserer Studentenversicherung ab 25 – direkt auf dem Campus.
Ich berate Sie gern:
Tammy Bieth
Hochschulberaterin
Tel. 01 51 - 57 89 11 46
uni.heidelberg@tk.de
Die Techniker

Liebe Studierende der Naturwissenschaften,

über die letzten Jahrzehnte hat sich die Region Heidelberg zu einem der bedeutendsten Zentren der Life Sciences weltweit entwickelt. Neben der Universität, die zu den ältesten und forschungsstärksten Europas gehört, beherbergt unsere Stadt auch zahlreiche weitere Forschungseinrichtungen wie das European Molecular Biology Laboratory (EMBL), das Deutsche Krebsforschungszentrum (DKFZ), oder das Max-Planck-Institut für medizinische Forschung (MPImF), die zusammen nahezu alle Teile des Spektrums bio-wissenschaftlicher Forschung abdecken.

Inmitten des vielfältigen Angebots der mit diesen Einrichtungen assoziierten Arbeitsgruppen kann es allerdings schwierig werden, die bestgeeignete Stelle für das nächste Laborpraktikum, die zukünftige Abschlussarbeit oder gar eine Promotionsstelle zu finden. Wir von der btS Heidelberg erstellen daher jährlich eine Lehrstuhlbroschüre, die Euch einen möglichst umfangreichen Überblick über verschiedenste Labore und AGs in Heidelberg ermöglichen soll. Das Ergebnis dieser Bemühungen – den ScieGuide Heidelberg 2022/23 – habt Ihr nun in seiner bereits fünften Auflage vor Euch. Wir hoffen, dass er Euch als Wegweiser auf Eurem akademischen Werdegang begleitet und Euch einen Eindruck von der Vielzahl an möglichen Forschungsrichtungen vermittelt.

Unser Dank gilt den an der Erstellung des ScieGuides beteiligten ehrenamtlichen Studierenden, den Arbeitsgruppenleiter:innen sowie unseren Kooperationspartner:innen, die uns die Mittel zum Druck dieser Broschüre zur Verfügung gestellt haben.

Wir wünschen Euch viel Spaß bei der Lektüre!

Euer Vorstandsteam der btS Heidelberg

Der ScieGuide erhebt keinen Anspruch auf Vollständigkeit. Wir freuen uns über jede zusätzliche Forschungsgruppe, die in der nächsten Ausgabe des ScieGuide vertreten sein will!

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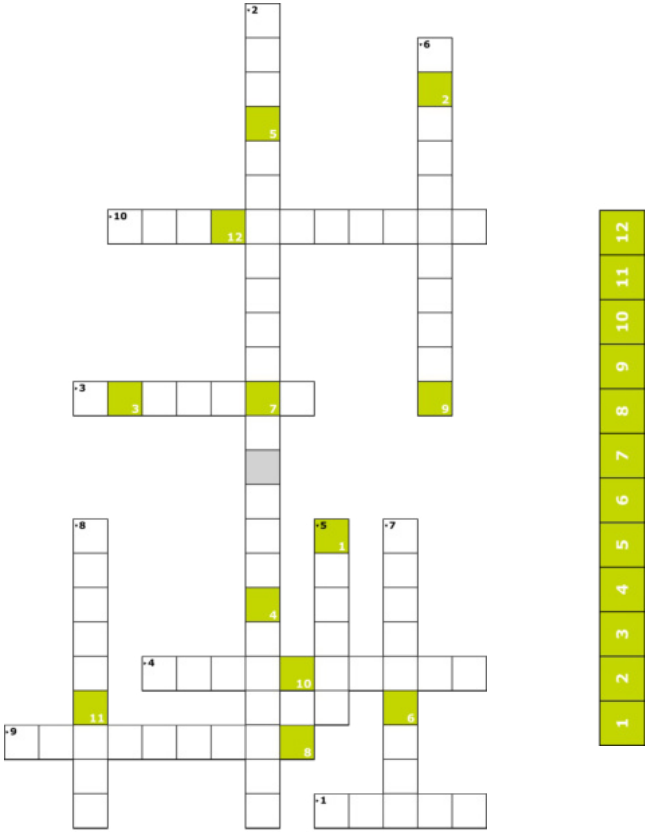

Waagerecht

1. Oxidationsmittel unter anderem in der Fettsäuresynthese.
3. Der Planet mit den meisten Monden im Sonnensystem.
4. Enzym für den klassischen Nachweis von ATP mittels Chemolumineszenz.
9. Hat einen Porphyrinringsystem, ist aber nicht im Blut unterwegs.
10. Zytokinklasse mit immunstimulierender, antiviraler undantitumoraler Wirkung

Senkrecht

2. Hat ihren Ursprung in obergärigen Bierhefen und dient als Modellorganismus, z.B. in der Molekularbiologie.
5. Entdeckte zusammen mit Kirchhoff die Elemente Rubidium und Caesium.
6. Erreger der Schlafkrankheit.
7. Membransysteme pflanzlicher Zellen und photoautotropher Bakterien, Name basiert auf dem griechischen Wort für Sack.
8. Nutzt Deep Learning zur Proteinstrukturvorhersage, seit 2021 als Open-Source-Lizenz verfügbar.

Lösungen auf Seite 184

btS
Die Life Sciences Studenteninitiative

Die **Life Sciences Studierendeninitiative** (btS) e.V. ist eine **bundesweit** operierende, **gemeinnützige**, **unabhängige** und **politisch neutrale** Studierendeninitiative.

Wir sind **Studierende** und **Doktoranden** aus **allen Bereichen der Life Sciences** und **unterstützen** ehrenamtlich die Lehre, **ergänzen** die Hochschulangebote und **vernetzen** Studierende, Doktoranden und Post-Docs mit der Industrie.

bts-ev.de

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EST. ★ '96
1996 GEGRÜNDET
seit 1996 eingetragener Verein (e.V.)

über
1200
Mitglieder

27 STANDORTE IN GANZ DEUTSCHLAND

Die **btS Heidelberg** freut sich immer über Zuwachs!
Wir treffen uns alle zwei Wochen, um unsere Projekte gemeinsam zu besprechen und zu planen.

Zeit und Ort erfährst Du auf:

https://bts-ev.de/heidelberg/
facebook.com/btSHeidelberg/
und
instagram.com/bts_heidelberg/

Die btS Heidelberg steht für...

Kontakt mit Firmen

Bei den von uns organisierten Firmenevents können die Teilnehmenden in spannenden Vorträgen und Workshops viel über verschiedene mögliche Arbeitgeber lernen. Ob Big Pharma, Biotech oder Consulting - hier ist für alle etwas dabei!

Networking

Beim digitalen Infoabend und Networking-Event mit Biertasting vor dem Semesterstart haben die Teilnehmer die btS in entspannter Atmosphäre kennen gelernt und einen abwechslungsreichen Abend verbracht.

Weiterbildung

In Zusammenarbeit mit der Pharma-akademie bieten wir regelmäßig ein einwöchiges AZAV-zertifiziertes GxP-Training an. Die rund 100 Teilnehmenden haben dabei die Gelegenheit, mit dem erworbenen Wissen ihre Berufschancen in der Industrie verbessern zu können.

Gemeinschaft

Neben der Organisation von tollen Events für Euch darf auch der Spaß und das Miteinander nicht zu kurz kommen. Deshalb treffen wir uns auch regelmäßig zum entspannten Beisammensein, wie hier im Flammkuchenhof Heidelberg.

Auf Jobsuche in den Life Sciences? Komm zur ScieCon!

Viele Firmen - ein Weg - Dein Job!

ScieCon München 2022

Die Life Sciences Karrieremesse

Jetzt wieder in Präsenz!

Was Dich erwartet...

- Gespräche mit Firmenvertretenden
- CV-Checks
- Bewerbungsfotos
- ein Live-Bewerbungsgespräch

... und vieles mehr!

Teilnahme ist kostenlos!

Weitere Infos unter:

https://bts-sciecon.de/m/

ScieCon München 2022

Heidelberg bietet verschiedene Graduiertenprogramme im naturwissenschaftlichen und medizinischen Bereich an. An exzellenten und international renommierten Forschungsinstituten wird so eine herausragende wissenschaftliche Ausbildung für Doktorand:innen sichergestellt.

Ruprecht-Karls-Universität Heidelberg

Die Universität Heidelberg ist die älteste Universität Deutschlands und kann sich unter den 50 weltbesten Universitäten behaupten. Der Dr. rer. nat. (Doktor der Naturwissenschaften) kann bei der Fakultät für Biowissenschaften, der Fakultät für Mathematik und Informatik, der Fakultät für Physik und Astronomie sowie der Fakultät für Chemie und Geowissenschaften erlangt werden. Die medizinische Fakultät Heidelberg und Mannheim bietet die Doktorgrade Dr. med., Dr. med. dent. und Dr. sc. hum an. Darüber hinaus stehen den Doktoranden verschiedene Graduiertenprogramme zur Verfügung, welche die Forschung während der Doktorarbeit mit Seminaren und Weiterbildungen ergänzen. Außerdem bietet die Universität Heidelberg das binationale Graduiertenprogramm "cotutelle de thèse" an. Doktoranden dieses Programms forschen an der Universität Heidelberg und einer zweiten Universität im Ausland, um zwei Doktorgrade von beiden Universitäten zu erlangen.

Die Zulassung in Heidelberg ist vom jeweiligen Gruppenleiter abhängig. Die Zulassung innerhalb des cotutelle-Vertrags ist an die Vorschriften der ausländischen Universität gebunden.

https://www.graduateacademy.uni-heidelberg.de/promovieren/index.html

Heidelberg Biosciences International Graduate School (HBIGS)

HBIGS wurde gegründet um talentierten Studierenden aus der ganzen Welt die Gelegenheit zu geben, an der Universität Heidelberg eine Doktorarbeit durchzuführen. HBIGS bietet herausragende Forschungsmöglichkeiten und eine exzellente Doktorandenausbildung. HBIGS umfasst ein breites Spektrum von natur-wissenschaftlichen Disziplinen: Strukturbiologie, Bioinformatik, Molekulare Medizin, Biotechnologie, Immunologie und Systembiologie.

Zulassungsrunden: Einmal pro Monat über das fast- oder regular track-Verfahren.

www.hbigs.uni-heidelberg.de

Deutsches Krebsforschungszentrum (DKFZ)

Die Helmholtz International Graduate School for Cancer Research ist ein internationales, interdisziplinäres Graduiertenprogramm in elementarer, computergestützter, epidemiologischer und translationeller Krebsforschung am DKFZ, dem größten biomedizinischen Forschungsinstitut Deutschlands. Zu den Forschungsschwerpunkten des DKFZs zählen die Ursachen und Mechanismen der Krebsentstehung sowie die Identifikation von neuartigen Werkzeugen für Diagnose, Behandlung und Prävention.

Zulassungsrunden: Zweimal pro Jahr, die Vorstellungsgespräche finden 8-10 Wochen nach Bewerbungsschluss statt.

www.dkfz.de/de/phd-program/

European Molecular Biology Laboratory (EMBL)

Das EMBL ist eine europäische, zwischenstaatliche Organisation mit mehr als 80 unabhängigen Forschungsgruppen im Bereich der Molekularbiologie, welche an sechs Standorten innerhalb Europas stationiert sind und ebenfalls ein internationales Graduiertenprogramm anbietet. Die Arbeitsgruppen am EMBL Hauptlabor in Heidelberg werden in vier zentrale Einrichtungen unterteilt: Zellbiologie und Biophysik, Entwicklungsbiologie sowie Struktur-biologie und Bioinformatik.

Zulassungsrunden: Zweimal pro Jahr, summer und winter recruitment rounds, die Vorstellungsgespräche finden etwa drei Monate nach Bewerbungsschluss statt

www.embl.de/training/eipp/

Max-Planck-Institut für medizinische Forschung (MPImf)

Das MPImf gehört zu der Max-Planck-Gesellschaft zur Förderung der Wissen-schaften e. V., einer unabhängigen, nichtstaatlichen und gemeinnützigen Vereinigung deutscher Forschungsinstitute. Für weitere Informationen über die jeweiligen Doktorandenprogramme sollten die Abteilungsdirektoren oder Forschungsgruppenleiter kontaktiert werden.

https://www.mr.mpg.de/14161632/graduates

Eine Doktorarbeit soll der nächste große Schritt in Eurem Leben sein? Sehr gut, denn es lohnt sich! Die Zeit ist ziemlich aufregend, wird Euch wahrscheinlich aber auch an Eure eigenen Grenzen bringen. Denkt immer daran, dass sich während der Promotion viele Dinge im Leben ändern können, über die Ihr jetzt noch nicht mal nachgedacht habt (Was kommt nach der Promotion?, Standortwechsel, Partner, Familienplanung, etc.). Daher haben wir hier einige wichtige Aspekte für Euch zusammengestellt:

Promotionsordnung

Einen Blick in die jeweilige Promotionsordnung ist immer lohnenswert. Dort stehen zum Beispiel die Anforderungen an die Zulassung, die Promotionsfächer (diese entscheiden über die Möglichkeiten Eure späteren Gutachter zu wählen) und die Regelpromotionszeit (für die Fakultät Biowissenschaften ist dies auf 3 Jahre festgelegt).

Projekt und Arbeitsbelastung

Ist der Vorschlag für das Promotionsthema gut gestellt? Ist das Forschungsprojekt realistisch und im gegebenen Zeitraum (3-4 Jahre) überhaupt umzusetzen? Es kommt durchaus vor, dass das Promotionsthema eine wissenschaftliche Sackgasse ist und sich die Ausrichtung eurer Doktorarbeit nochmals ändert. Wie ist die erwartete Arbeitsbelastung vom Gruppenleiter/Betreuer? Obwohl nicht vertraglich festgelegt, fordern einige Projekte oder auch Gruppenleiter Wochenendarbeit, Überstunden oder teilweise Arbeiten in der Nacht (z.B. bei stark frequentierten Geräten, wie Mikroskopen). Wird im Vertrag eine Lehrtätigkeit (z.B. die Betreuung von Saalpraktika) vorgeschrieben? Dies kann unter Umständen mehrere Wochen pro Jahr in Anspruch nehmen.

Forschungsgruppe und Betreuer

Passt der Betreuer oder Gruppenleiter, sowie die Gruppe selbst zu mir? Denkt daran, dass Ihr während der Promotion einen Großteil Eurer Zeit in dem Labor verbringen werdet. Ein Tipp ist, mit den Gruppenmitgliedern selbst ein wenig Zeit zu verbringen, um die Arbeitsatmosphäre und Anforderungen besser einschätzen zu können. Wünsche ich mir eine enge Betreuung oder schätze ich mich so eigenständig ein, dass ich relativ unabhängig das Projekt durchführen kann? Gerade in größeren Arbeitsgruppen ist eine enge Betreuung schwieriger.

Bezahlung, Urlaubstage und sonstige Regelungen

Reicht mir der Lohn für meinen gewünschten Lebensstandard? Die Entlohnung nach TV-L E13 (Tarifvertrag für den öffentlichen Dienst der Länder, Entgeldstufe 13) ist für Doktorandenstellen die Regel und kann online eingesehen werden. Für Doktorandenstellen in den Naturwissenschaften werden meist 50 - 65 % Verträge vergeben (je nach Dienstzeit

macht das teilweise 500 Euro pro Monat mehr oder weniger auf dem Konto aus). In der Regeln werden 30 Urlaubstage pro Jahr festgelegt; es gibt allerdings auch Verträge, in denen nur 20 Urlaubstage pro Jahr vereinbart sind. Ebenfalls wichtig sind sonstige vertragliche Regelungen, z.B. zur Altersvorsorge.

Stipendium ja/nein?

Promotionsstipendien haben in Deutschland eher einen schlechten Ruf. Der Vorteil ist eine relative Unabhängigkeit von den finanziellen Mitteln Eures Betreuers. Manche Doktorandenstellen sind allerdings direkt an ein Stipendium gebunden. Denkt daran, dass Ihr mit einem Stipendium in der Regel keine Sozialversicherungs-, Renten- oder Krankenversicherungsbeiträge zahlt. Oft werden Aufstockungsverträge angeboten. Wenn Ihr im Stipendium nicht privat krankenversichert sein wollt (ca. 100 Euro monatlich), müsst ihr euch freiwillig krankenversichern - das kostet bis zu 400 Euro monatlich. Seid Euch auch darüber im Klaren, dass Ihr nach dem Absolvieren einer Doktorarbeit eventuell eine kurze Zeit lang arbeitslos sein werdet. Mit einem Stipendium ohne eine lohnsteuerpflichtige Nebenbeschäftigung rutscht Ihr nach Abschluss direkt in Arbeitslosengeld II (Hartz IV), sofern keine Weiterbeschäftigung möglich ist.

Checkliste für die Bewerbung

Lebenslauf: Habe ich einen aktuellen Lebenslauf?

Motivation oder Motivationsschreiben: Was ist meine Motivation in der gegebenen Gruppe/in dem Graduiertenprogramm meine Doktorarbeit zu machen? Was habt Ihr von der Promotion und was ist Euer Mehrwert, den Ihr dem Gruppenleiter/Betreuer gebt?

Empfehlungsschreiben: Bereitet Euch darauf vor, dass oft mindestens zwei Referenzschreiben verlangt werden. Denkt daran, dass die Referenzschreiben direkt von Euren angegebenen Referenzen angefordert werden können (ohne, dass Ihr die Empfehlungsschreiben je selbst in der Hand gehalten habt) und sprecht diese Personen deshalb unbedingt im Vorfeld an.

Elektronische und beglaubigte Kopien von relevanten Dokumenten: Transkript oder Masterurkunde, Zeugnisse, polizeiliches Führungszeugnis (wird allerdings meist direkt angefragt).

Sprachzertifikat: Manche Graduiertenprogramme erfordern Sprachzertifikate, wie z.B. TOEFL oder IELTS. Diese Sprachzertifikate kosten Geld und bis Ihr Eurer Zertifikat habt, können schon mal ein paar Monate vergehen. Auch die Vorbereitungszeit und der Aufwand für die Tests ist nicht zu unterschätzen.

Let Life *Sciences* meet you

Karrierethemen der Life Sciences

Der Karriereblog der btS

- **Welche Unternehmensgröße passt zu mir?**
- **Naturwissenschaftliche Promotion in der Industrie**
- **Berufsbilder in den Life Sciences**

Und viele weitere Themen...

...für Deinen Berufseinstieg in den Life Sciences.

Wir möchten mit unserem Blog auf diverse Fragestellungen zur Karriere und den Berufsaussichten in den Life Sciences eingehen. Hier findest Du viele Infos zur beruflichen Orientierung in & nach dem Studium.

Vielfältig, inspirierend, lesenswert.
Schau jetzt vorbei
https://qr.bts-siecon.de/sc_karriereblog

btS e.V. | Von Studierenden, für Studierende.

auch auf

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Die Life Sciences Studierendeninitiative

Übersicht der Forschungsbereiche

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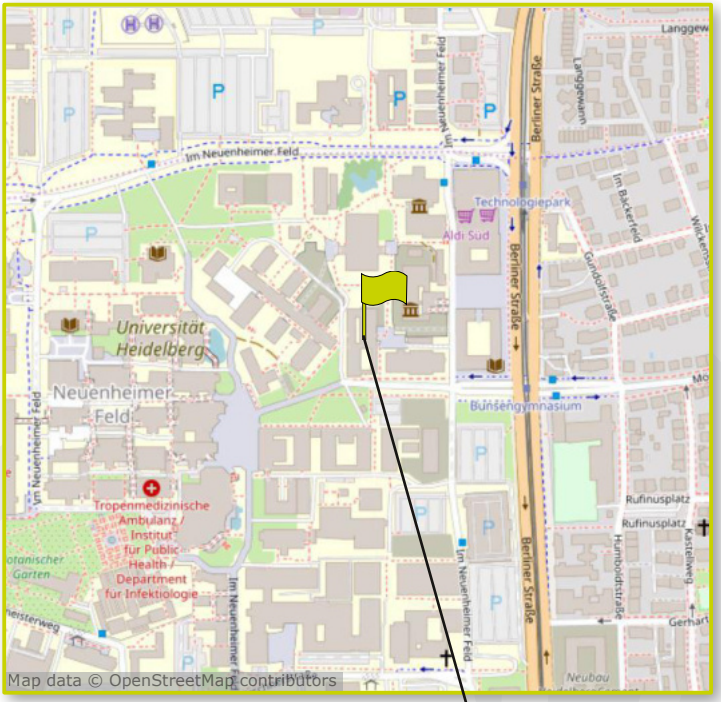
BioQuant



Cryo-Electron Tomography of Virus-Host Interactions

Research focus

We are interested in studying how viruses interact with cellular membranes and lipids during infection. Many enveloped viruses must cross the cell membrane during entry and exit. To do so, viruses developed or hijacked protein machinery, which remodel, fuse or cut membranes. We use and further develop cryo-electron microscopy techniques in conjunction with other imaging methods as fluorescence microscopy and imaging mass spectrometry to solve the puzzle of viral-membrane interactions of influenza A virus, Ebola virus and coronaviruses.

Key publication

Klein, S., Cortese, M., Winter, S.L. *et al*. SARS-CoV-2 structure and replication characterized by in situ cryo-electron tomography. Nat Commun 11, 5885 (2020). https://doi.org/10.1038/s41467-020-19619-7.

Methods and specific features

- Cryo-electron microscopy and tomography
- Correlative light and electron microscopy
- Scanning electron microscopy
- Virological Methods
- Structural biology
- Image processing

Opportunities in this group

Bachelor thesis: No.

Internships/Lab rotation: Yes, within Master program of Biochemistry, Molecular Biotechnology, Infectious Diseases with focus on pathogens, membranes and imaging methods.

Master thesis: Yes, for excellent students with a major in biochemistry, molecular biotechnology or infectious diseases, a prior intership in our group is required for a master thesis.

Contact

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Klick me!

Modeling of Biological Processes

Research focus

Research in the group focuses on one side on the development of computational methods for the modeling, simulation and analysis of biochemical networks. On the other hand, application projects on relevant biological systems are of major importance for the group. Thus, on the methodological side, we are constantly developing algorithms that allow a more thourough understanding of the inner workings of biochemical systems. These algorithms are made available for the scientific community by integration in our software package COPASI (ca. 17000 downloads per release). The group is also heavily involved in the development of standardized data exchange. Apart from method development we have been applying the methods in projects modeling both signalling as well as metabolic networks in different organisms, often with collaborators in house or on campus. As an example, understanding information processing in calcium signalling has been one of the major topics.

Key publication

Hoops S, Sahle S, Gauges R, Lee C, Pahle J, Simus N, Singhal M, Xu L, Mendes P, Kummer U. COPASI--a COmplex PAthway SImulator. Bioinformatics. 2006 Dec 15;22(24):3067-74. doi: 10.1093/bioinformatics/btl485. Epub 2006 Oct 10. PMID:17032683.

Methods and specific features

Computational modeling using different approaches, e.g.

- differential equations
- stochastic simulations
- agent-based models
- whole-genome scale models

Opportunities in this group

Bachelor thesis: Yes, for students that have attended introductory courses on modeling.

Internships/Lab rotation: Yes, mostly in the scope of a master program and only with basic knowledge on modeling.

Master thesis: Yes. Again, only for students with sufficient knowledge on modeling and computational approaches.

PhD: Whenever there are positions available.

HiWi/Research Assistant: Occasionally, limited in time.

Contact

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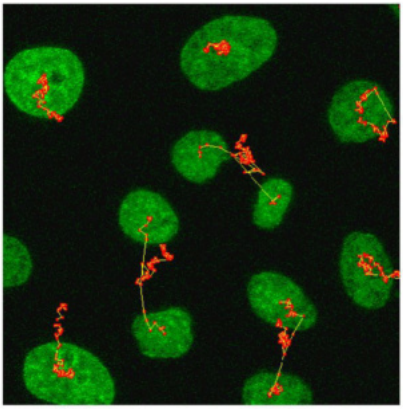
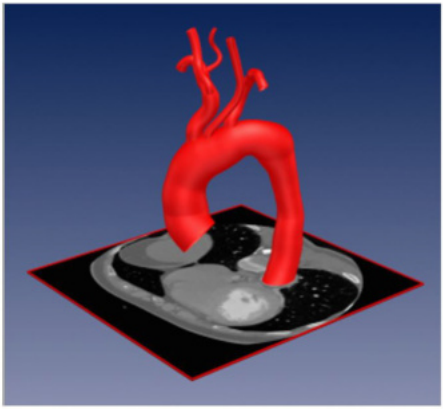
Klick me!

Biomedical Image Analysis





Research focus

The research group Biomedical Computer Vision (BMCV) develops methods and algorithms for computer-based analysis of biological and medical images. A main aim is to derive quantitative information about cellular and subcellular structures from microscopy data to be used for computational modeling. We have developed a wide spectrum of novel advanced image analysis methods for cell segmentation and tracking, particle detection and tracking, non-rigid image registration, vessel segmentation, and landmark localization comprising deep learning methods, model-based methods, and probabilistic methods. The developed methods have been successfully used in different applications to study virus infection, cell migration and division, and the genome architecture.

Key publication

Wollmann T and Rohr K. (2021) Deep Consensus Network: Aggregating predictions to improve object detection in microscopy images, *Medical Image Analysis* 70, 102019.

Methods and specific features

- Cell segmentation
- Cell tracking
- Particle tracking
- Colocalization
- Cell classification
- Image registration
- Vessel segmentation
- Landmark localization
- Model-based methods
- Probabilistic methods
- Deep learning, Machine learning

Opportunities in this group

Bachelor thesis: Yes, for interested students with experience in Image Analysis or Machine Learning.

Internships/Lab rotation: Yes, for Master students with a background in Image Analysis, Machine Learning or Bioinformatics.

Master thesis: Yes, for interested students with experience in Image Analysis or Machine Learning.

PhD: Yes.

HiWi/Research Assistant: Yes, occasionally.

Contact

PD Dr. Karl Rohr

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Computational Systems Medicine

Research focus

Our goal is to acquire a functional understanding of the deregulation of signalling networks in disease and to apply this knowledge to develop novel therapeutics. We focus on cancer, auto-immune and fibrotic disease. Our research is hypothesis-driven and tailored towards producing mathematical models that integrate diverse data sources. We collaborate closely with experimental groups.

A key emphasis is to build models that are both mechanistic (to provide understanding) and predictive (to generate novel hypotheses). To build these models, we combine existing biochemical knowledge with functional data. A major focus of our group is the development of logic models of signaling networks. We train these models with data generated with mass spectrometry and antibody-based technologies. We are also very interested in the use of single-cell data.

In parallel, we analyse genomic and phenotypic data. We combine this information with our prior knowledge of the underlying pathways. Thereby, we aim to improve our ability to dissect the mode of action of therapies and provide avenues for developing new ones. While our research is driven by applications, we develop open-source computational tools that we share freely with the scientific community.
Finally, we support scientific crowdsourcing, specifically collaboratives competitions, through the DREAM challenges.

Key publication

Eduati F *et al*. Patient-specific logic models of signaling pathways from screenings on cancer biopsies to prioritize personalized combination therapies. Molecular systems biology, 2020.

Methods and specific features

- Dynamic modeling (logic based, ODE based)
- Bioinformatic and data analysis tools (R/Python)
- Machine learning
- Network biology tools and resources

Opportunities in this group

Bachelor thesis: Yes, at least 6 months. Basic bioinformatic knowledge and programming needed.

Internships/Lab rotation: Yes, at least 6 months. Basic bioinformatic knowledge and programming needed.

Master thesis: Yes, at least 6 months. Basic bioinformatic knowledge and programming needed.

PhD: Yes.

HiWi/Research Assistant: Yes, at least 6 months. Basic bionformatic knowledge and programming needed.

Contact

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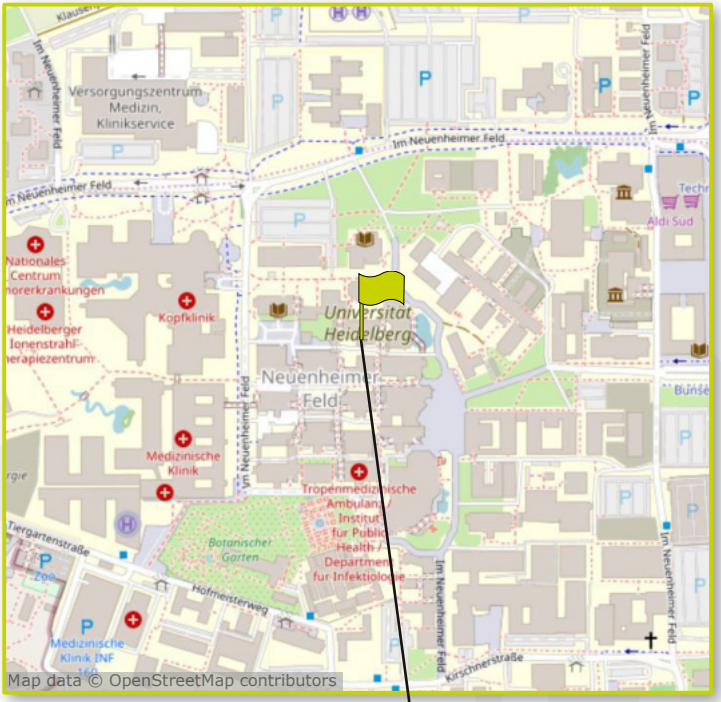
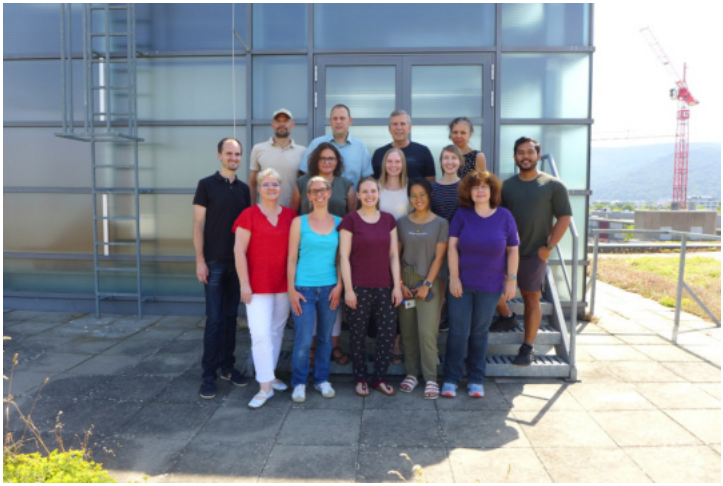
BZH

Biochemie-Zentrum der Universität Heidelberg



AG Brunner: S. 32
AG Jeske: S. 34
AG Schlaitz: S. 36
AG Schuck: S. 38
AG Sinning: S. 40

Molecular Mechanism of Circadian Rhythms and Molecular Clocks



Research focus

Most organisms have evolved circadian clocks to anticipate environmental changes associated with the 24h night-day cycle of earth rotation. Circadian clocks modulate rhythmic expression of a large number of genes and thus generate the potential to control biochemical, physiological and behavioral functions in a time-of-day specific manner. Circadian clocks are cell- autonomous oscillators. Eukaryotic circadian clocks are composed of a network of interconnected positive and negative feedback loops that produce rhythmic expression and modification of one or more clock proteins. Circadian oscillations are self-sustained and persist without environmental cues with a ca. 24 h period. In nature, environmental signals, so-called zeitgebers, are transduced to the circadian clock to synchronize the clock with the 24 h period of earth rotation. The strongest zeitgebers are light, temperature and nutrients. Using the filamentous fungus *Neurospora crassa* as well as mammalian cell culture as model organisms, we aim to understand how the circadian clock works as a program that coordinates complex expression profiles in a temporal fashion. While in *Neurospora*, we additionally investigate transcription induced inactivation of promoters and transcriptional memory, our focus in cell culture is on the coordination of the circadian clock and the cell cycle.

Key publication

Diernfellner, A. C. R. & Brunner, M. (2020) Phosphorylation Timers in the *Neurospora crassa* Circadian Clock. *J Mol Biol*, doi:10.1016/j.jmb.2020.04.004

Methods and specific features

- Protein biochemistry (overexpression, purification, blotting etc.)
- PCR, qPCR, Next Generation Sequencing
- Cloning, transformation, transfection, CRISPR-Cas
- Reporter Assays, Bioluminescence, Fluorescence
- To some extent Bioinformatics / Modelling

Opportunities in this group

Bachelor thesis: In principle, yes, depending on capacity. Should have first molecular biological hands-on experience.

Internships/Lab rotation: In principle, yes, depending on capacity. Should have first molecular biological hands-on experience.

Master thesis: In principle, yes, for excellent students with a major in a relevant subject (biochemistry, molecular biology). A prior internship in our group would be a major asset.

PhD: If position available (usually advertised). Enquiries/Applications generally welcome at all times (please include CV, references, motivation letter).

HiWi/Research Assistant: Rarely, limited in time

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Klick me!

Molecular Functions of Germline Proteins

Research focus

In the lab, we are using a multidisciplinary approach to investigate proteins and protein complexes with essential functions during germ cell formation and early embryonic development. The research focusses on understanding molecular mechanism underlying piRNA biogenesis and piRNA-mediated transposon silencing of transposon mRNAs, processes which are highly critical during gametogenesis and early animal development of *Drosophila*.

In particular, we are currently focusing our studies on LOTUS domain-containing proteins (Kubíková et al., 2020, Biol Chem) and on ATP-dependent RNA helicases. To unravel the molecular mechanisms of how these proteins function in the piRNA pathway, we combine RNA/protein biochemistry, X-ray crystallography, and cell culture techniques with *Drosophila* genetics.

Key publication

Jeske, M., Müller, C.W., Ephrussi, A. (2017). The LOTUS domain is a conserved DEAD-box RNA helicase regulator essential for the recruitment of Vasa to the germ plasm and nuage. Genes Dev. 31(9), 939-952.

Methods and specific features

- Highly interdisciplinary approach
- Recombinant protein production from *E. coli* and insect cells; diverse protein purification techniques
- Protein interaction studies using in vitro (GST pull down, ITC, etc.) and cell culture-based assays (ReLo: Salgania et al. 2022, bioRxiv)
- Structure determination of protein-protein and protein-RNA complexes using X-ray crystallography; AlphaFold modeling; prospectively cryoEM
- Enzymology of ATP-dependent RNA helicases
- *Drosophila* genetics, transgenesis, western blotting, immunostaining, confocal fluorescence microscopy, real-time PCR

Opportunities in this group

Bachelor thesis: Yes, for excellent biochemistry students (or related).

Internships/Lab rotation: Yes, for excellent biochemistry students (or related), minimum length is 3 months.

Master thesis: Yes, for excellent biochemistry students (or related). A prior internship in our group is a prerequisite.

PhD: Prospectively from March 2023. In addition, initial funding is possible for excellent biochemistry students (or related) with intended application for a fellowship.

HiWi/Research assistant: Yes, for excellent biochemistry students (or related).

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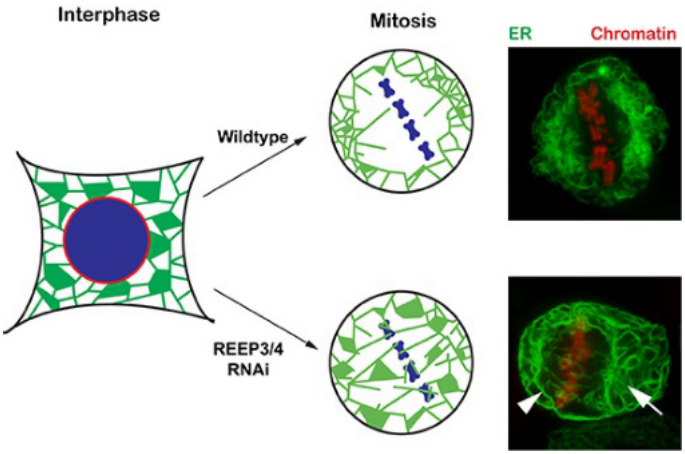
Klick me!

Organelle Dynamics during Mitosis



Research focus

Eukaryotic cells carry out their various functions in distinct compartments, for instance in membrane-bound organelles. Membrane-bound organelles have characteristic shapes and intracellular distributions, which correlate with their physiological roles. Yet, how organelle morphology and positioning are established and how they promote organelle functions is only partially understood. To unravel the functional roles of organelle morphogenesis, we need to elucidate the mechanisms underlying organelle organization. Interphase organelle organization is known to depend on membrane-shaping proteins, which interact with and deform cellular membranes, and on microtubules, which move and position organelles. For mitosis, organelles undergo striking morphological remodeling and spatial reorganization. We have identified the proteins REEP3 and REEP4, which establish the morphology and distribution of the endoplasmic reticulum (ER) in mitotic cells. REEP3 and REEP4 possess a membrane-shaping reticulon homology domain and associate with microtubules, and both of these properties bring about the distinct organization of the ER during mitosis. More recently, we discovered that REEP4 localizes also to the nuclear membrane and functions in nuclear pore complex (NPC) formation during late mitosis. Currently, we aim to understand how the different functions of REEP3 and REEP4 are controlled. Further, we want to uncover how the ER contributes to mitotic cell division and whether ER helps to coordinate the segregation of chromosomes and organelles.

Key publication

Golchoubian B, Brunner A, Bragulat-Teixidor H, Neuner A, Akarlar BA, Ozlu N, Schlaitz AL. 2022. Reticulon-like REEP4 at the inner nuclear membrane promotes nuclear pore complex formation. J Cell Biol 221(2):e202101049.

Methods and specific features

- Mammalian cell culture including genome editing by CRISPR/Cas
- Advanced light microscopy including: Super-resolution microscopy and Live cell confocal microscopy
- Image analysis and quantification
- Protein biochemistry and analysis of protein interactions, e.g. by Co-immunoprecipitations and Proximity-dependent labeling (BioID)
- Molecular biology (e.g. PCR, qPCR)

Opportunities in this group

Internships/Lab rotation: Yes, normally for students of the relevant Master's programs at Heidelberg University.

Master thesis: Yes, a prior internship is usually required.

PhD: As advertised on the lab web site.

HiWi/Research assistant: Occasionally.

Contact

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Organelle Homeostasis

Biogenesis and Degradation of Endoplasmic Reticulum

ER homeostasis (a semi-accurate fantasy)

1 – the unstressed, happy ER. The ER surrounds the nucleus as the nuclear envelope and extends outward as the peripheral ER.

2 – the ER experiences protein folding stress. The unfolded protein response kicks in and activates genes for chaperones and lipid biosynthesis. The ER expands to make more space for new protein folding machinery.

3 – the stressed ER. Chaperones and ER-associated degradation do what they can to deal with misfolded proteins.

4 – the ER prepares for ER-phagy. Parts of the ER are being rearranged into ER whorls.

5 – ER whorls (orange) detach from the rest of the ER, reducing ER size and perhaps taking damaged ER with them.

6 – the stress has been resolved and the ER is back to normal.

Research focus

We are interested in understanding

(1) How cells adjust the architecture of their organelles to current physiological needs and

(2) How cells degrade damaged or redundant organelle components.

Specifically, we are investigating how the size and shape of the endoplasmic reticulum (ER) is determined through coordinated biogenesis and degradation. ER biogenesis is driven by a signalling pathway called the unfolded protein response and involves the generation of ER tubules and sheets. Degradation of ER can occur by two principal mechanisms: the degradation of individual ER proteins by the proteasome and the degradation of large portions of ER by autophagy (self-eating). A particularly fascinating and poorly understood type of ER-selective autophagy is micro-ER-phagy, which involves the generation of large ER membrane whorls. These ER whorls are recognized and degraded in lysosomes by yet unknown mechanisms we are busy unravelling.

Key publication

Schäfer et al. (2020). ESCRT machinery mediates selective microautophagy of endoplasmic reticulum in yeast. EMBO Journal, 39:e102586

Methods and specific features

- Yeast as a model organism
- Light microscopy, including live cell and time-lapse imaging and quantitative image analysis
- Electron microscopy, including correlative light electron microscopy
- Genetic screens, including high through-put microscopy and protein-protein interaction screens
- Biochemisty, including various protein degradation assays

Opportunities in this group

Bachelor thesis: Yes, as part of the Bachelor Program Biowissenschaften.

Internships/Lab rotation: Yes, typically as part of the Master Programs Molecular Biosciences, Biochemistry or Molecular Biotechnology.

Master thesis: Yes, a prior internship in our group is a prerequisite for a master thesis.

PhD: As advertised on the lab's web site.

Contact

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Klick me!

Macromolecular Machines studied by an Integrated Structural Biology Approach

Research focus

Our goal is to understand structure and function of macromolecular assemblies with central roles e.g. in protein folding, targeting and membrane protein biogenesis. We aim at mechanistic insights by a combination of integrated structural biology with biochemical and *in vivo* analyses.

(1) We dissect the delivery pathways for membrane proteins e.g. by the universally conserved signal recognition particle (SRP), and by the GET (guided entry of tail-anchored proteins) pathway. After collecting structural snapshots of the SRP and the GET system using both x-ray crystallography and cryo-EM, we now focus on the membrane-associated steps and in particular on the protein-lipid interplay. Recently, we extended our efforts to integral membrane proteins with central roles in protein glycosylation as well as in the Wnt pathway.

(2) During synthesis at the ribosome, proteins are subject to enzymes for modification and chaperones that assist in folding. These factors share overlapping binding sites at the ribosomal surface and often affect translation. We dissect their impact on protein homeostasis, and at the end, we want to understand their carefully orchestrated interplay to finally obtain a complete picture.

(3) We study the MTREC complex, a novel 11-subunit exosome targeting compex in *S. pombe*, that directs non-coding RNAs to degradation. We perform structure-function analyses, and we are particularly interested in the role of RNA modifications for target RNA recruitment.

Key publication

McDowell et al. (2020) Structural basis of tail-anchored membrane protein biogenesis by the GET insertase complex, *Mol Cell* 80: 72-86.e7. PMID: 32910895.

Methods and specific features

To study complex macromolecular assemblies, we combine *in vitro* and *in vivo* analyses. X-ray crystallography and cryo-EM are our key methods, but we also use NMR spectroscopy and SAXS. We use a variety of biochemical and biophysical techniques to precisely characterize molecular interactions and interfaces. These include ITC, BLI, MST, SEC-MALS, fluorescence-based methods (nanoDSF), cross-linking mass spectrometry (XL-MS), CRAC, or hydrogen-deuterium exchange mass spectrometry (HDX-MS). We systematically optimize protein constructs for expression, purification and crystallization using state-of-the-art cloning and protein production tools, carrier driven crystallization, nanobodies, etc. We use *E. coli*, yeast and insect cells as well as mammamlian cell culture for protein production. We have established a protein crystallization platform with state-of-the-art robotics and imaging (https://xtals.bzh.uni-heidelberg.de/). For data collection we use world leading synchrotron radiation facilities – mainly the ESRF in Grenoble. We have been centrally involved in establishing cryo-EM on campus, which we now use for screening and data collection. We also use the cryo-EM facilities at the EMBL in Heidelberg and at the ESRF in Grenoble.

Opportunities in this group

Bachelor thesis: Yes, for excellent students of Biochemistry and Chemistry.

Internships/Lab rotation: Yes, for excellent students of Master programmes in Biochemistry, Molecular Biotechnology, Cell biology and Chemistry.

Master thesis: Yes, for excellent students with a strong interest in our research topics and methodology.

PhD: Yes, for excellent students with strong motivation for the analysis of molecular machines using integrative structural biology.

Contact

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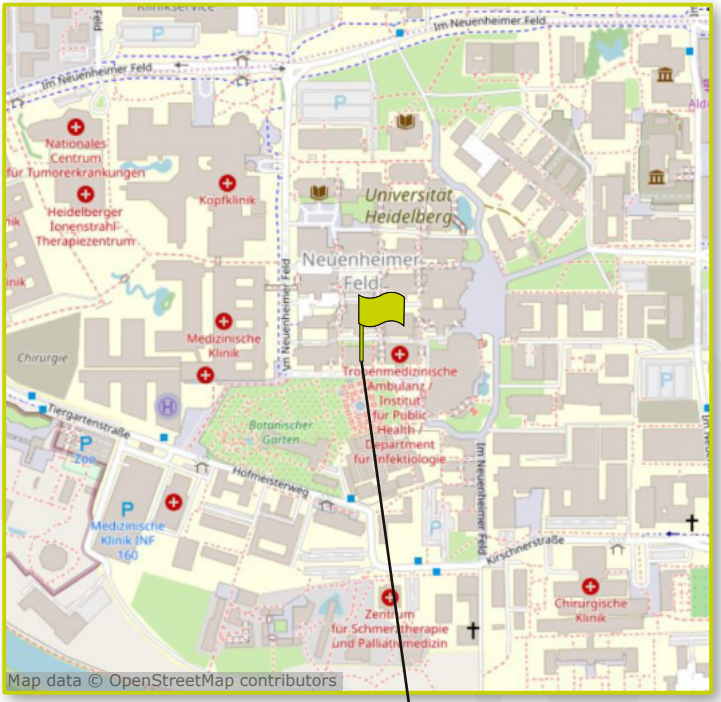
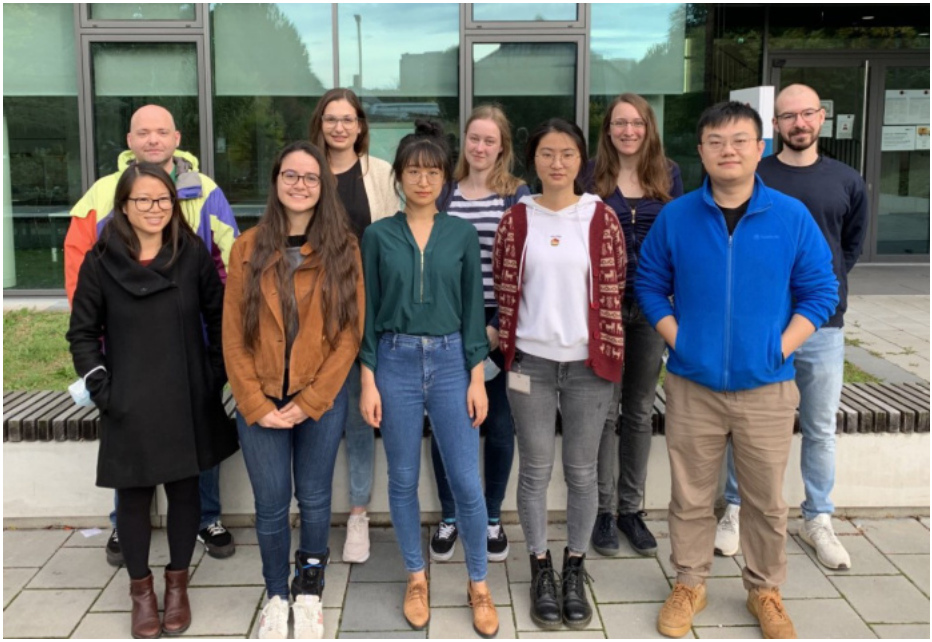
Klick me!

CIID

Center for Integrative Infectious Disease Research



Hepatitis Virus-Host Interactions



Research focus

With about 20 million infections each year, hepatitis E virus (HEV) represents a significant global health burden. Despite a growing awareness, the comprehension of this virus and its life cycle at the molecular level remains scarce. A contributing factor is the necessity to grow the virus in cell culture systems, which are usually based on aberrant cancer cells.
In order to overcome these limitations, our lab is culturing and differentiating stem cells, yielding more physiologically relevant and authentic cell culture systems permissive for HEV infection. Using these systems, we study each step of the HEV life cycle, including cell entry, genome replication, assembly, and secretion from (polarized) cells. We further study the innate and adaptive immune response to HEV infections and explore novel treatment options. Our studies are supported by a strong network of collaborations and state of the art technologies available on the outstanding campus environment of Heidelberg University.

Key publication

Dao Thi VL, Wu X, Belote RL, Andreo U, Takacs CN, Fernandez JP, Vale-Silva LA, Prallet S, Decker CC, Fu RM, Qu B, Uryu K, Molina H, Saeed M, Steinmann E, Urban S, Singaraja RR, Schneider WM, Simon SM, Rice CM (2020). Stem cell-derived polarized hepatocytes. Nature communications. 11:1677 Nat Comm.

Methods and specific features

- Advanced tissue culture: Human embryonic/induced pluripotent stem cell-derived cultures and human adult stem cell-derived organoids and their differentiation into HEV-permissive tissues
- Genetic manipulation: si/shRNA, lentiviral transduction, CRISPR-Cas9
- Virological and cell biological methods: HEV production, purification, and infection; infection read-out by immunblot, luciferase assays, immunflourescent stainings, FACS
- Flourescence imaging: confocal, high resolution, and quantitative image analysis

Opportunities in this group

Bachelor thesis: Yes, for excellent students with a strong interest in Virology.

Internships/Lab rotation: Yes, for excellent students of Master programmes in Biochemistry, Molecular Biotechnology, and Infectious Diseases, with a strong interest in Virology.

Master thesis: Yes, if you have completed an internship with us before.

PhD: Depends on available funding.

HiWi/Research Assistant: Occasionally.

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Klick me!

Cell Biology and Immunology of HIV Pathogenesis

Research focus

Our research addresses the cell biology, immunology and pathogenesis of HIV-1 infection with an emphasis on CD4+ T lymphocytes. One focus of our studies is on the molecular mechanisms of action by which the HIV-1 pathogenicity factor Nef reprograms host cell vesicular transport, signal transduction and motility to optimize HIV-1 spread in the host and to accelerate disease progression. Another important aspect of our work is on the host innate immune system in HIV infection and on viral evasion mechanisms. This includes dissecting how the intrinsic immunity factor SERINC5 impairs HIV-1 particle infectivity and how this activity is antagonized by the viral protein Nef, but also studies to elucidate which barriers prevent productive HIV-1 infection of resting CD4+ T lymphocytes. These HIV-related studies involve the development of complex 3D culture systems for studying the relationship between host cell motility and HIV-1 spread in tissue. Finally, we are also interested in the cell biology of CD4 T cell activation and differentiation. In this context, we particularly focus on the newly identified role of nuclear actin filament formation for CD4 T cell help.

Key publication

Kaw, S., Ananth, S., Tsopoulidis, N., Morath, K., Coban, M.B., Hohenberger, R., Bulut, O., Klein, F., Stolp, B. and Fackler, O.T. (2020). Expression of HIV-1 pathogenesis factor NEF in CD4 T cells impairs antigen-specific B cell function. Embo J., 39:e105594, DOI 10.15252/embj.2020105594.

Methods and specific features

- Our work involves the use of complex primary cell culture models, *in vivo* analyses in mice and studies on HIV replication and pathogenesis.
- These studies apply immunology, biochemistry and cell biology approaches, with a particular focus on imaging and flow cytometry.
- The laboratory is located in the new Center for Integrative Infectious Disease (CIID) research building with its state-of-the art imaging facility at the heart of the Heidelberg life science campus.
- We offer an international and highly interactive environment to address projects at the interface of immunology, biochemistry, cell biology, and virology.

Opportunities in this group

Bachelor thesis: Yes, for interested students with basic background in Virology, immunology and/or cell biology.

Internships/Lab rotation: Yes, within the Master Program "Infectious Diseases", but also other Life Science Master Programs.

Master thesis: Yes, a prior internship in our group is prerequisite for a master thesis.

PhD: Temporarily possible proliferates.

HiWi/Research Assistant: Occasionally, limited in time.

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Klick me!

Transmission of the Malaria-Causing Parasite from Mosquitoes to Mice

Research focus

We investigate the biology of the *Plasmodium* sporozoite. This is the form of the malaria parasite transmitted by mosquitoes. It is formed by an unusual process of schizogony in oocysts at the mosquito gut, enters the salivary glands of the mosquito and is spat into the skin by the bite. Within the skin the parasite moves extremely fast to search and enter a blood vessel from where it floats to the liver to enter into liver cells. We are interested in how the parasite is formed and how it moves. We also attenuate the parasites genetically to test new types of experimental vaccines.

Key publication

Spreng B, Fleckenstein H, Kübler P, Di Biagio C, Benz M, Patra P, Schwarz US, Cyrklaff M and Frischknecht F. (2019) Microtubule number and length determine cellular shape and function in Plasmodium. EMBO Journal. doi: 10.15252/embj.2018100984

Methods and specific features

We use a large range of modern microscopy techniques, such as confocal microscopy and cryo electron tomography. We also use standard genetic methods to generate transgenic parasites in order to investigate differences in their motility and infectivity to mosquitoes and mice. Together with colleagues we also use different biophysical methods such as optical traps to investigate force generation by the parasite.

Opportunities in this group

Bachelor thesis: Yes, but you need to apply early as we usually are 4-5 times oversubscribed.

Internships/Lab rotation: Yes, but you need to apply very early.

Master thesis: Yes, most become co-authors on publications.

PhD: Yes, pending on funding.

HiWi/Research assistant: Yes, pending on how many we currently have.

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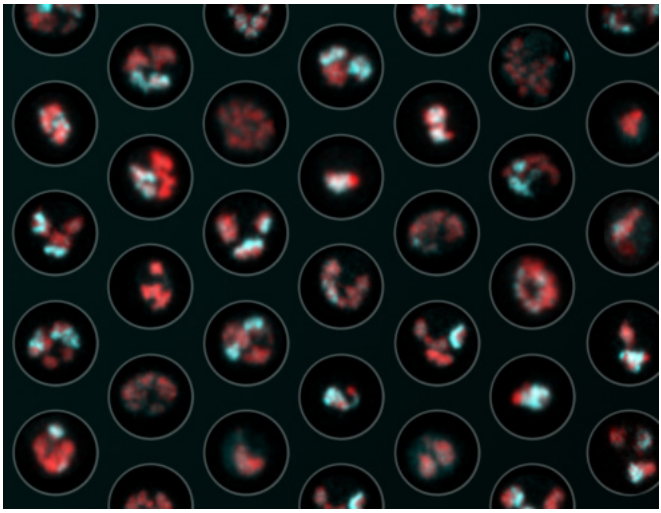
Asynchrony of Nuclei in Multinucleated Cells



Research focus

We investigate how individual nuclei of a multinucleated cell can retain a high degree of autonomy. Cells usually proliferate by duplicating their genome and subsequently dividing into two daughter cells. The malaria-causing parasite *Plasmodium falciparum*, however, proliferates by a remarkably different mode: Multiple rounds of DNA replication and closed mitosis occur, forming a multinucleated cell before daughter cells assemble. Although the nuclei reside in a shared cytoplasm, they multiply asynchronously.

Ongoing projects to study the apparent autonomy of the nuclei aim at:

1. understand how asynchrony is introduced and maintained during nuclear multiplication;
2. elucidate the regulatory circuits that drive asynchronous nuclear multiplication;
3. use our molecular insight to develop novel specific small molecule inhibitors that target *Plasmodium*'s unusual cell division cycle.

Understanding how the nuclei of the malaria-causing parasite can behave like cells within cells will not only highlight new intervention strategies to tackle malaria but also inform on how cells can be organized.

Key publication

Klaus *et al.*, 2022. Asynchronous nuclear cycles in multinucleated *Plasmodium falciparum* enable rapid proliferation. Science Advances. 8(13):eabj5362 PMID:35353560.

Methods and specific features

To investigate the apparent autonomy of the nuclei in *Plasmodium falciparum*, we are employing:

- Different imaging modalities
- Molecular genetic tools
- Chemical genetic tools
- Proteomics

In collaboration, we are also developing mathematical models, which describe the proliferation of the malaria parasite.

Opportunities in this group

Bachelor thesis: We are always looking for students who are curious about the way *Plasmodium* proliferates.

Master thesis: We are always looking for students who are curious about the way *Plasmodium* proliferates.

PhD: We are currently looking for a PhD student starting in fall 2022. Please get in touch if you are also curious about the way *Plasmodium* proliferates.

HiWi/Research Assistant: We are always looking for students who are also curious about the way *Plasmodium* proliferates.

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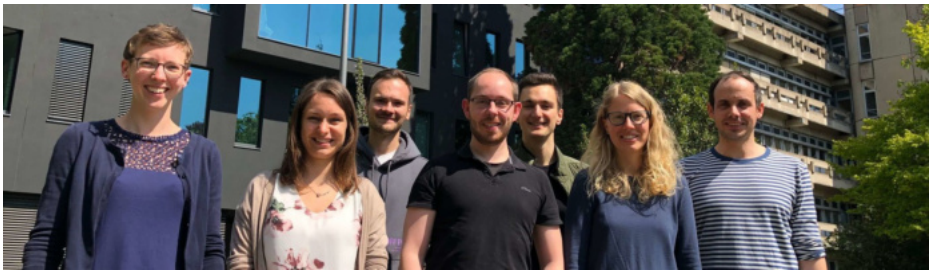
Klick me!

Divergent Nuclear Division Mechanisms in Malaria-Causing Parasites



Research focus

Despite being key to rapid proliferation of malaria parasites in the human blood and other life cycle stages the mechanisms of cell division are still poorly understood. Our vision is to generate an extensive cell biological and genetic framework to dissect critical events during nuclear division. The study of this highly dynamic and small scale process requires exquisite temporal and spatial resolution. Hence, we are using a combination of advanced imaging techniques such as live cell, super-resolution and correlative microscopy to study key structural elements of the division machinery. Thereby we hope to uncover new targets within this essential pathway and contribute to the fight against malaria.

Key publication

Simon C.S., Funaya C., Bauer J., Voss Y., Machado M., Penning A., Klaschka D., Cyrklaff M., Kim J., Ganter M., Guizetti J.*. (2021) An extended DNA-free intranu-clear compartment organizes centrosome microtubules in malaria parasites. Life Science Alliance doi:10.26508/lsa.202101199.

Methods and specific features

- Live cell imaging
- Super-resolution microscopy (U-ExM, STED,…)
- Electron microscopy
- Biochemistry
- Genome editing
- *Plasmodium falciparum* blood stage culture

Opportunities in this group

Bachelor thesis: Yes, for excellent and motivated candidates.

Internships/Lab rotation: Yes, for students with a strong interest in malaria cell biology and experience in cell culture.

Master thesis: Yes, for students with a strong interest in malaria cell biology and experience in cell culture.

PhD: Depending on the funding situation.

HiWi/Research Assistant: Occasionally.

Contact

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Klick me!

Dynamics of Events in HIV-1 Replication

Research focus

We are interested in the biology of the human immunodeficiency virus (HIV-1). With our work, we want to contribute to a detailed understanding of the intricate interactions of this important pathogen with its host cell during the viral replication cycle, and compare the pathways used by HIV-1 with that of other retroviruses.

The interaction between virus and host cell is highly dynamic, involving ordered and regulated formation, transport, transformation and dissociation of (nucleo)protein complexes. Biochemical, electron microscopic and structural studies provide detailed images of virions and information about the composition subviral complexes. However, the bulk data and 'snapshots' obtained using these methods do not reflect the dynamics of events occurring in the infected cell. In contrast, modern fluorescence imaging techniques enable us to zoom in on individual viruses, directly observing transport processes and protein interactions within living cells.
Currently we are fascinated by the mature HIV-1 capsid. This characteristic cone-shaped structure is not simply a disposable container for the virus genome, as initially believed. Rather, it has multiple functions as a master orchestrator of the entire early phase of HIV-1 replication, from cell entry to integration of the viral DNA into the host cell genome. In order to follow these dynamic processes, we develop fluorescently labeled HIV-1 derivatives and probes that allow us to follow individual events in virus-cell interaction with high time resolution. Microscopy is combined with biochemical and virological analyses to elucidate fate and function of the retroviral capsid in post-entry replication.

Key publication

Schifferdecker S, Zila V, Müller TG, Sakin V, Anders-Össwein M, Laketa V, Kräusslich HG, Müller B. Direct Capsid Labeling of Infectious HIV-1 by Genetic Code Expansion Allows Detection of Largely Complete Nuclear Capsids and Suggests Nuclear Entry of HIV-1 Complexes via Common Routes. MBio 2022; doi: 10.1128/mbio.01959-22.

Methods and specific features

- Tissue culture (cell lines and primary cells) and standard molecular biology methods
- Virological and cell biological methods (virus purification, infectivity assays, immunoblot, immunofluorescence, FACS)
- Fluorescence imaging (mainly confocal, STED and TIRF microscopy; Minflux, in collaboration) and image analysis
- Genetic code expansion and click chemistry
- Protein purification and analysis, BioID

Opportunities in this group

Bachelor thesis: Yes, for good students with a special interest in our type of work. A previous lab rotation with us is advantageous.

Internships/Lab rotation: Yes, but you should apply well in advance.

Master thesis: Yes, for motivated and curious students with a specific interest in virology and imaging. A previous lab rotation in our group is an advantage.

PhD: Yes, dependent on funding. Open positions will be advertised on our homepage and through HBIGS.

HiWi/Research Assistant: Occasionally available (for students with some experience in basic molecular biology methods).

Contact

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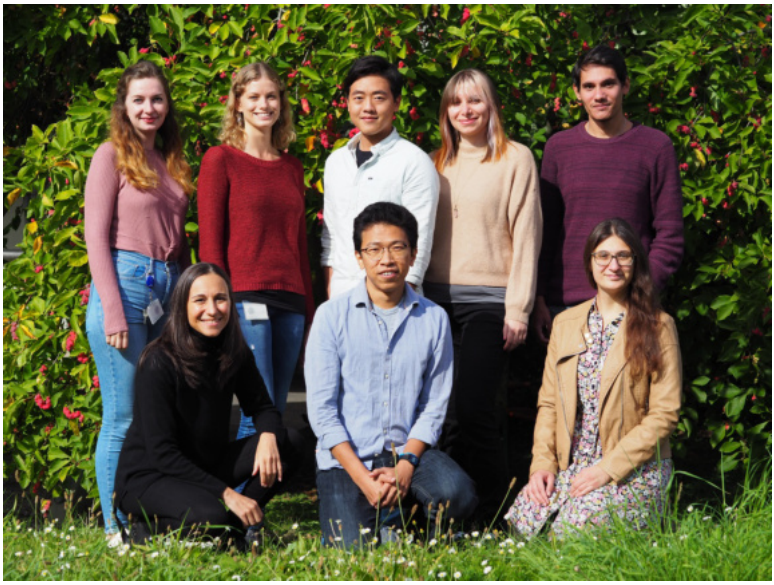
Klick me!

Translational Control by RNA Viruses



Research focus

Throughout the infection, viruses elicit multiple host cell responses including innate immune and stress responses. Viral double-stranded RNA replication intermediates trigger the activation of the stress sentinel Protein kinase R, which mediates the phosphorylation of eIF2α, a critical factor for translation initiation. As an almost immediate result, polysomes disassemble, protein synthesis is suppressed. Stalled mRNAs condensate with RNA-binding proteins and form membrane-less stress granules, which formation is dynamic, reversible and driven by cytosolic phase separation. To establish productive infections, viruses have evolved mechanisms to overcome translational attenuation that results from stress response induction. My laboratory is trying to understand how RNA viruses control the host translation machinery and the cellular stress response to ensure their progeny production. We explore the strategies evolved by different members of the Flaviviridae family such as hepatitis C virus, dengue virus, Zika virus and West Nile virus to antagonize or inversely to utilize the host stress response pathway.

Key publication

Roth, H., Magg, V., Uch, F., Mutz, P., Klein, P., Haneke, K., Lohmann, V., Bartenschlager, R., Fackler, O.T., Locker, N., Stoecklin, G., Ruggieri, A. (2017). Flavivirus infection uncouples translation suppression from cellular stress responses. mBio 8(1):e02150-16.

Methods and specific features

- Virology (virus production, infections) only in biosafety level 2 area (ex. work with Zika virus, lentiviruses)
- Cell culture (stable cells, CRISPR/Cas9 knockout technology)
- Molecular biology (cloning, WB, …)
- RNA methods (*in vitro* RNA transcription, *in vitro* RNA translation, polysome profiling, qPCR,…)
- Quantitative live-cell microscopy
- Immunofluorescence analysis

Opportunities in this group

Bachelor thesis: Yes, for Bachelor students with biochemistry and molecular biology background.

Internships/Lab rotation: Yes.

Master thesis: Yes, a prior internship in our group is prerequisite for a master thesis.

PhD: Based on funding opportunities of the lab.

HiWi/Research Assistant: Based on needs. Students are always welcome to ask.

Contact

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Klick me!

Molecular Biology of Hepatitis B- and Hepatitis D Virus / Host Interactions

Research focus

My group investigates the molecular mechanisms of Hepatitis B (HBV) - and Hepatitis D Virus (HDV) / host interactions with a focus on the early events (entry) of infection, the identification of receptors and the structural analysis of virus receptor interactions. Using these receptor(s), we develop novel cell culture systems for both viruses and study their molecular biology (molecular mechanisms of replication and persistence) and the innate immune responses induced during infection. In our translational research program we are developing entry inhibitors for HBV/HDV infection (with Hepcludex/Myrcludex being approved in 2020 as the first treatment of HDV infection) and hepatotropic drugs for the therapy of liver diseases. We are also developing a point of care (POC) diagnostic assay to easily detect HDV infections, which is used in world wide epidemiological studies.

Key publication

Lempp FA, Ni Y, Urban S. Hepatitis delta virus: insights into a peculiar pathogen and novel treatment options. 2016 Nature Reviews Gastroenterol. Hepatol. 13(10):580-9.

Methods and specific features

- All types of cell culture methods including work with primary human hepatocytes.
- Various transfection and transduction methods for gene silencing and trans complementation.
- All standard molecular biology methods.
- Virological and cell biological methods e.g. infectivity tests, IC50 determination of antiviral drugs, ELISA, immunofluorescence, FACS, confocal microscopy.
- Genetic code expansion (amber suppression) and click chemistry labelling approaches of viral and cellular proteins combined with high resolution imaging.

Opportunities in this group

Bachelor thesis: Yes, for excellent students with experience in Molecular Biology. Early application is desirable.

Internships/Lab rotation: Yes, for students of our Master Program "Infectious Diseases" and the master program "Biotechnology".

Master thesis: Yes, for excellent students with a specific interest in virology, who absolved a prior internship in my group.

PhD: Yes, depending on funding opportunities.

HiWi/Research Assistant: Yes, preferentially for students who were associated to my group before (e.g. after an internship or a bachelor thesis).

Contact

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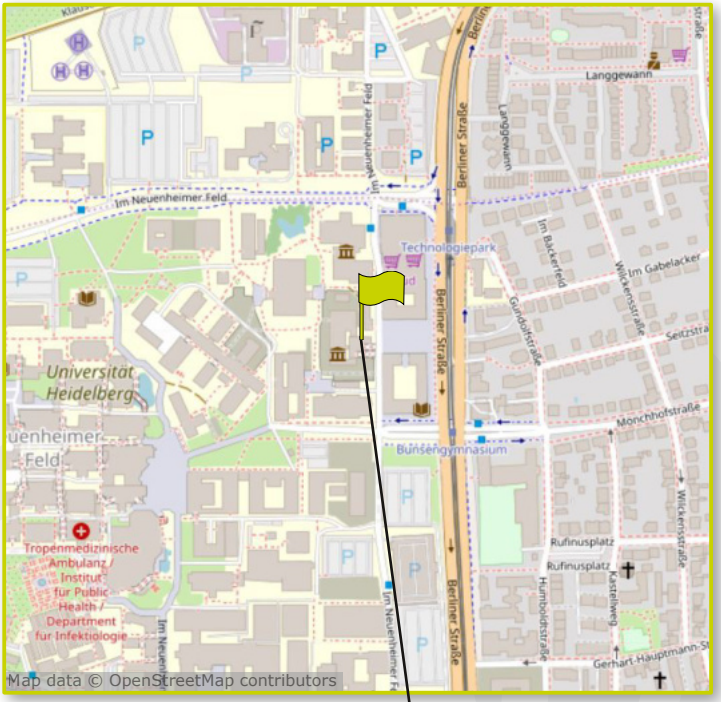
Klick me!

COS

Centre for Organismal Studies



AG Maizel: S. 62

Cell and Developmental Biology of Plants

Research focus

My lab is interested in how plants reliably shape their organs. Unlike animals, plants form organs throughout their whole life. This is a crucial determinant of their ability to adapt to their environment. We use the model plant *Arabidopsis thaliana* as a model and in particular how new roots are formed. By its simple organisation and the availability of numerous tools, the formation of new roots is an excellent model to understand the rules governing the morphogenesis of plants organs. In addition, these lateral roots are very important for the plant physiology, providing anchorage nutrient uptake.

Key publication

Stöckle, D. et al. Microtubule-based perception of mechanical conflicts controls plant organ morphogenesis. Science Advances **8**, eabm4974 (2022)

Methods and specific features

My lab uses a mix of traditional molecular genetics, cell biology and high end microscopy together with quantitative analysis and modelling.

- Microscopy: live imaging by confocal and light sheet microscopy.
- Molecular methods: CRISPR/Cas, PCR, GreenGate cloning, transgenesis.
- Cell and histology techniques: clearing, stainings.

Opportunities in this group

Bachelor thesis: Yes, for students with interest in plant development and/or microscopy and a creative mind!

Internships/Lab rotation: Yes, students from the MCB, MAPS and developmental biology majors but also from molecular biotechnology. Creativity and hard work are a must.

Master thesis: Yes, a prior internship in our group is prerequisite for a master thesis. M.Sc. students from the MCB, MAPS and developmental biology majors but also from molecular biotechnology are encouraged to apply. In all cases, we look for students highly motivated by the topic, hard working and creative.

PhD: Yes, pending availability of funding (from the lab or from fellowship). We expect from PhD student a very high dedication and interest for the topic, and open and creative mind.

HiWi/Research Assistant: Occasionally, limited in time.

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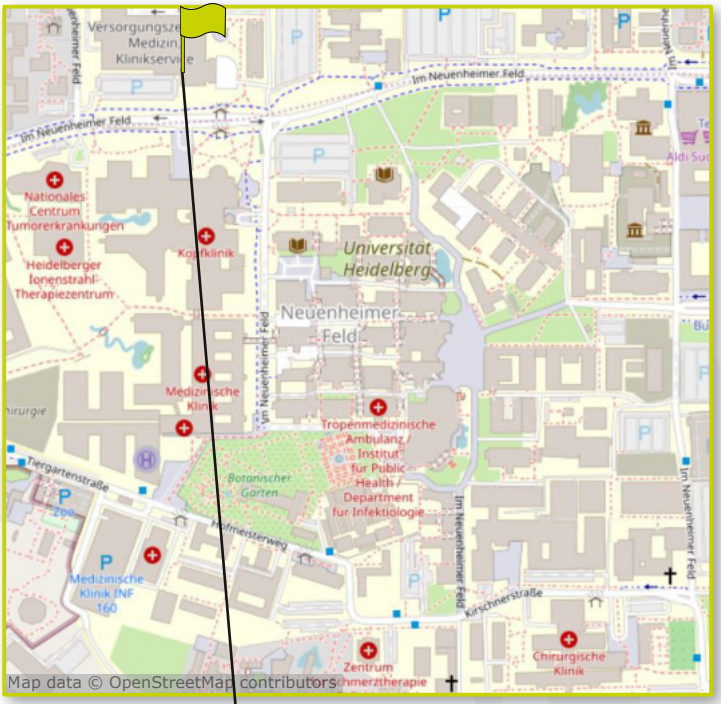
Klick me!

Dietmar - Hopp - Stoffwechselzentrum



AG Jung-Klawitter: S. 66
AG Peters: S. 68

Inborn Errors of Neurotransmitter and Pterin Biosynthesis

Research focus

We are interested in inborn errors of metabolism with a special focus on defects in neurotransmitter biosynthesis and metabolism. This rare group of diseases includes defects in the biosynthesis of tetrahydrobiopterin (BH4) as well as defects in dopamine, serotonin, and GABA biosynthesis. As a model we use patient-specific induced pluripotent stem cells (iPSCs) with CRISPR-generated isogenic control iPSC lines as well as differentiated somatic cell types (neurons, glia) and organoids to elucidate the pathophysiology of the diseases. We are interested especially interested in:

- gaining a better understanding of the complex pathophysiology of these diseases
- obtaining better genotype/phenotype correlations
- the identification of new therapeutic targets and diagnostic markers

Key publication

Jung-Klawitter, S, Opladen, T (2018). Induced pluripotent stem cells (iPSCs) as model to study inherited defects of neurotransmission in inborn errors of metabolism. J Inherit Metab Dis. 2018 Nov;41(6):1103-1116. doi: 10.1055/s-0038-1673630

Methods and specific features

- Cell culture: generation of induced pluripotent stem cells; stem cell culture; differentiation of stem cells (2D, 3D); cultivation of eukaryotic cells; transfection; transduction
- Molecular methods: DNA and RNA isolation; cDNA synthesis; PCR applications; qRT-PCR, mutagenesis; CRISPR/Cas9; cloning; sequencing; western blot analyses
- Analytical methods: enzyme activity assays; GC-MS, Tandem-MS and HPLC; fluorescence microscopy
- In cooperation: RNA-Sequencing (bulk, single cell); Metabolomics

Opportunities in this group

Bachelor thesis: Yes, basic knowledge in cell culture and molecular biology methods and an internship in the group would be helpful.

Internship/Lab rotation: Yes.

Master thesis: Yes, basic knowledge in laboratory techniques and a short internship necessary.

PhD: Yes; experience in relevant methods, strong motivation, persistence and creativity necessary.

HiWi/Research assistant: Occasionally.

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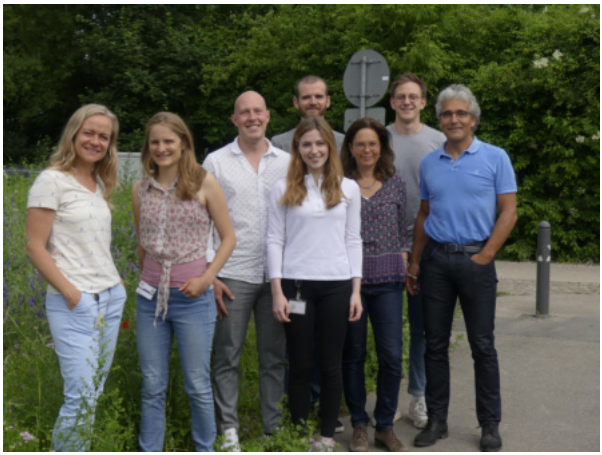
Klick me!

Regulation of Dipeptide Metabolism in Health and Disease



Research focus

As part of the Collaborative Research Center (CRC) 1118, we identify and describe metabolic pathways that are dysregulated in diabetes and other disease.

We are interested in understanding:

- How the metabolism of dipeptides is dis-regulated in diabetes and other disease and
- How can we prevent the dis-regulation and the subsequent biological consequences of reactive metabolites and post-translational modifications (PTM)

We are currently investigating the previously almost unknown dipeptide metabolism in genetically modified cells, mice and humans. In addition to providing amino acids, there is some evidence that dipeptides also possess further functions. To this end, we are identifying and characterizing the enzymes responsible, the function of dipeptides, and dipeptide shifts depending on disease and its pathogenesis. The impact on histological and functional consequences such as proliferation rates, growth, GFR, proteinuria, and blood pressure are studied.

Key publication

Weigand T, Colbatzky F, Pfeffer T, …Peters V (2020). A Global Cndp1-Knock-Out Selectively Increases Renal Carnosine and Anserine Concentrations in an Age- and Gender-Specific Manner in Mice. Int. J. Mol. Sci: 22:4887

Methods and specific features

- Genetically modified renal cell models (CRISP/Cas)
- Carnosinase 1 and 2 knockout mice
- RNAseq
- Analytical methods: HPLC, Tandem-MS
- Protein chemistry
- Metabolomics/Lipidomics
- Enzymology (recombinant enzymes)
- Transepithelial resistance
- Post-translational modifications (such as S-nitrosylation, cysteinylation, carbonylation and sumolyation)
- Formation of hydrogen sulfide in living cells
- Immunohistochemistry
- Oxidative stress markers
- Molecular methods: DNA and RNA isolation; cDNA synthesis; PCR applications; qRT-PCR

Opportunities in this group

Bachelor thesis: Yes, for interested students with basic experience in biochemistry.

Internship/Lab rotation: Possible.

Master thesis: Yes, for excellent students with interest in metabolism and its regulation.

PhD: Yes.

HiWi/Research assistant: Yes.

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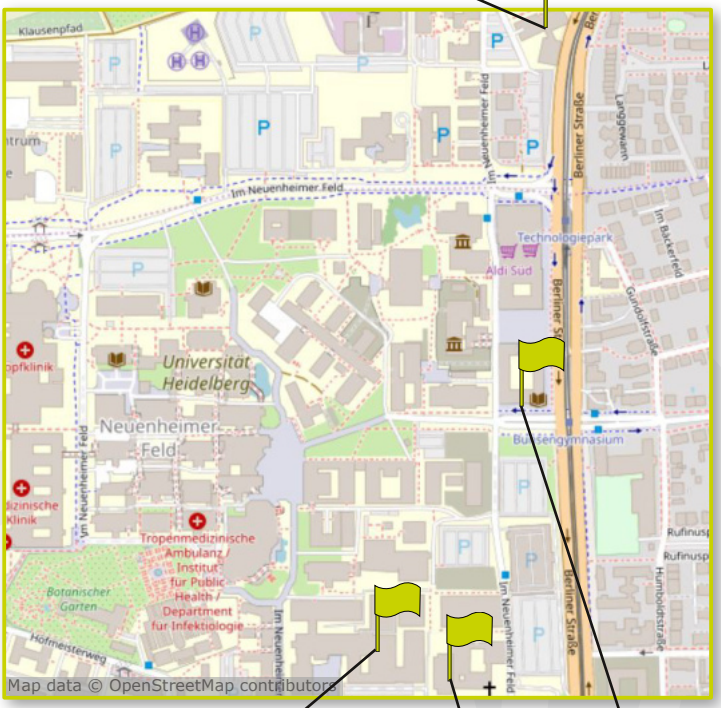
Klick me!

DKFZ

Deutsches Krebsforschungszentrum

AG Kutscher: S. 80
AG Palm: S. 86
AG Teleman: S. 90



AG Brors S. 72

AG Dick: S. 74
AG Essers: S. 76
AG Loges: S. 82
AG Mall: S. 84
AG Riemer: S. 88

AG Kloor: S. 78

Angewandte Bioinformatik

Fokus der Forschung

Wir entwickeln und nutzen bioinformatische und statistische Methoden, um die Entwicklung von Tumoren zu verstehen. Diese Methoden setzen wir ein, um Veränderungen auf der Ebene der DNA (Genomsequenzierung), der RNA (RNA-Sequenzierung) und der Epigenetik (Methylierungen) zu untersuchen. Dabei interessiert uns vor allem, wie Krebs entsteht und welche molekularen Schalter zum Fortschreiten und zur Resistenzentwicklung einer Krebserkrankung führen. Einen besonderen Beitrag dazu liefern Einzelzellanalysen von Tumoren und ihrer Umgebung. Unsere Erkenntnisse nutzen wir, um zu untersuchen, wie man Krebspatienten mit personalisierten Therapien besser behandeln kann. Dazu arbeiten wir eng mit Onkologen aus dem Nationalen Centrum für Tumorerkrankungen in Heidelberg zusammen. Auch international sind wir an großen Initiativen beteiligt, z.B. dem Internationalen Krebsgenomkonsortium, dem Internationalen Humanen Epigenomkonsortium und der Pan Prostate Cancer Genetics Group.

Schlüsselpublikation

Sieverling, L., Hong, C., Koser, S.D. et al. Genomic footprints of activated telomere maintenance mechanisms in cancer. Nat Commun 11, 733 (2020). https://doi.org/10.1038/s41467-019-13824-9

Methoden

- Prozessierung und Analyse von Genomsequenzdaten (whole-exome, whole-genome), Detektion von Einzelnukleotidvarianten, Kopienzahlaberrationen, Insertionen/Deletionen und strukturellen Varianten
- Analyse von RNA-Sequenzierungsdaten: Mapping, Transkriptabundanz, Detektion von differentieller Genexpression, Fusionen, Pathway-Analysen
- Analyse epigenetischer Daten (DNA-Methylierung, ChIP-seq, DNaseI-seq, ATAC-seq)
- Einzelzell-Sequenzanalysen (scGenomics, scRNAseq, scTCR, barcodegd sequencing, scATAC-seq)
- Methoden des maschinellen Lernens: Support Vector Maschinen, Random Forest, Clusterverfahren, verschiedene Arten von Regression (z.B. lasso, ridge regression)
- Programmiersprachen: Bash, Python, R, Perl

Möglichkeiten in dieser Gruppe

Bachelorarbeit: Ja, für Studierende mit Erfahrung in Bioinformatik
Praktika/Laborrotation: Ja, im Rahmen des Masterprogramms Molekulare Biotechnologie
Masterarbeit: Ja, für Studierende mit Erfahrung in Bioinformatik
Doktorarbeit: Ja, bei Vorerfahrung in Bioinformatik
HiWi/Forschungsassistenz: Nach Verfügbarkeit

Kontakt

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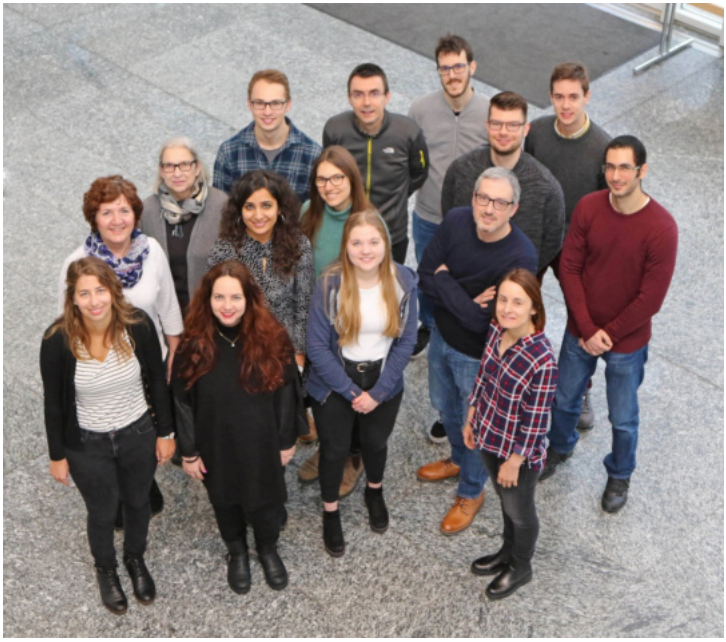
Klick me!

Redoxregulation



Research focus

1) We aim to understand the detailed molecular mechanisms by which redox signals are transmitted inside cells.

2) We make use of mechanistic insights to create tools that enable monitoring and manipulating redox signals inside living cells and model organisms.

3) We employ these tools to obtain more detailed understanding of redox homeostasis in either healthy or malignant situations. We are interested in intervention strategies that enhance cytoprotective signals in healthy cells and disrupt them in malignant cells.

Key publication

Morgan, B., Van Laer, K., Owusu, T.N., Ezerina, D., Pastor-Flores, D., Amponsah, P.S., Tursch, A., and Dick, T.P. (2016). Real-time monitoring of basal H2O2 levels with peroxiredoxin-based probes. Nature Chemical Biology *12*, 437-443.

Methods and specific features

Development and application of genetically encoded biosensors for real-time measurement of metabolites in living cells and model organisms.

- Genome editing and genetic screening
- Small molecule screening
- Protein biochemistry and enzymology

Opportunities in this group

Bachelor thesis: no.

Internships/Lab rotation: yes.

Master thesis: yes.

PhD: yes.

HiWi/Research Assistant: as needed.

Contact

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Klick me!

Inflammatory Stress in Stem Cells

Research focus

The focus of our research is to understand the impact of inflammatory stress on the HSC compartment via the effect of the pro-inflammatory cytokines on quiescent HSCs and their bone marrow niche. We investigate the sensing, response and recovery of the stem cells and the niche. This will allow us to better understand the link of inflammation and the HSC compartment: what are the mechanisms by which the HSC compartment is reassuring the successful restoration of homeostasis of the blood system following successful elimination of the infection and how are these HSCs themselves protected from pathogenic insults? And how does the impact of inflammatory stress on stem cells and their niche induce or influence malignant transformation in the bone marrow? Furthermore, we investigate how homeostatic heterogeneity in interferon signaling in the hematopoietic system impacts on disease development, progression and therapy resistance in myeloproliferative neoplasms.

Key publication

Haas S, Hansson J, Klimmeck D, Loeffler D, Velten L, Uckelmann H, Wurzer S, Prendergast ÁM, Schnell A, Hexel K, Santarella-Mellwig R, Blaszkiewicz S, Kuck A, Geiger H, Milsom MD, Steinmetz LM, Schroeder T, Trumpp A, Krijgsveld J, Essers MA. (2015). Inflammation-induced emergency megakaryopoiesis driven by hematopoietic stem cell-like megakaryocyte progenitors. Cell Stem Cell 17: 422-34

Methods and specific features

- In vivo analysis hematopoiesis in animal models
- FACS
- Gene expression (sc and bulk RNAseq, qPCR)
- *In vitro* bone marrow organoids
- Bone marrow imaging
- Leukemia models

Opportunities in this group

Bachelor thesis: Yes, for students with a molecular biology or cell biology background.

Internships/Lab rotation: Yes, within the scope of cancer biology, cell biology, molecular biology related master programs.

Master thesis: Yes, for excellent students of cancer biology, cell biology, molecular biology related master programs. MD thesis also possible for MD students with strong interest in basic research (minimum time for MD thesis 1 year).

PhD: Applications via the DKFZ international PhD program.

HiWi/Research Assistant: occasionally.

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Klick me!

Immune Biology and Evolution of Mismatch Repair-Deficient Cancer (Department of Applied Tumor Biology)

Research focus

DNA repair mechanisms ensure genomic stability of dividing cells. One of the essential DNA repair systems is the Mismatch Repair (MMR) system responsible for the correction of small insertion/deletion loops during DNA replication. When the MMR system is unfunctional, the mutation rate of a cell skyrockets, which enables malignant transformation. MMR-deficient tumors may develop sporadically, or in the context of the most common inherited tumor syndrome, Lynch syndrome. Due to a germline variant in one of the MMR genes, Lynch syndrome carriers are at high risk of developing various tumors during their lives. There is a big unmet clinical need for the development of effective preventive approaches for these patients. Interestingly, mutations accumulating in MMR-deficient cells not only contribute to carcinogenesis, but also trigger the generation of immunogenic neoantigens. We have deciphered relevant mutational and immunological targets arising during the evolution of MMR-deficient cancers and tested a first-in-human vaccine against non-viral cancer preclinically and in a Phase I/IIa clinical trial. We currently develop novel diagnostic approaches for Lynch syndrome and MMR deficiency using artificial intelligence. We cooperate with renowned scientific groups worldwide on various topics, including:

Cancer immune surveillance, cancer vaccines and prevention, artificial intelligence, machine learning, mathematical modeling, tumor phylogeny, tumor evolution and strong translational focus.

Key publication

Gebert et al. Recurrent Frameshift Neoantigen Vaccine Elicits Protective Immunity With Reduced Tumor Burden and Improved Overall Survival in a Lynch Syndrome Mouse Model. Gastroenterology. 2021 Oct;161(4):1288-1302.

Methods and specific features

- Fragment length analysis
- Targeted Sequencing
- Next Generation Sequencing
- PCR, qPCR
- Digital image analysis
- Bioinformatics
- Artificial intelligence, including machine learning-based image analysis
- Mathematical modelling
- Gene expression analysis
- *In vitro*, *in vivo* and *ex vivo* experiments
- Protein analysis (immunohistochemistry, immunofluorescence, WB)
- Tissue immune profiling
- Immune monitoring (ELISpot, ELISA, killing assays)

Opportunities in this group

Bachelor thesis: Yes. For excellent students with strong interest and background in molecular tumor biology and/or bioinformatics (depending on capacity).

Internship/Lab rotation: Yes. Usually within a master program (depending on capacity).

Master thesis: Yes. For excellent students with strong interest in translational cancer research including tumor immunology and/or bioinformatics (depending on capacity).

PhD thesis: Yes. For excellent students typically in frame of PhD programs (depending on capacity).

Hiwi/Research assistant: Occasionally.

Contact

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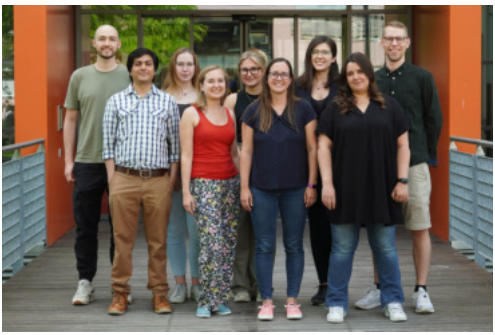
Klick me!

Developmental Origins of Pediatric Cancer



Research focus

Cancer is a disease phenotype often caused by abnormal, uncontrolled cell division. In adults, external factors, such as lifestyle choices, environmental exposures, or occupational hazards commonly underlie tumorigenesis. In children, however, these external factors play a smaller role. Instead, pediatric cancer is thought to arise from a block of developmental maturation. Therefore, effectively treating pediatric cancer will require a thorough knowledge of normal development, including the cellular function of the genes involved. For example, in medulloblastoma, a highly aggressive embryonal brain tumor, a differentiation block in distinct progenitor cell types gives rise to four tumor subgroups. Each subgroup has its own clinical features, prognosis, and treatment options. Although 70% of diagnosed children survive over five years, current treatments severely compromise quality of life. Learning more about medulloblastoma disease modalities in relation to their developmental origins will guide patient-specific treatment, increasing remission rates and reducing long-term toxicity. Researchers have identified probable genetic causes using -omic analyses of patient samples. However, rigorous functional validation of putative disease-causing genes and the corresponding cell states is still required. By studying basic neural development, we may better understand pediatric tumor initiation and progression. Our group's long-term goal is to understand normal brain development and elucidate the progression to malignancy. We use induced pluripotent stem cell models and mouse models investigate the role of oncogenes and tumor suppressor genes during development and tumorigenesis. Ultimately, we want to develop mechanism-of-action-based treatments with reduced toxicity for children with brain tumors.

Key publication

Kutscher LM*, Okonechnikov K*, Batora NV*, Clark J, Silva PBG, Vouri M, van Rijn S, Sieber L, Statz B, Gearhart MD, Shiraishi R, Mack N, Orr BA, Korshunov A, Gudenas BL, Smith KS, Mercier AL, Ayrault O, Hoshino M, Kool M, von Hoff K, Graf N, Fleischhack G, Bardwell VJ, Pfister SM, Northcott PA^, Kawauchi D^ (2020) Functional loss of a non-canonical BCOR-PRC1.1 complex accelerates SHH-driven medulloblastoma formation. *Genes Dev* **34**:1161–1176.

Methods and specific features

- Mouse models
- Induced pluripotent stem cells
- Imaging
- Transcriptomics
- We use the relevant molecular and cell biology techniques to answer the research question at hand, collaborating with other labs when necessary.

Opportunities in this group

Bachelor thesis: Yes, depending on space. The minimum time for a bachelor's thesis is five to six months.

Internships/lab rotation: Yes, depending on space. The minimum amount of time for a lab rotation is four months.

Master thesis: Yes, depending on space. A prior internship in the laboratory is required. The minimum time for a Master's thesis is six months.

PhD: Yes, depending on funding.

HiWi/Research Assistant: Yes, depending on needs.

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Klick me!

Personalized Medical Oncology: Endothelial-Immune Interactions, Resistance Development, Characterization of Rare Mutations in Driver Oncogenes and Liquid Biopsies

Research focus

We identify novel mechanisms driving cancer progression and therapy resistance with a focus on the tumor microenvironment. From these insights we derive novel targets and treatments for individualized cancer therapies. After preclinical validation we translate them into clinical studies. For example, we found that the interaction of AML cells with the bone marrow stroma elicits upregulation of its ligand Gas6 driving therapy resistance of AML cells and immunosuppression via engaging its receptor Axl in AML or immune cells, respectively. This pathway can be inhibited by the small molecule Axl inhibitor Bemcentinib which we translated into a clinical trial in relapsed AML patients (BGBC003, NCT02488408). In a reverse translation program attached to the trial we are dissecting patterns of response and resistance with innovative single cell sequencing technologies in order to inform further development of Axl-targeting.

In addition, we investigate patterns of response and resistance to targeted and immune therapies in cancer with a focus on precision oncology and NSCLC by utilizing innovative solid & liquid biopsy technologies (Janning et al., 2022, Ann Onc; 2017, Cancers). Here, we apply microfluidics techniques as well as single cell sequencing and -imaging technologies to enrich & analyze tumor cell as well as other cellular and subcellular components present in tumors and/or body fluids of cancer patients. Thereby, we identify unknown potential resistance mechanisms which we investigate in-depth at the functional level in cellular and animal cancer

models concerning their capability to drive cancer progression and therapy resistance. Potentially druggable candidates are subsequently translated to clinical trials.

Overall, we aim to discover novel tumor-promoting mechanisms at the interface between tumor and host, derive novel therapies and dissect mechanisms of response and resistance in cancer patients.

Key publication

Wroblewski M, Bauer R, Cubas Córdova M, Udonta F, Ben-Batalla I, Legler K, Hauser C, Egberts J, Janning M, Velthaus J, Schulze C, Pantel K, Bokemeyer C, Loges S. Mast cells decrease efficacy of anti-angiogenic therapy by secreting matrix-degrading granzyme B. Nat Commun. 2017 Aug 16;8(1):269

Methods and specific features

- International team consisting of clinicians, clinician scientists and basic researchers
- Preclinical models including organoids
- Circulating tumor cells (CTC)
- Innovative single cell multiomics
- Structural modeling and bioinformatic analyses (collaboration with Benedikt Brors, DKFZ)
- NSCLC patient cohorts
- FACS, RT qPCR
- Histology

Opportunities in this group

Master thesis: Yes, for motivated students (biochemistry, molecular biology or similar).

PhD thesis: Yes, depending on the availability of funding.

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Klick me!

Cell Fate Engineering and Disease Modeling

Research focus

One of the most exciting concepts in biology is the plasticity of cell fate that allows cellular identity to be reset. This plasticity is essential for normal development, but several human diseases are also associated with unwanted changes in cell identity. For example, dedifferentiation and adoption of stem cell-like properties are cancer hallmarks and aberrant gene expression is linked to neuropsychiatric diseases.

Our research mission is to understand the mechanisms that determine and maintain cell fate with the goal to understand and treat human diseases associated with loss of cell identity.

Key publication

Mall, M., Kareta, M., Chanda, S. et al. Myt1l safeguards neuronal identity by actively repressing many non-neuronal fates. Nature 544, 245–249 (2017). https://doi.org/10.1038/nature21722

Methods and specific features

Our enthusiastic team uses a combination of biochemistry, mouse models, single cell and functional genomics as well as state-of-the-art cell reprogramming, stem cell and organoids technologies to engineer cell fate decisions and model human development and disease. The current focus of the lab is to study the molecular mechanisms that regulate cell identity and to understand human disorders that are associated will loss of cell identity such as mental disorders and cancer.

Opportunities in this group

Internships/Lab rotation: We offer limited internship and rotation positions for a minimum duration of 4 months to excellent students from the Master Programs in Biochemistry, Molecular Biosciences and Molecular Biotechnology at the University of Heidelberg, as well as to outstanding external candidates. Please send your application to Dr. Moritz Mall with a statement about your research interest, as well as your current transcripts and CV.

Master thesis: Based on availability we offer excellent students with interest in neuroscience, stem cell biology and transcriptional regulation thesis opportunities. Please contact Dr. Moritz Mall with a statement about your research interest, as well as your current transcripts and CV to learn more.

PhD: We are continuously looking for ambitious PhD candidates to study the mechanisms that regulate cell fate during development and disease. Please apply via the International PhD Program of the DKFZ.

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Regulation of Cellular Metabolism

Research focus

Metabolism supplies the bioenergetic and biosynthetic pathways which underlie all cellular functions. To match the metabolic demands of different physiological and pathological states, cells therefore must tightly control nutrient uptake and usage. For example, growing cells increases nutrient uptake to double in mass, whereas starving cells tap into alternative nutrient sources to survive.

Our lab investigates fundamental principles of metabolic regulation in mammalian cells. To understand how cells acquire nutrients, we characterize their import pathways. Here, we are especially interested in metabolic roles of endocytosis and the lysosome. To understand how cells switch between different nutrient acquisition strategies, we study their regulation by signal transduction. Here, we focus on the mTORC1 and Ras signaling pathways, which transduce inputs from nutrients and growth factors, respectively. Dysregulated metabolism has emerged as a hallmark of cancer. Hence, we investigate how cancer cells gain metabolic autonomy to support uncontrolled growth, and promote metabolic flexibility to navigate nutrient-poor tumor microenvironments.

Key publication

Ratto E, Chowdhury SR, Siefert NS, Schneider M, Wittmann M, Helm D, Palm W. 2022 Direct control of lysosomal catabolic activity by mTORC1 through regulation of V-ATPase assembly. *Nature Communications; in press*

Methods and specific features

Our lab uses a broad range of cell biological and biochemical techiques to address our research questions from multiple angles, including live imaging, proteomics and metabolite tracing. To discover new metabolic regulators, we conduct genome-wide CRISPR screens in pathophysiologically relevant metabolic environments in cell culture and in mouse models.

Opportunities in this group

Internships/lab rotation: Yes, excellent students from the Master Programs in Biochemistry, Molecular Biosciences or Molecular Biotechnology at Heidelberg University, as well as outstanding external students are welcome to apply.

Master thesis: Yes, excellent students with a strong background in biochemistry or cell biology are welcome to apply.

PhD: Yes, ambitious and motivated scientist who are interested in addressing fundamental questions at the intersection of signaling and metabolism are invited to apply to the DKFZ PhD program.

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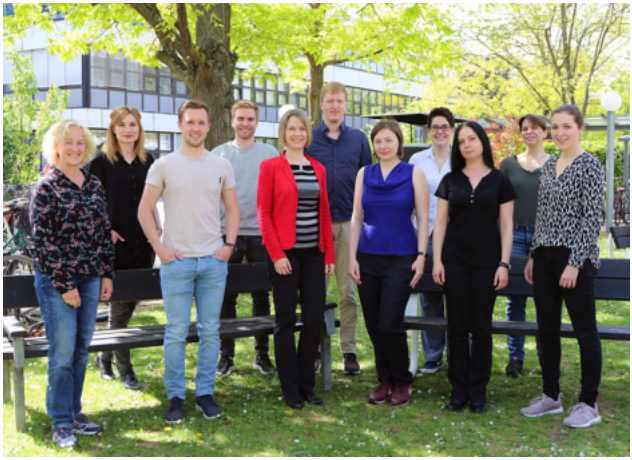
Klick me!

Cancer Immunotherapy Design Based on Validated T Cell Epitopes



Research focus

Cancer immunotherapies aim to make use of the two hallmarks of the immune system, specificity of antigen recognition and development of immunological memory. Thus, immunotherapies could be designed to only affect tumor cells and no healthy tissue, and they could also be effective against future metastases. Among different immunotherapy approaches, therapeutic cancer vaccinations aim at activating a patient's immune system so that it eradicates an existing tumor or cancer precursor lesions. To this end, the tumor cells must have characteristics that allow the immune system to differentiate them from healthy cells. These so-called tumor specific antigens can either be of viral origin or derive from tumor-specific mutations.

The overall aim of this group is to generate a therapeutic cancer vaccine against human papillomavirus (HPV)-induced malignancies. We characterize potential target epitopes by immunopeptidomics, i.e. assessment by mass spectrometry if they are HLA-presented on a tumor cell`s surface. Identified epitopes are tested for immunogenicity; and we examine various vaccine delivery and adjuvant formulations. Moreover, we are developing tumor models that allow assessing the efficiency of our vaccines and investigating ways of improving the trafficking of vaccination-induced T cells to the tumor site.

As the established immunopeptidomics workflow is highly sensitive, we are also applying it to a current area of immunotherapy research: the identification of tumor-mutation-derived neoepitopes. All these studies contribute to an optimal formulation of therapeutic cancer vaccines,

aiming at the effective induction of adaptive immune responses in cancer patients, or at target identification for adoptive T cell therapies.

Key publication

Kruse S, Büchler M, Uhl P, Sauter M, Scherer P, Lan TCT, Zottnick S, Klevenz A, Yang R, Rösl F, Mier W, Riemer AB (2018). Therapeutic vaccination using minimal HPV16 epitopes in a novel MHC-humanized murine HPV tumor model. OncoImmunology, 8(1): e1524694.

Methods and specific features

- Immunopeptidomics, incl. sample preparation, mass spectrometry and data analysis
- Immunogenicity assays: ELISpots, intracellular cytokine staining, cytotoxicity assays
- Working with epitope prediction servers
- Molecular cloning
- Expansion of (primary) tissue samples/cells
- In vivo immunogenicity and efficacy testing, orthotopic tumor models

Opportunities in this group

Bachelor thesis: Yes, for students with experience/training in T cell immunology. Should be in context with a long internship, e.g. "Praxissemester"

Internships/lab rotation: Yes, in the scope of the Master programs "Molecular Biosciences" (Majors Infectious Diseases and Cancer Biology) and "Molecular Biotechnology". All lab rotations are for a minimum of 8 weeks.

Master thesis: Yes, at least 6 months. A previous internship in the group is preferred.

PhD: Exclusively through the DKFZ Graduate School.

Contact

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Klick me!

Signaling and metabolic pathways that control tissue and cell growth using Drosophila and human systems

Research focus

The Teleman Lab is interested in understanding cell and tissue growth. Unlike the cell cycle, the mechanisms controlling cell growth and tissue growth are comparatively less well understood. We study two aspects of this problem: metabolism and signaling.

• Metabolism: To grow, cells and tissues need to make biosynthetic building blocks to accumulate mass. This requires the activation of metabolic pathways that support anabolism and fight oxidative stress.

• Signaling: Cellular anabolic metabolism is regulated by signaling pathways such as the insulin pathway or the mTORC1 pathway. These signaling pathways sense and respond to growth factors and nutrient levels. We investigate the regulation and dynamics of these signaling processes controlling metabolism and energy consumption.

This research has implications for both basic biology and cancer biology:

• Basic biology: Tissue growth and size control represents one of the unsolved fundamental mysteries in developmental biology. How does a tissue know what size to become, and when to stop growing? How does a tissue measure its size? The underlying mechanisms are not known.

• Cancer biology. For a tumor to form, the cells not only need to proliferate but they also need to grow. Understanding the molecular mechanism controlling cell growth, and the metabolic pathways that generate biomass, is an important part of understanding cancer.

Since signaling pathways are highly conserved from flies to human, we use Drosophila as a model organism for gene discovery and organismal studies. We then translate our findings into mammalian systems to study the implications for metabolic disorders and cancer.

Key publication

Nůsková H, Serebryakova MV, Ferrer-Caelles A, Sachsenheimer T, Lüchtenborg C, Miller AK, Brügger B, Kordyukova LV and **Teleman AA**. Stearic acid blunts growth-factor signaling via oleoylation of GNAI proteins. (2021) *Nature Communications*. 12:4590. doi: 10.1038/s41467-021-24844-9

Methods and specific features

Research on tissue and cell growth covers many different topics thereby requiring an integrated approach. Our work spans topics from the identification of new cancer gene functions and translational control mechanisms, to the regulation of signaling pathways by metabolites. The lab uses a wide range of techniques, from cell/tissue culture and biochemical approaches to *in vivo* genetics and organismal phenotyping.

Opportunities in this group

Internships/lab rotation: Yes - Master students of the Molecular Biosciences or Biochemistry course, or outstanding students from outside are welcome to apply.

Master thesis: Yes, often a lab rotation precedes the master thesis. Highly motivated, talented and curious students are welcome to apply.

PhD: Yes for excellent students who are highly motivated and interested in signaling and growth and the underlying biochemistry. Students who like to work and contribute to a vibrant international environment.

HiWi/Research assistant: Yes.

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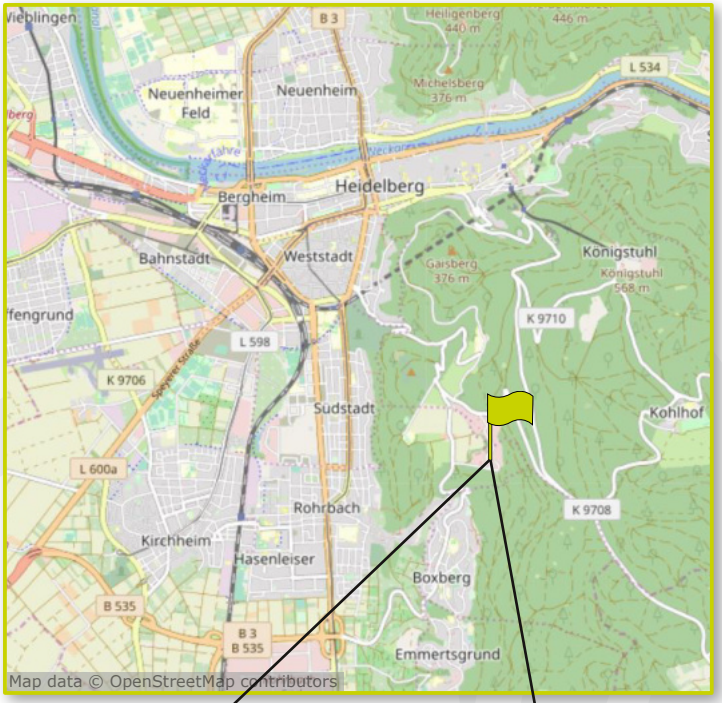
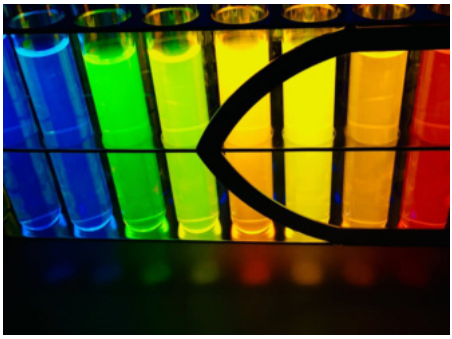
The European Molecular Biology Laboratory



Building Next-Generation Fluorescent Tools for Biological Imaging



Research focus

Our group aims at developing novel chemical tools to push the frontier of fluorescence imaging and allow interrogation of biological systems at the molecular, cellular and organismal levels. We design and build innovative probes by combining the superior fluorescence properties of synthetic fluorophores with the specificity of genetically encoded protein scaffolds.

This approach, at the interface of synthetic chemistry and protein engineering, has the promise to overcome many limitations of currently available reporters. As tool-builders, we work in close collaboration with microscopists and biologists who implement our tools to ultimately increase our understanding of complex cellular functions. Our current research interestes include:

- Development of new fluorophore scaffolds and fluorogenic labeling strategies
- Light-responsive fluorophores for super-resolution microscopy
- Synthetic dyes for deep-tissue imaging

Key publication

Deo, Abdelfattah *et al*. (2021) The HaloTag as a general scaffold for far-red tunable chemigenetic indicators. Nature Chemical Biology 17:718-723.

Methods and specific features

Projects in the group rely on organic synthesis and standard purification and characterization methods (NMR, HPLC, LCMS, chromatography, etc…).

We characterize the photophysical properties using steady state UV-Visible and fluorescence spectroscopy.

Several projects additionally involve biochemistry and protein engineering to engineer new protein tags.

Opportunities in this group

Bachelor thesis: Yes for excellent student with expertise in Organic Chemistry or Biochemistry, for a minimum duration of 4 months.
Internships/lab rotation: Yes for excellent student with expertise in Organic Chemistry or Biochemistry.
Master thesis: Yes for excellent student with expertise in Organic Chemistry or Biochemistry.
PhD: Limited possibilities, only via the EMBL PhD Program.

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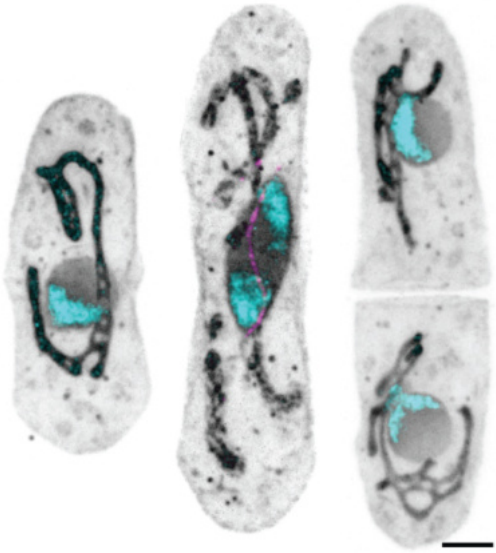
Klick me!

Evolutionary Cell Biology of the Nucleus



The fission yeast S. pombe at different cell cycle stages imaged using expansion microscopy. DNA is in cyan, the mitotic spindle in the center cell in magenta, and a non-specific protein stain - preferentially labelling mitochondria and the nucleus in these cells - in gray.
Scale = 1.5 µm.

Research focus

The nucleus, the one organelle that all eukaryotes share, is over 2 billion years old with universal functions in housing and protecting the genome and compartmentalizing the cell. Yet, different eukaryotes across the tree have evolved strikingly divergent strategies to organize and remodel the nucleus through the cell cycle. In our group, we apply the tools of experimental cell biology, comparative genomics, and directed evolution to fission yeast, budding yeast, and protist models to understand this apparent contradiction – aiming in the process to discover universal principles of nuclear organization, and in the long term, reconstruct the evolutionary history of this unique structure at the heart of cellular life.

Key publication

Dey G.*, Culley S., Curran S., Schmidt U., Henriques R., Kukulski W. and Baum B. (2020). Closed mitosis requires local disassembly of the nuclear envelope. Nature 585(7823):119-123. DOI: 10.1038/s41586-020-2648-3.

Methods and specific features

- Live cell microscopy, high-throughput genetics, cell biology and biochemistry in fission and budding yeast
- Adapting super-resolution microscopy and expansion microscopy techniques for protists and fungal models
- Experimental lab evolution of budding and fission yeast
- Development of new protist models for cell biology, including *Ichthyosporea*, acellular slime moulds, and deep-branching fungal relatives
- Improving tools for comparative genomics and phylogenetics
- Environmental sampling and cytoskeletal profiling of understudied marine protists from coastal waters (new in 2022-2024)

Opportunities in this group

Bachelor thesis: Yes, from students with some amount of lab experience (microbiology, molecular biology, cell biology or biochemistry in any model system).

Internships/lab rotation: Yes, we are always keen to hear from students interested in carrying out internships and rotations with us – but ideally, a minimum of 12 weeks for experimental projects and 8 weeks for computational projects.

Master thesis: Yes. Lab experience with non-mammalian model systems is a bonus but not required; experience with comparative genomics, structural bioinformatics or phylogenetics also a plus.

PhD: Applications through the EMBL International PhD programme only, no direct applications to lab. We are not actively recruiting students in the 22-23 cycle.

HiWi/Research assistant: Enquire if interested.

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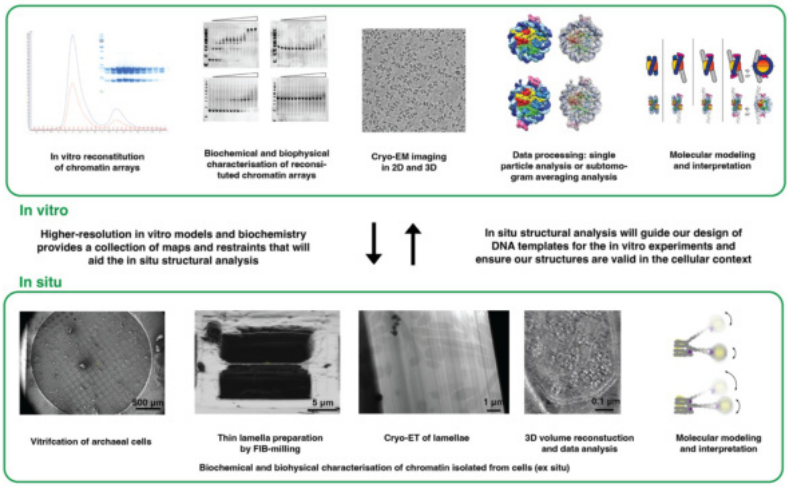
Klick me!

Organisational Principles and 3D Architecture of Archaeal Chromatin



Research focus

Our group aims to understand the mechanisms and evolutionary principles of genome packaging and chromatin 3D organisation by studying archaea using a combination of biochemistry, biophysics, and high-resolution structural biology in near-native contexts.

The genomes of all eukaryotes and most archaea are organised into chromatin, a complex of DNA and histone proteins. Chromatin allows for efficient packaging of the genome and adds multiple layers of regulation of DNA repair, replication, and transcription. Chromatin emerged before the divergence of the Archaea and Eukarya, suggesting a shared ancient role of chromatin in gene expression regulation. Although archaea display many hallmarks of eukaryotic chromatin structure, they have also evolved unique features that allow them to adapt to extreme environments.

However, structural knowledge about archaeal chromatin remains extremely limited. Thus, our group uses a combination of top-down and bottom-up structural approaches to understand the molecular architecture of chromatin in archaea.

As a top-down approach, we employ in situ cryo-electron tomography (cryo-ET) and subtomogram averaging analysis to characterise chromatin in near-native conditions inside archaeal cells. As a bottom-up approach, we reconstitute chromatin complexes of interest in vitro and characterise their structure and function. Using cryo-electron microscopy (cryo-EM), we aim to obtain high-resolution structures of archaeal chromatin complexes. This integrated approach can provide us with a complete picture of chromatin arrangement in archaea, and shed light on the evolutionary origins of chromatin organisation.

Key publication

Dodonova, S. O. (2020). Nucleosome-bound SOX2 and SOX11 structures elucidate pioneer factor function. Nature, 580(7805), 669-672.

Methods and specific features

- Biochemistry. Protein expression and purification, chromatin *in vitro* reconstitution
- Biophysics. Biophysical characterization of proteins and protein-DNA complexes (EMSA, nano-DSF, mass-photometry, DLS)
- Structural biology with the focus on cryo-EM and cryo-ET, including cryo-EM sample preparation by plunge-freezing, FIB-milling; 2D and 3D imaging (tomography), data analysis by single particle approach and/or subtomogram averaging

Opportunities in this group

Bachelor thesis: Yes, for students with prior experience in protein biochemistry. Due to extended beurocracy connected to Bachelor at EMBL, positions are limited.

Internships/lab rotation: Yes. Students with experience and interest in biochemistry are especially welcome; and/or students with cryo-EM experience.

Master thesis: Yes, for students who have done an internship in the lab, or with experience in protein/protein-DNA complex biochemistry. Due to extended beurocracy connected to Masters at EMBL, positions are limited.

PhD: Application through the centralised EMBL PhD program: www.embl.org/about/info/embl-international-phd-programme/application/.

HiWi/Research assistant: Yes, students with biochemistry experience and/or cryo-EM sample preparation/imaging are welcome to get in contact.

Contact

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Klick me!

Assembly Mechanisms of Protein-RNA Complexes at the Single-Molecule Level

Research focus

Assembly of protein-RNA complexes (RNPs) is a most fundamental process in all life forms. Our current understanding is based merely on the interaction of pre-formed protein and RNA molecules but in a cell, it is much more complicated. The RNA starts to fold and the proteins start to bind to the nascent RNA already while it is emerging from the RNA polymerase. Furthermore, many cellular factors affect this process, such as RNA modification, RNA processing or the formation of biomolecular condensates. Finally, many processes are coupled to each other (such as transcription and translation in bacteria) and therefore behave differently than if studied in isolation.

So, how can we visualize how these very dynamic and complex processes work and evolve over time?

Our lab is using single-molecule fluorescence microscopy to directly track in real-time the formation of single protein-RNA complexes in physiological relevant context by studying how i) RNA folding, ii) RNA modification, iii) RNA processing, iv) the binding of ligands, v) the processes of transcription and vi) condensate formation and vii) different macromolecular machines are functionally coupled and shape RNP assembly. We then combine this with structural biology, biochemical assays and in vivo experiments in order to gain a more complete and quantitative understanding of how RNA folds and RNPs assemble in context.

Key publication

Duss O, Stepanyuk GA, Puglisi JD, Williamson JR. (2019) Transient protein-RNA interactions guide nascent ribosomal RNA folding. *Cell* 179(6), 1357-1369.

Methods and specific features

- Single molecule fluorescence microscopy: for tracking conformational and compositional dynamics of single RNAs, proteins and macromolecular complexes/machines over minutes to hours using multiple colors.
- Cryo electron microscopy and tomography (in collaboration): for obtaining structural information on the snapshots that we can then put into order using our single-molecule real-time experiments.
- Biochemical assays: we are reconstituting active complex biochemical systems *in vitro*, such as the complete bacterial transcription-translation coupling system or eukaryotic RNA modification machineries. This allows us manipulate the systems with full control of all the components.
- *In vivo* experiments: we have started to also develop systems to track macromolecular dynamics and structure in vivo.

Opportunities in this group

Bachelor thesis: Only in exceptional cases and for computational projects; minimum 6 months.

Internships/lab rotation: Yes, with background in Biochemistry, Biophysics, Structural Biology, Molecular Biology, Chemistry or Physics. Minimum 6 months (wetlab) or 4 months (computational).

Master thesis: Yes, with background in Biochemistry, Biophysics, Structural Biology, Molecular Biology, Chemistry or Physics.

PhD: Yes, but applications via the EMBL International PhD program (https://www.embl.org/about/info/embl-international-phd-programme/).

HiWi/Research assistant: Occasionally.

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Klick me!

Pricinples of Transcriptional Regulation and its Role in Cell Fate Decisions during Development

Research focus

Complex patterns of gene expression are a key driver of embryonic development, defining cell fates during embryogenesis. This is largely regulated by enhancers, which function in complex 3D topologies with promoters. Mutations in enhancers are often associated with human diseases and evolutionary changes.
Our group has two central questions:

1. How a single genome generates such a diversity of cells, tissues and organs during development?
2. How do transcriptional networks effectively fine-tune and control cell "differentiation" during development?

To shed light onto on these questions, we optimize and implement new methods for use within complex multi-cellular *Drosophila* embryos as well as mammalian stem-cell derived "organoids" as model systems. We make use of the unbiased systems-wide approach of genomics, combining it with genetics, high-resolution imaging, and computational approaches to understand how the genome is regulated and organized during development. We are currently combining genetic and optogenetic perturbations with (single cell) genomics and imaging approaches to understand how enhancers function during developmental programmes.

Key publication

Furlong EEM, Levine M. Developmental enhancers and chromosome topology. Science. 2018 Sep 28;361(6409):1341-1345. Doi: 10.1126/science.aau0320.

Methods and specific features

The Furlong group is a mixture of 'wet lab' biologists and computational biologists, and people that do both.

The bench experimental work applys state-of-the-art genomics approaches, genome engineering and imaging approaches to address different questions related to genome regulation. The computational projects involve collaborating with the experimental biologists to analyze their genomics data, and integrate diverse large scale datasets, interpret and present results. Our group is highly profient in:

- Genetic manipulation techniques (genome editing)
- Light induced protein perturbation (optogenetics)
- Immunoflourescence, FISH and imaging-based assays
- Microscopy
- Single-cell omics (ATAC-seq, RNA-seq)
- Chromatin capture assays (Hi-C, Micro-C, Capture-C)
- Diverse Next Generation Sequencing (NGS) techniques
- Computational analysis of NGS data
- Data integration and some types of machine learning

The research group is highly international, gender balanced, interactive and fun. We have multiple international collaborations with colleagues to jointly solve biological questions. In addition to internal lab meetings and journal clubs, EMBL offers excellent training opportunities via seminars and conferences free to attend virtually.

Bachelor thesis: Occasionally, based on availability, and a commitment to stay at least 5 months - see information provided by EMBL's Scientific Visitor program.

Internships/lab rotation: We sometimes host masters graduates who are seeking further training before a PhD and are able to commit at least 5 months via the EMBL Scientific Visitor program.

Master thesis: Yes, most common visitor category in the group - for enthusiastic students enrolled in a program of relevance (i.e within Life Sciences) - a commitment of six months at the least is preferred.

PhD: Yes, via EMBL's International PhD program. Sometimes, short-term PhD visitors registered elsewhere supported by travel fellowships (EMBL, SDB etc) arriving to exchange knowledge and further their training

HiWi/Research assistant: Occasionally – minimum for 5 months. Prior lab experience is required

Contact

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Klick me!

Design Principles of Early Animals: From Development to Regeneration

Research focus

Our research is driven by the principle that change is the only constant in life. We aim to understand how the interplay between genetic and environmental factors shapes animal development, regeneration, and evolution. We are taking advantage of the biology of our distant relatives, the cnidarians, and especially the sea anemone *Nematostella vectensis*, which offers a platform to study how dynamic interactions between organisms and their environments impact a wide range of biological processes.

1. We recently described that the number of sea anemone tentacles depends on the amount of food they consume, and we are interested in addressing how nutrients activate post-embryonic programs.
2. We also linked organism behavior and morphogenesis. We study how the nervous system controls muscular hydraulics to coordinate body movement and morphogenesis.
3. We study regeneration to dissect how the interplay between local and systemic factors drives *de novo* organogenesis, and we screen for environmental drivers of regeneration beyond physical injury.

Key publication

Ikmi A, Steenbergen P, Anzo M, McMullen M, Stokkermans M, Ellington L, and Gibson M (**2020**). Feeding-dependent tentacle development in the sea anemone *Nematostella vectensis*. ***Nature communications**, Sept 02; 11:4399*.

Methods and specific features

Our group uses a wide range of experimental approaches:

- Imaging across scale (e.g., Confocal and light-sheet microscopy)
- Spatial transcriptomics and single-cell sequencing
- Computational analyses & biophysical modelling
- Precise genetic manipulation and transgenesis (e.g., gene-editing & inducible genetic system)

Opportunities in this group

Bachelor thesis: Yes, if the student is interested in genome-editing using the CRISPR/Cas9 system.

Master thesis: Yes, please contact me if you are interested in one of the questions described in the research focus section.

HiWi/Research assistant: Yes, we are looking for a research assistant to help with the husbandry of sea anemones.

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Klick me!

Cryo-EM Technology Development

Research focus

Our team develops high-throughput and fully automated pipelines to enable large-scale cryo-EM sample preparation and screening. This multidisciplinary project will integrate the work of engineers, software developers, image analysists, and molecular biologists developing new approaches to address some of the major rate-limiting steps that currently affect the throughput and the success rate of cryo-EM projects. Our pipeline will integrate specimen handling, sparse-matrix screening, and biochemical characterisation workflows to explore sample stability within a wide range of buffer conditions. The produced screening conditions will be applied to a range of cryo-EM supports by newly developed vitrification devices able to provide controlled and efficient preparation of cryo-grids. We will integrate the existing imaging routines with new software applications to establish a fully automated pipeline that will cover all the imaging steps required for large-scale cryo-EM sample screening. Our pipeline will rely on minimal operator dependency and will provide full tracking of the samples throughout the entire process. We will establish a dedicated data management system implemented with a secure web interface for project planning and real-time remote inspection of the results.

Key publication

Mattei S, Ban A, Picenoni A, Leibundgut M, Glockshuber R, Boehringer D. (2020) **Structure of native glycolipoprotein filaments in honeybee royal jelly**. *Nat Commun* 11(1). doi: 10.1038/s41467-020-20135-x.

Methods and specific features

- Cryo-electron microscopy
- Cryo-electron tomography
- Cryo-correlative light and electron microscopy
- Image processing
- Robotics
- Data management

Opportunities in this group

Bachelor thesis: Only exceptionally, mostly for students with programming experience.

Internships/lab rotation: Yes, especially for software developers or interns with programming experience.

Master thesis: Yes, for physicists, computational scientists and biochemists.

PhD: PhD positions are available through the official EMBL PhD programme

Contact

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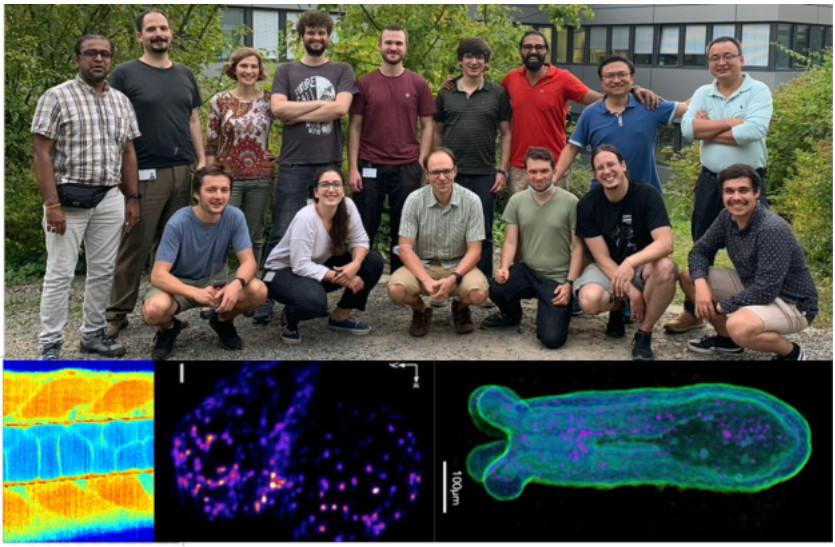
Klick me!

Advanced Optical Tools for Bio-Imaging



Research focus

Our group innovates new optical tools and methods ('microscopes') that allow to observe cellular processes and dynamics in living organisms in non-invasive ways. In particular, we develop optical imaging techniques that aim to push the frontiers of microscopy to record from deep and highly scattering, living tissues, such as the mouse. This includes our work on multi-photon microscopy which is geared towards obtaining high spatial resolution in deep brain areas. We also work on other novel microscopy methods such as photoacoustics or light-sheet microscopy with applications in imaging structural and functional processes *in vivo*. Furthermore, we are developing so-called Brillouin microscopy, an emerging technique in the life sciences that has great potential to offer new insights into 3D cellular and tissue visco-elasticity and their role in the development of entire organisms.

Key publication

L. Streich, *et al*. High-resolution structural and functional deep brain imaging using adaptive optics three-photon microscopy. **Nature Methods 18**, 1253-1258 (2021).

Methods and specific features

- Advanced light microscopy
- Multi-photon microscopy
- Photoacoustics
- Brain-imaging in awake mice
- *In-vivo* imaging of model organisms (*C. elegans*, zebrafish, mice, *Nematostella*, etc.)

Opportunities in this group

Bachelor thesis: No.
Internships/lab rotation: Yes, but minimum duration is 3-6 months.
Master thesis: Yes, prior background in microscopy or physics/engineering or computer science is advantageous.
PhD: Yes, please apply through the EMBL PhD program.
HiWi/Research assistant: Occasionally, limited.

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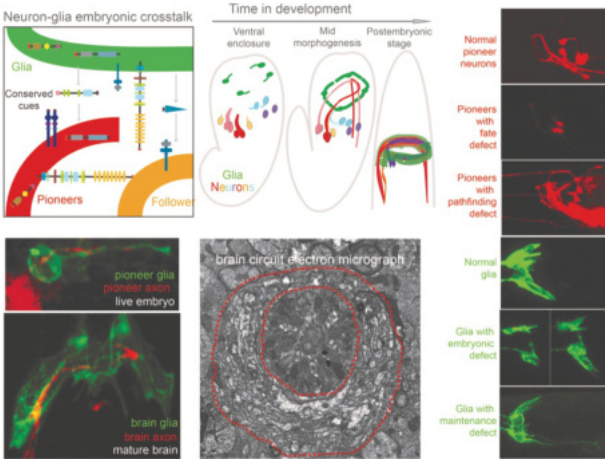
Klick me!

Mechanisms of Nervous System Assembly and Maintenance

Research focus



Assembly of functional nervous systems is fundamental for life and behavior and relies on intricate interactions between neurons and glia, both essential sculptors of circuits. In the embryo, cells with diverse fates and morphologies interact to give rise to well-defined circuit architecture that needs to be maintained throughout animal life. Dissecting mechanisms of circuit architecture is tantalizing. Cell properties, behaviors, and the molecular events that pioneer assembly or ensure the fidelity of nervous system maintenance remain elusive. We study pioneer neurons and glia of specific molecular signature that initiate hierarchical brain assembly, and the diverse molecular cues acting in neurons and glia to build and maintain circuit assembly.

Our goal is to understand the morphogenesis and interactions of pioneer neurons and glia, and events underlying hierarchical brain formation. How cells of developing circuits establish specialized morphologies to coordinate assembly *in vivo*? How do they interact spatio-temporally while specifying their fates? What principles pattern circuit assembly across species? How neuroglia ensure the maintenance of circuit architecture throughout animal's life and interactions with the environment?

We map nervous system development and maintenance *in vivo* by dissecting:

- Molecular pathways establishing specification and morphogenesis of pioneer cells
- Neuron–glia crosstalk that synergistically guide circuit assembly and connectivity
- Communication of neurons and glia with neighboring tissues and ECM
- Genes and environmental factors that affect circuit maintenance

These studies will advance our understanding of fundamental principles of live nervous system formation and provide insights into neuron-glia interactions in health and disease.

Key publication

Rapti G*, Li C, Shan A, Lu Y, Shaham S.*. (2017) *Corresponding author

Glia initiate *C. elegans* brain assembly through non-canonical Chimaerin/Furin axon guidance. Nature Neuroscience 2017 Oct; 20 (10):1350-1360. doi: 10.1038/nn.4630.

Methods and specific features

To dissect mechanisms driving formation of the nervous system, we employ a series of multi-disciplinary approaches. These include molecular biology, advanced genetics, genome engineering including CRISPR/Cas9 technology, live timelapse embryonic imaging and quantitative approaches, and in collaboration protein biochemistry and electron microscopy for neurodevelopment phenomics, photomanipulation and bioinformatics. We primarily study animals and embryos of the live model organism *C. elegans*. This valuable system features transparent embryos with morphogenesis that we can track at single-cell resolution, traceable lineages, mapped nervous system anatomy and connectivity, a sequenced genome and available single-cell RNA transcriptomics. It features cell types and genes shared with other invertebrate and vertebrate species and allows for sophisticated large-scale genetics. We are also establishing collaborations and projects for comparative studies of nervous system development, employing vertebrate cell culture and other live organisms including invertebrate models and mouse embryos.

Opportunities in this group

Internships/lab rotation: Yes, for excellent students of Master Programs in Biochemistry, Molecular Biosciences, Cell biology or Neurobiology. Preferably, internships duration is for at least four months.

Master thesis: Yes, for excellent and motivated students with a background in cell biology, molecular biology, biochemistry or neurobiology.

PhD: Only via the EMBL international PhD program.

HiWi/Research assistant: Possible.

Contact

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Klick me!

Spatial Biology from Molecules to Tissues: High-Dimensional Investigation of Cellular Organisation

Research focus

We aim to understand the spatial features and organisational principles of biological structures ranging from nanoscale complexes to subcellular compartments, cells, and tissues. To enable comprehensive investigation, we develop molecular tools and methods for advanced imaging, and employ multimodal approaches.
Our projects include:

- Expanding our technology suite by:
  - Building a high-throughput single-cell platform for spatial multi-omic profiling of cell states, utilising integrated imaging, sequencing, and machine learning.
  - Developing new correlative and multimodal imaging workflows for comprehensive profiling of cellular phenotypes.
- Identifying new biomarkers, establishing new reporters and approaches to probe and modulate the organisation of organelles and membraneless assemblies and investigate how biomolecular condensates intertwine with the molecular cell state and the cell's response to stress factors.
- Applying these approaches to address the fundamental question of how single-cell identity relates to spatial and molecular organisation. These efforts will help to uncover the complexity of intricate diseases like cancers and neurodegeneration at the single-cell level, and will provide new insights into cellular homeostasis, disease formation, and drug response.

Key publication

Saka SK *et al*. Immuno-SABER enables highly multiplexed and amplified protein imaging in tissues. Nature Biotechnology 2019 31427819. doi:10.1038/s41587-019-0207-y.

Methods and specific features

Our group is very interdisciplinary and works at the intersection of different fields, combining a range of methods and expertise including:

- Molecular and cell biology
- Cell culture and mammalian tissue preparations
- Multiplexed Immunofluorescence and smFISH (including SABER-FISH, Immuno-SABER and other multiplexing methods)
- Advanced fluorescence microscopy
- Integrated imaging and RNA-sequencing assays
- Spatial biology and spatial omics
- DNA engineering/nanotechnology
- Neurobiology and cancer
- Bioinformatics
- (single-cell) RNA-Seq
- Image analysis
- Biomolecular condensates

Opportunities in this group

Bachelor thesis: We are interested in hosting research students pursuing a bachelor degree in other instutions for their research phase (background in molecular/cell biology, bioinformatics).

Internships/lab rotation: We welcome long-term interns and rotation students (ideally > 4 months research stays), who have prior labwork experience.

Master thesis: We are interested in hosting research students pursuing an MSc degree in other instutions, for their research phase (background in molecular/cell biology, microscopy, bioinformatics – ideally with prior research experience).

PhD: PhD opporutnities are possible through the EMBL PhD Program, depending on the recruitment cycle.

HiWi/Research assistant: We are open to evaluating HiWi/Research assistant applications with molecular/cell biology lab experience.

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Klick me!

Bacterial Cellular Networks and Interactions of Bacteria with the Environment, the Host, Viruses and other Microbes

Research focus

Microbes play a key role in human and planetary health. The group uses high-throughput approaches to unravel the physiology of commensal and pathogenic bacteria during interactions with the environment in the context of:

- drug treatment (antibiotics or human drugs)
- drug combinations
- experimental evolution
- interactions with other microorganisms
- interactions with and defence against bacteriophages
- interactions with human host cells in the gut microbiome
- interactions with macrophages during intracellular infection

We systematically map the role of microbes in environmental and human ecosystems to uncover fundamental relationships stabilizing or destabilizing these systems.

Key publication

Maier, L., Goemans, C. V, Wirbel, J., Kuhn, M., Eberl, C., Pruteanu, M., Müller, P., Garcia-Santamarina, S., Cacace, E., Zhang, B., *et al*. (2021). Unravelling the collateral damage of antibiotics on gut bacteria. Nature 599, 120–124.

Methods and specific features

The group uses a variety of different methods including:

- High-throughput genetics and phenotyping for model and non-model bacteria in diverse controlled or complex enviroments
- Molecular and cellular microbiology to uncover underlying mechanisms and study bacterial physiology (e.g., genetic manipulation of commensals, pathogens and gut microbes)
- Biochemistry – protein activity/interactions, complex formation/ reconstitutions, structure-function analysis
- High-throughput imaging
- Proteomics – inlcuding establishing new methods for activity proteomics in bacteria (with Savitski Lab)
- Metabolomics (with Metabolomics CF)
- Next-generation sequencing & genomics (with Sequencing CF)

Opportunities in this group

Internships/lab rotation: Yes, for Master students.
Master thesis: Yes.
PhD: Via the EMBL International PhD Programme: https://www.embl.org/about/info/embl-international-phd-programme/.

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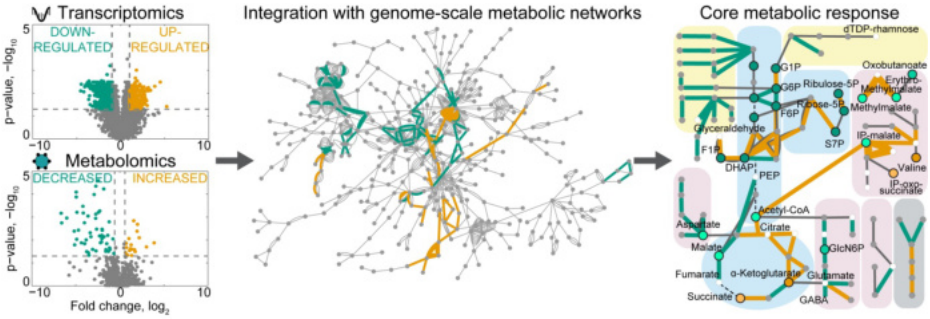
Klick me!

Multi-Omics-Based Modelling of Microbial Ecosystems



Research focus

The Zimmermann-Kogadeeva group combines computational modelling and multi-omics data integration to investigate how microbes adapt to their surroundings, and how metabolic adaptations of individual bacteria shape the functional outcome of microbial communities and their interactions with the host and the environment.

Our team develops and expands computational and experimental approaches to:

- Identify uncharacterised metabolic functions in bacteria and elucidate them by combining metabolic modelling with laboratory experiments.
- Leverage multi-omics integration techniques to quantify metabolic interactions in microbial communities.
- Combine mathematical modelling with machine learning to aid experimental design and predict the behaviour of microbial systems.

Key publication

Zimmermann M, Zimmermann-Kogadeeva M, Wegmann R, Goodman AL. Separating host and microbiome contributions to drug pharmacokinetics and toxicity. Science Vol 363 Issue 6427, (2019).

Methods and specific features

- Genome-scale metabolic modelling
- (Pharmaco)kinetic modelling
- Graph-based approaches for multiomics integration
- Machine learning
- Metabolomics
- Metagenomics
- Metatranscriptomics
- Systems biology of bacterial metabolism
- *in vitro* and *in vivo* interactions in microbial communities
- Stable 13C isotope labelling experiments

Opportunities in this group

Internships/Lab rotation: Upon request, we welcome students with interdisciplinary backgrounds, from mathematics and computer science to biology, biotechnology and pharmacology.

Master thesis: Upon request, we welcome students with interdisciplinary backgrounds, from mathematics and computer science to biology, biotechnology and pharmacology.

PhD: Within the EMBL International PhD Programme
https://www.embl.org/about/info/embl-international-phd-programme/

HiWi/Research assistant: Occasionally, limited in time.

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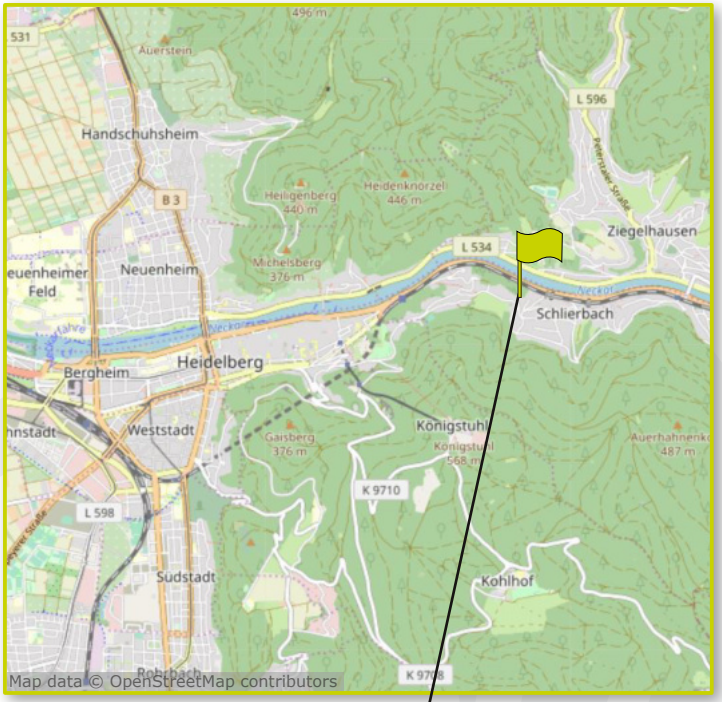
Klick me!

HITS

Heidelberg Institute for Theoretical Studies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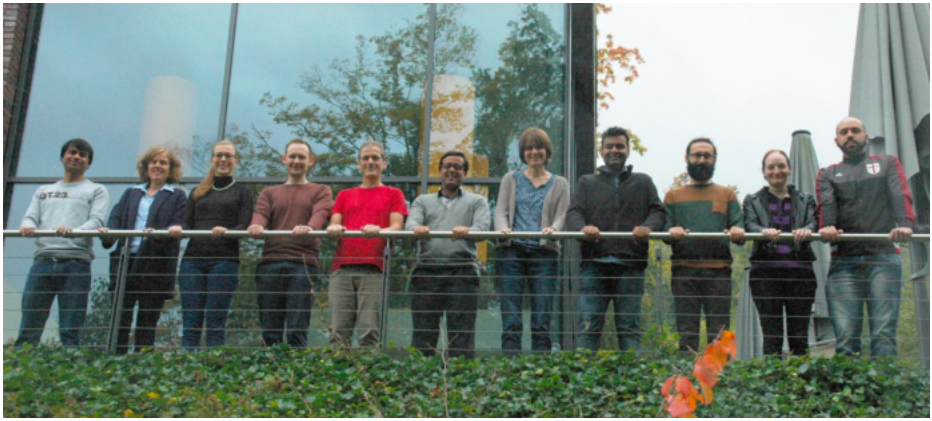
AG Wade S. 120

Molecular and Cellular Modeling



Research focus

Molecular recognition, binding and catalysis are fundamental processes in cell function. The ability to understand how macromolecules interact with their binding partners and participate in complex cellular networks is crucial to prediction of macromolecular function, and to applications such as protein engineering and structure-based drug design.

We are primarily interested in understanding how biomolecules interact. What determines the specificity and selectivity of a drug-receptor interaction? How can proteins assemble to form a complex, and what shape can the complex take? How is the assembly of a complex influenced by the crowded environment of a cell? What makes some binding processes quick and others slow? How do the motions of proteins affect their binding properties?

These questions are illustrative of the types of problem we address in our projects via the development and application of computational approaches to the study of biomolecular structure, dynamics, interactions, and reactions. We take an interdisciplinary approach, entailing collaboration with experimentalists and concerted use of computational approaches based on physics and bio-/chemo-informatics.

The research group is located at Heidelberg Institute for Theoretical Studies (HITS) (www.h-its.org).

Key publication:

Öztürk MA, De M, Cojocaru V, Wade RC (2020). Chromatosome Structure and Dynamics from Molecular Simulations, Annu. Rev. Phys. Chem. 71(1):101-119

Methods and specific features

We develop and apply a broad spectrum of computational techniques including:

- Molecular dynamics simulation
- Brownian dynamics simulation
- Continuum electrostatics
- Molecular docking and design
- Interactive, web-based visualization tools.

We make software developed in the group available for download or as webservers.

Opportunities in this group

Internships/Lab rotation: Yes, experience with scientific computing preferred.

Bachelor thesis: Yes, experience with scientific computing preferred.

Master thesis: Yes, with relevant prior internship or Bachelors' thesis.

PhD: Yes, degree in biophysics, biochemistry, physics, bioinformatics or related discipline required.

HiWi/Research Assistant: Yes, experience in programming/system administration required.

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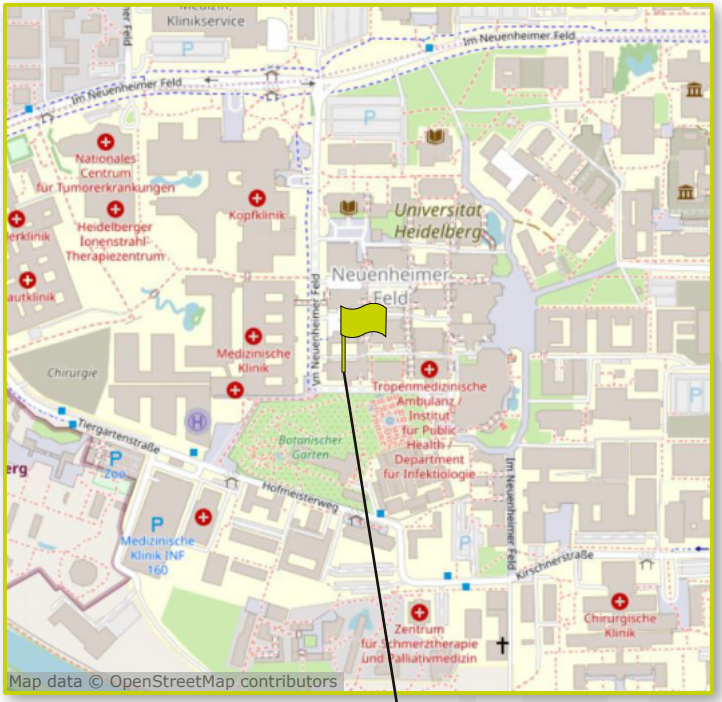
Klick me!

IPMB

Institut für Pharmazie und Molekulare Biotechnologie



AG Fricker: S. 124

AG Jäschke: S.1262

Drug Transport across the Blood Brain Barrier, Development of Innovative Drug Delivery Systems

Research focus

1) Transport mechanisms across the blood brain barrier with focus on ABC-export proteins, signaling events underlying transporter expression and function

2) Development of innovative drug delivery systems to overcome the blood brain barrier

3) Development of innovative formulations for peroral peptide and protein administration

Key publications

Engaging neuroscience to advance translational research in brain barrier biology. Neuwelt EA, Bauer B, Fahlke C, Fricker G, Iadecola C, Janigro D, Leybaert L, Molnár Z, O'Donnell ME, Povlishock JT, Saunders NR, Sharp F, Stanimirovic D, Watts RJ, Drewes LR. Nat Rev Neurosci. 2011 Mar;12(3):169-82.

Methods and specific features

- Electrophoresis
- rtPCR
- Transport experiments
- Cell culture
- Confocal laser scanning microscopy
- HPLC
- LC-MS
- Animal studies (drug targeting studies)

Opportunities in this group

Internships/Lab rotation: Yes

Bachelor thesis: Yes

Master thesis: Yes, prior internship is necessary.

PhD: Yes, if open position available.

HiWi/Research Assistant: Yes.

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Gert.fricker@uni-hd.de
+49 6221 / 548336
Consultation hours: Wednesday, 1-3 pm.

Klick me!

Chemische Biologie und Biochemie von Nukleinsäuren

Fokus der Forschung

Neue biologische Funktionen von RNA: Hier untersuchen wir vor allem die Rolle von natürlich vorkommenden Nukleinsäuremodifikationen. Wir haben durch eine neuentwickelte Kombination von chemoenzymatischer Anreicherung und Next-Generation Sequencing RNAs in Bakterien entdeckt, die kovalent mit dem universellen Redoxkofaktor NAD verknüpft sind. Wir untersuchen aktuell, welche biologischen Funktionen diese Modifikation hat. Außerdem suchen wir nach weiteren natürlichen RNA-Modifikationen.

RNA-Imaging: Leider gibt es keine natürlichen „Green fluorescent RNAs", mit denen man zelluläre RNAs für die Mikroskopie sichtbar machen kann. Wir entwickeln Kombinationen aus RNA-Aptameren und synthetischen Farbstoffderivaten, um RNAs in lebenden Zellen mikroskopisch zu visualisieren.

Photoschaltbare Nukleinsäuren: Im Kontext der Synthetischen Biologie, aber auch der Bionanotechnologie besteht ein hohes Interesse daran, Prozesse durch externe Stimuli wie bspw. Licht zwischen verschiedenen Zuständen hin- und herzuschalten. Wir entwickeln photoschaltbare Nukleotide und bauen diese in DNA ein. Anschließend studieren wir, wie Struktur und Funktion der DNA sich durch Bestrahlung mit Licht verändern.

Außerdem untersuchen wir den evolutionären Ursprung des genetischen Codes.

Schlüsselpublikation

H. Cahová, et al. and A. Jäschke (2015). NAD captureSeq indicates NAD as a bacterial cap for a subset of regulatory RNAs. Nature 519, 374-377. doi: 10.1038/nature14020

Methoden

- Molekularbiologische Methoden: PCR, Klonierung, Transkription, SELEX, Next-Generation sequencing uvm.
- Biochemische Methoden: Proteinexpression und Aufreinigung, Enzymassays, RNA-Protein-Interaktionsstudien uvm.
- Zell- und Mikrobiologische Methoden: Transfektionen in Pro- und Eukaryoten, Fluoreszenzmikroskopie.
- Chemisch-präparative Methoden: moderne mehrstufige organische Synthese mit Schutzgruppenchemie, Intertbedingungen, Kreuzkupplungen, Fotochemie etc.
- Analytische Methoden: Eigene NMR- und Massenspektrometrie, HPLC, UV-vis, CD, Fluoreszenzspektroskopie, diverse Imaging-Systeme.

Möglichkeiten in dieser Gruppe

Bachelorarbeit: Ja, in Molekularer Biotechnologie, Chemie, Biochemie und Biologie.

Praktika/Laborrotation: Ja, in Molekularer Biotechnologie, Chemie, Biochemie, Biologie (jeweils Bachelor oder Master) und Pharmazie (Wahlpflichtfach). Minimum 6 Wochen.

Masterarbeit: Ja, in Molekularer Biotechnologie, Chemie, Biochemie und Biologie. Ein vorher absolviertes Praktikum in diesem Arbeitskreis ist wünschenswert.

Doktorarbeit: Es stehen regelmäßig Stellen und Projekte zur Verfügung. Bitte fragen Sie an.

HiWi/Forschungsassistenz: Abhängig vom aktuellen Bedarf. Bitte fragen Sie an.

Kontakt

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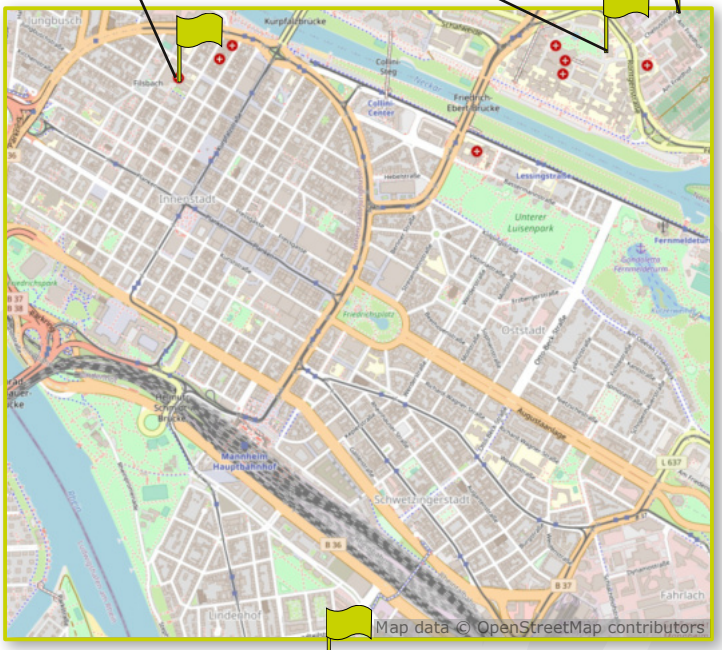
Klick me!

Mannheim

AG Grinevich: S. 134

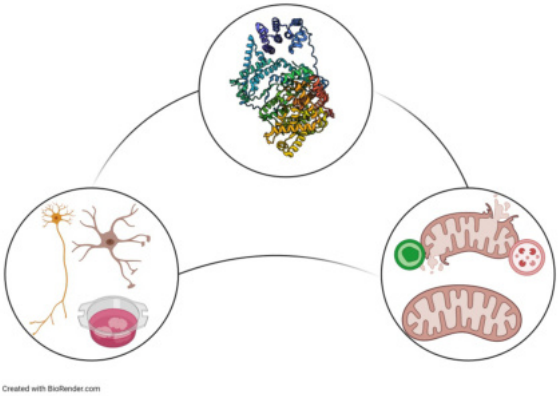
AG Bonekamp: S. 130
AG Islinger: 136

CCU Dermatooncology: S. 132



AG Mack: S. 138
AG Wiedemann: S. 140

Cellular and Organellar Compensatory Mechanisms to Mitochondrial Dysfunction



Research focus

Mitochondrial diseases are among the most common group of inherited metabolic disorders and are characterized by defects in mitochondrial oxidative phosphorylation. They are clinically heterogeneous, but often present with a number of severe neurological symptoms. Immense progress has been made in understanding the metabolic consequences of end-stage mitochondrial dysfunction, however, we lack insight into the early, cell-type specific cellular responses to mitochondrial dysfunction and how yet unidentified early mechanisms might modulate the severity of mitochondrial disorders.

We recently developed first-in-class inhibitors of mitochondrial transcription (IMTs) specifically targeting the mitochondrial RNA polymerase POLRMT. Mutations in POLRMT cause neurological disease in human patients, rendering IMTs a unique tool to model mitochondrial dysfunction in different neuronal and glial cell types.

The use of IMTs enables a time-resolved understanding of cellular and organellar compensatory mechanisms to mitochondrial dysfunction at a time when a cell can still respond. We are particularly interested in understanding early mitochondrial stress and signaling responses, mechanisms of interorganellar compensation and effects on neural plasticity. Thus, we aim to gain insight into cellular susceptibility to mitochondrial disorders and progressive mitochondrial dysfunction in age-related pathologies to enable the identification of potential interventions at an early stage.

Key publication

Bonekamp, N.A. *et al*. (2020): Small-molecule inhibitors of human mitochondrial DNA transcription. *Nature*. Dec;588(7839):712-716.

Methods and specific features

- Primary cell culture (neurons, glia cells, organotypic slices)
- Mouse models of mitochondrial disease
- Immunohistochemistry/immunocytochemistry
- Light-microscopy (confocal, live cell)
- Time-course inhibitor studies
- Biochemistry (immunoblotting, BN-PAGE, in-gel actvity assays of mitochondrial OXPHOS complexes, organelle pull-down)
- Quantitative proteomics

Opportunities in this group

Bachelor thesis: Yes, possible.
Internships/Lab rotation: Yes, typically as part of the Master Program Molecular Biosciences (or similar).
Master thesis: Yes, a prior internship in our group is prefered.
PhD: Occasionally, please inquire directly.

Contact

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Basic, Translational and Clinical Research on Skin Cancer

Research focus

The Clinical Cooperation Unit Dermato-Oncology is engaged in the diagnosis and therapy of skin tumors. Research results obtained are transferred directly into clinical practice. The main focus is on malignant melanoma, a tumor that originates from the pigment cells of the skin. The Clinical Cooperation Unit Dermato-Oncology conducts several translational research projects, including different Phase I-IV clinical trials, with innovative melanoma therapies.

Translational research focuses on stem cell features of melanoma cells, target identification to overcome resistance mechanisms, immunosuppression in melanoma, and prognostic and predictive melanoma biomarker.

Key publication

see pubmed Utikal J or Utikal JS or Umanksy V

Methods and specific features

- Different methods established (cellular biology, molecular biology, immunology)
- Work with clinical material from patients possible

Opportunities in this group

Bachelor thesis: Yes, for interested students in the field of oncology.

Internship/lab rotation: Yes, within the TMR Master Program of the Medical Faculty Mannheim.

Master Thesis: Yes, for interested students in the field of oncology.

PhD: Yes, for interested students in the field of oncology.

HiWi/Research assistant: Occasionally announced.

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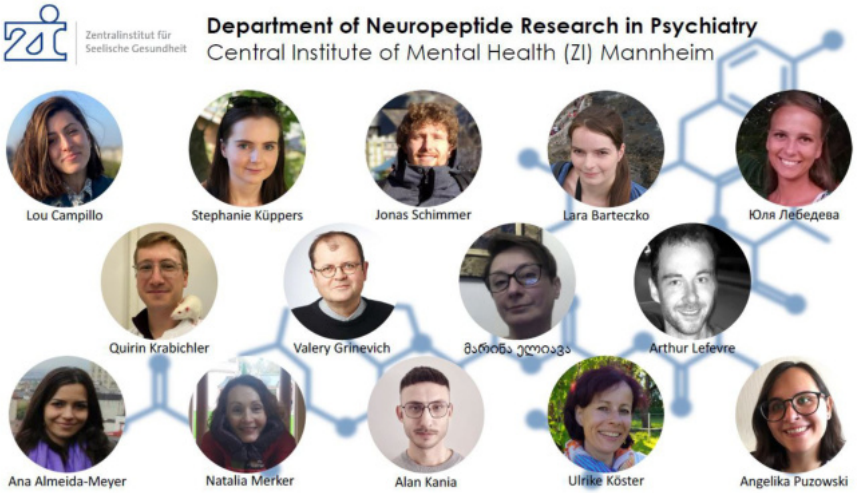
Klick me!

Neuropeptide Signaling in the Brain in Orchestration of Various Forms of Behvaiors



Research focus

Our research interests are:

1. Development of novel technologies for activity-dependent labelling and manipulation of neuropeptide neurons.
2. Deciphering the functional organization of neuropeptide brain circuits.
3. Studying the role of neuropeptides in pathophysiological mechanisms of human mental diseases to assess novel therapeutic approaches by manipulating neuropeptide signaling.

Key publication

Tang, Y., Benusiglio, D., Lefevre, A., Hilfiger, L., Althammer, F., Bludau, A., Hagiwara, D., Baudon, A., Darbon, P., Schimmer, J., Kirchner, M.K., Roy, R.K., Wang, S., Eliava, M., Wagner, S., Oberhuber, M., Conzelmann, K.K., Schwarz, M., Stern, J.E., Leng, G., Neumann, I.D., Charlet, A., **Grinevich, V**. (2020): Social touch promotes inter-female communication via activation of parvocellular oxytocin neurons. *Nature Neurosci*. doi: 10.1038/s41593-020-0674.

Research highlight: Bray, N. Social contacts. *Nature Reviews Neuroscience* (2020). https://doi.org/10.1038/s41583-020-0365-4.

Methods and specific features

- Viral vectors
- Transgenic rats
- Optogenetics
- Chemogenetics
- Anatomy
- IMARIS
- Fiberphotometry
- Fear conditioning
- Pain measures
- Social behavior

Opportunities in this group

Bachelor thesis: Yes, for students interested in Neuroscience.
Internships/Lab rotation: Yes, in the scope of Master Program "Neuroscience".
Master thesis: Yes, for excellent students in major "Neuroscience".
PhD: Yes, for students with their own fellowships.
HiWi/Research Assistant: Occassionally possible.

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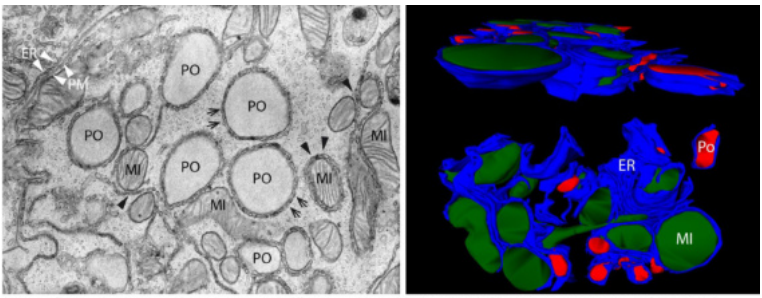
Klick me!

Significance of Peroxisomes for the Lipid Homeostasis of the Central Nervous System and Other Organs



Organelle contact sites in hepatocytes: As illustrated by a EM image and a 3D-reconstruction of EM serial sections, peroxisomes (PO) and mitochondria (MI). Are frequently sorrounded by a network of tightly associated endoplasmic reticulum (ER). Our research is focused on unraveling the function of such organell contact sites in health and disease.

Research focus

Peroxisomes are ubiquitous cellular organelles with essenential functions in the lipid metabolism of eukaryotes. In humans, mutations in genes coding for peroxisomal proteins cause severe disorders with a prominent neurodegenerative pathology, which often lead to death in early childhood. Our group is engaged in unraveling mechanistic aspects of the neuronal pathology of peroxisomal disorders. To this end, we focus on understanding the impact of alterations in lipid composition of cellular or organelle membranes to the phenotype development. In particular, we aim at understanding how these metabolic changes induce the observed degenerative processes and why they lead to the primarily neurologic phenotype characterized by a decline in motor and cognitive skills. Moreover, a recent focus of our research is directed to unveiling the functional significance of so-called "tethering-proteins" and the associated mebrane contact zones which appear to act as physical hubs for an intracellular, metabolic communication network among different organelles like peroxisomes and the ER and which may be the molecular background of a novel class of organelle disorders.

Key publication

Darwisch *et al*. 2020, Cerebellar and hepatic alteration in ACBD5-deficient mice are associated with unexpected, distinct alteration in cellular lipid homeostasis. *Comm. Biol*. 3:713.

Methods and specific features

Generally, we combine *in vivo* work on knockout mouse models with *in vitro* experiments performed in primary or permanent cell cultures. With respect to the methods applied we make use of the following techniques:

- Real time qPCR
- *In vitro* expression of protein variants or protein kockdown by RNAi
- Protein interactions assays (pull-down strategies, BN-PAGE)
- Split-GFP assays (e.g. for the analysis of membrane contact sites)
- Confocal Microscopy
- Live Cell Imaging
- Transmission electron microscopy
- Subcellular Fractionation, organelle isolation
- Quantitative proteomics (in cooperation with Proteomics Core Facility Mannheim)
- Differentiation of embryonal mouse fibroblasts and human iPSCs
- Neuronal hippocampal primary cultures

Opportunities in this group

Bachelor thesis: Yes, practical experience in cell culture, microscopy techniques or basic methods in molecular biology/protein biochemistry (Western Blotting, PCR, Molecular Cloning, etc.) are a prerequisite.

Internships/Lab rotation: Yes, for students from the graduate programs "Molecular Biosciences".

Master thesis: Yes, for students from the graduate program "Molecular Bioscience" with the major Neuroscience or Molecular and Cellular Biology.

PhD: Currently no open position.

HiWi/Research Assistant: No.

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Klick me!

Metabolic Engineering of Bacteria

Research focus

Welcome to the Lab of Matthias Mack! We study species of the genus *Streptomyces*. These remarkable bacteria make their home in the soil, where they have to battle for nutrients and survival with millions of other microorganisms. Streptomycetes produce an arsenal of compounds that can be used to communicate with - or kill - other microbes and are the source of most of our antibiotics. Our work on these fascinating bacteria covers everything from the biochemistry of antibiotic production and gene regulation, to microbial community interactions. In addition to our work on Streptomycetes we investigate the important biotechnological product riboflavin in different microorganisms with the goal to identify novel targets for metabolic engineering. We constructed a large variety of classical synthetic hosts to over synthesize riboflavin and, most importantly, also started to use autotrophic organisms as a chassis for future CO_2-based biotechnological production processes. Moreover, my group hosts scientists working on a variety of different biotechnological projects in close cooperation with industrial partners. All our projects, however, deal with microorganisms and molecular biology techniques. Following my PhD in molecular microbiology I worked for Hoffmann-La Roche in Basel prior to my appointment as professor for microbiology. I started an own group focusing on the aerobic bacterium *Streptomyces davaonensis* and the powerful antibiotic roseoflavin. We study the biosynthesis of roseoflavin, its uptake and metabolism by target cells, the mode of action of roseoflavin and the resistance mechanism of the producer.

Key publication

Schneider, C., Konjik, V., Kissling, L., and Mack, M. 2020. The novel phosphatase RosC catalyzes the last unknown step of roseoflavin biosynthesis in Streptomyces davaonensis, Mol Microbiol 114, 609-625.

Methods and specific features

We study the physiology of bacteria and fungi at the molecular level using biochemical techniques and genetic engineering tools. We cultivate microorganisms (*Escherichia coli*, Streptomyces species, Bacillus species and yeasts) in 5 mL to 10 L scale. We overproduce proteins (enzymes and regulators) using a variety of expression hosts. We purify proteins (using ÄKTA chromatography systems) and measure their activity (in case of enzymes) or otherwise determine their molecular function (e.g. RNA- or DNA binding) in case of regulators. We design and develop novel assays for enzymes and determine substrate and product levels using HPLC/MS. We genetically modify microorganisms using CRISPRcas9 based systems. In streptomycetes we use PCR-targeting for genome editing. We study riboswitches using reporter gene experiments and in vitro transcription/translation. We measure protein/protein interactions using bacterial two-hybrid systems. We determine RNA-protein interactions using a yeast three-hybrid system. In cooperation with other groups we determine crystal structures of proteins and carry out genome, metabolome, transcriptome and/or proteome analyses. In cooperation with the University of Göttingen we use proximity-dependent biotin identification (BioID) to find interacting proteins in the close vicinity of a protein of interest in living cells.

Opportunities in this group

Bachelor thesis/Internships/Lab rotation: Yes, for interested students with basic experiences in microbiology, biochemistry and molecular biology.

Master thesis: Yes, for interested students with excellent experiences in microbiology, biochemistry and molecular biology.

PhD: Yes, for interested students with excellent experiences in microbiology, biochemistry and molecular biology.

HiWi/Research assistant: Occasionally within industry projects.

Contact

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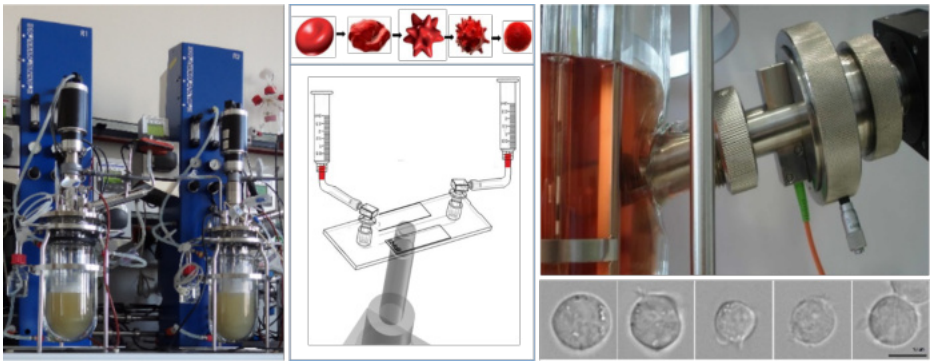
Klick me!

Cell Culture Technology and Process Monitoring



Research focus

We are primarily interested in the monitoring of biotechnological processes and biological samples. In cooperation with internal and external partners, we work with mammalian cells but also with yeast, prokaryotes and – recently – human parasites. An important focus is the development and application of *in situ* microscopes and the development of image analysis algorithms. With all this, we try to answer diverse questions like "Can we monitor viability and apoptosis of animal cells in a bioreactor in real time?", "How much storage lesion do red blood cell concentrates show over time?" or "What is the amount of filamentous bacteria in a waste water treatment basin?" Our work is highly interdisciplinary and is interesting for people with a knack for pipets, screwdrivers and IT alike.

Key publication

Sierra F DA, Melzak KA, Janetzko K, Klüter H, Suhr H, Bieback K, Wiedemann P (2017): Flow morphometry to assess the red blood cell storage lesion. Cytometry A 91(9), 874-882. DOI: 10.1002/cyto.a.23127

Methods and specific features

- Cell culture technology including fully regulated bioreactors
- *in situ* light microscopy
- Development of microscopes including all the respective hard- and software
- Image analysis algorithm development including neural networks and deep learning

Opportunities in this group

Bachelor thesis: Yes, for motivated students with a background in some of the topics mentioned above. Less than five months lab work do not really make sense.

Master thesis: Yes, for motivated students with a strong background in some of the topics mentioned above.

PhD: Yes, depending on funding. Please be motivated, determined and well organized.

HiWi/Research assistant: Yes, depending on funding.

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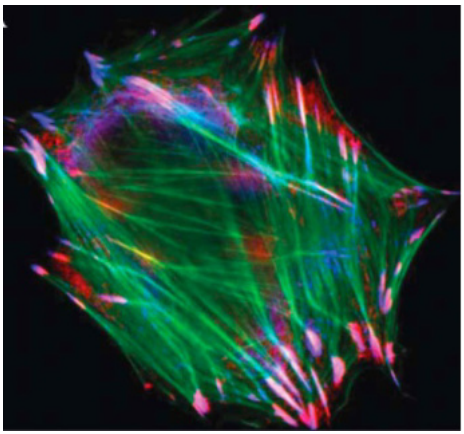
MPIMR

Max-Planck-Institut für Medizinische Forschung / MPI for Medical Research

AG Cavalcanti-Adam: S. 144
AG Fischer: S. 146
AG Göpfrich: S. 148
AG Hell: S. 150

Mechanobiology of Cell Adhesion



Research Focus

Altered mechanical and chemical properties of tissues are common traits of diseases, such as cancer and developmental disorders. We are interested in understanding how cells sense and integrate mechanical and biochemical signals from their environment.
We focus on the regulation of molecular and cellular forces generated by the interactions of cell surface receptors involved in cell-extracellular matrix adhesion and cell-cell adhesion.

- Cell-extracellular matrix adhesion: integrins are transmembrane receptors which bind to extracellular matrix molecules. They have a central role in how cells sense and respond to the mechanics of their environment. Forces mediated by integrins are transduced to the actin cytoskeleton and activate signaling for cell survival and growth.
- Cell-cell adhesion: cadherins are receptors which enable the linkage between adjacent cells. In epithelial cells the integrity of cadherin-mediated adhesions is crucial for the maintenance of tissue integrity and for the coordination of collective migration.

We investigate how the local regulation of integrin and cadherin-mediated forces affects cell migration, growth and differentiation. We also work on determining how intercellular adhesions impact on cell-matrix adhesion forces.

Key Publication

Wei Q, Holle A, Li J, Posa F, Biagioni F, Croci O, Benk AS, Young J, Deng J, Zhang M, Inman GJ, Spatz JP, Campaner S, Cavalcanti-Adam EA*. (2020) BMP-2 signaling and mechanotransduction synergize to drive osteogenic differentiation via YAP/TAZ. ***Advanced Science,*** *1902931-1902936, doi: 10.1002/advs.201902931*.

Methods and specific features

Our lab is interdisciplinary, being our research in the field of mechanobiology, at the interface between biology and physics. We design microscopy tools to measure molecular forces, e.g. using DNA-based tension probes, and cell-generated forces using traction force microscopy. We also combine these tools with surface micro- and nano-patterning approaches and fabrication of soft materials to mimic the mechano-chemical features of the extracellular environment. In the lab, the optochemical control of cell adhesion is implemented in cell culture and biochemical approaches.

Opportunities in this group

Bachelor thesis: Yes, for interested students with basic experience in Biology or related fields.

Internships/Lab rotation: Yes, in the scope of the Molecular Biotechnology program, with a focus on Biophysical Chemistry. Please apply very early since we are usually oversubscribed.

Master thesis: Yes, a prior internship in our group is prerequisite for a Master thesis. Students with a major in Biological Sciences and Physics are encouraged to apply.

PhD: Possible from time to time.

HiWi/Research Assistant: Occasionally, depending on project availability.

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Klick me!

Virus-Host Interactions in Protists

Research Focus

We study the ecology and evolution of DNA viruses infecting single-celled eukaryotes (protists) from natural ecosystems. Our main model is the marine heterotrophic flagellate *Cafeteria* sp., but we also work on freshwater protists and algae.

Our focus lies on giant DNA viruses, which have particles in the 0.2-1.0 µm range and genomes that can exceed one megabase. A second group of smaller DNA viruses called virophages often parasitizes giant viruses. We are interested in this tripartite host-virus-virophage interaction and its eco-evolutionary consequences.

We isolate novel protist and virus strains in laboratory culture, using enrichment methods for water and soil samples.

We characterize the infection cycles of protist viruses by molecular biology methods and electron microscopy, and sequence, assemble and annotate their genomes for a better understanding of the various roles viruses play in the environment.

Key Publication

Fischer and Hackl (2016). Host genome integration and giant virus-induced reactivation of the virophage mavirus. Nature 540: 288-291.

Methods and specific features

- Microscopy
- Electron microscopy
- Culturing
- PCR & qPCR
- Flow cytometry
- DNA extraction
- DNA sequencing (e.g. Nanopore)
- Virus purification
- Bioinformatics with a focus on genome assembly and comparative genomics

Opportunities in this group

Bachelor thesis: Yes, combined with a prior internship in our group. Must be self-organized and highly motivated.

Internships/Lab rotation: Yes, with a minimum duration of 8 weeks, longer if possible.

Master thesis: Yes, combined with a prior internship in our group. Must be self-organized and highly motivated.

PhD: Currently not available.

HiWi/Research Assistant: Please inquire.

Contact

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Klick me!

Biophysical Engineering of Life

Research Focus

Can we construct a cell from non-living matter? In search for answers, bottom-up synthetic biology has successfully encapsulated functional sets of biomolecules inside lipid vesicles, yet a "living" synthetic cell remains unattained. Instead of relying exclusively on biological building blocks, the integration of new tools can be a shortcut towards the assembly of active and eventually fully functional synthetic cells. This is especially apparent when considering recent advances in DNA nanotechnology. DNA nanotechnology allowed us to engineer various functional parts for synthetic cells, which, meanwhile have found diverse applications as biophysical probes in cell biology. Recently, we engineered functional DNA-based mimics of a cytoskeleton. These cytoskeletons are capable of stimuli-responsive reversible assembly, cargo transport and can deform giant unilamellar lipid vesicles (GUVs) from within. We further demonstrate the division of GUVs based on phase separation or spontaneous curvture increase and osmosis rather than the biological building blocks of a cell's division machinery. We derive a parameter-free analytical model which makes quantitative predictions that we verify experimentally. The osmolarity increase can be triggered by enzymatic reactions or by light-triggered release of caged compounds. Ultimately, by coupling GUV division to their informational content and their function, we aim for a prototype of a synthetic cell capable of evolution.

Key Publication

Zhan, P., Jahnke, K., Liu, N. & Göpfrich, K. Functional DNA-based cytoskeletons for synthetic cells. Nature Chemistry (2022), https://www.nature.com/articles/s41557-022-00945-w.

Methods and specific features

- DNA and RNA origami
- 3D Laserprinting
- Microfluidics
- Confocal microscopy
- Lipid vesicles
- Atomic force microscopy

Opportunities in this group

Bachelor thesis: Spaces are very limited, please include a CV and transcript in your email.

Internships/Lab rotation: Spaces are very limited, please include a CV and transcript in your email.

Master thesis: Yes, please include a CV and transcript in your email.

PhD: Yes, typically after a HiWi/internship to ensure good fit with the group.

HiWi/Research Assistant: Spaces are very limited, please include a CV and transcript in your email.

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Klick me!

Optical Nanoscopy

Research Focus

The ultimate goal of biological super-resolution fluorescence microscopy is to provide three-dimensional resolution at the size scale of a fluorescent marker. In the Hell Group, our focus is on developing novel fluorescence microscopes with spatial resolutions down to a few nanometers. Our most recent contribution to the field is MINFLUX, a breakthrough concept, which achieves true molecular resolution. So far, we have demonstrated MINFLUX nanoscopy can provide resolutions in the range of 1 to 3 nm for structures in fixed and living cells.

MINFLUX and other super resolution techniques (MINSTED, STED, RESOLFT, GSDIM) utilize labels which have a reversible transition or switching of fluorescence between a bright and a dark state. Consequently, the group is also interested in developing new and innovative fluorescent markers and labeling methodologies.

The majority of current and future efforts in the group concentrate on the development of the MINFLUX concept and compatible labeling methodologies.

The group is divided between two sites, MPI for Medical Research in Heidelberg and MPI for Multidisciplinary Sciences in Göttingen. Opportunities for talented and hard-working students are available at both locations.

Key Publication

Gwosch, K.C., Pape, J.K., Balzarotti, F. *et al*. MINFLUX nanoscopy delivers 3D multicolor nanometer resolution in cells. Nat Methods 17, 217–224 (2020). https://doi.org/10.1038/s41592-019-0688-0.

Methods and specific features

The research of the group focuses on:

- Super-resolution microscopy techniques, including MINFLUX and STED
- Development of new and innovative fluorescent markers
- Live-cell-compatible labeling concepts

Opportunities in this group

Bachelor thesis: Yes, depending on capacity and preferably for at least 3 months. Placements are highly competitive and early applications are recommended.

Internships/Lab rotation: Yes, depending on capacity and preferably for at least 3 months. Placements are highly competitive and early applications are recommended.

Master thesis: Yes, for excellent and highly motivated students. A prior internship in the group is an advantage.

PhD: Yes, for outstanding students who are hard working and highly motivated.

HiWi/Research Assistant: According to demand.

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Göttingen: https://www.mpibpc.mpg.de/hell/
http://www.4pi.de/

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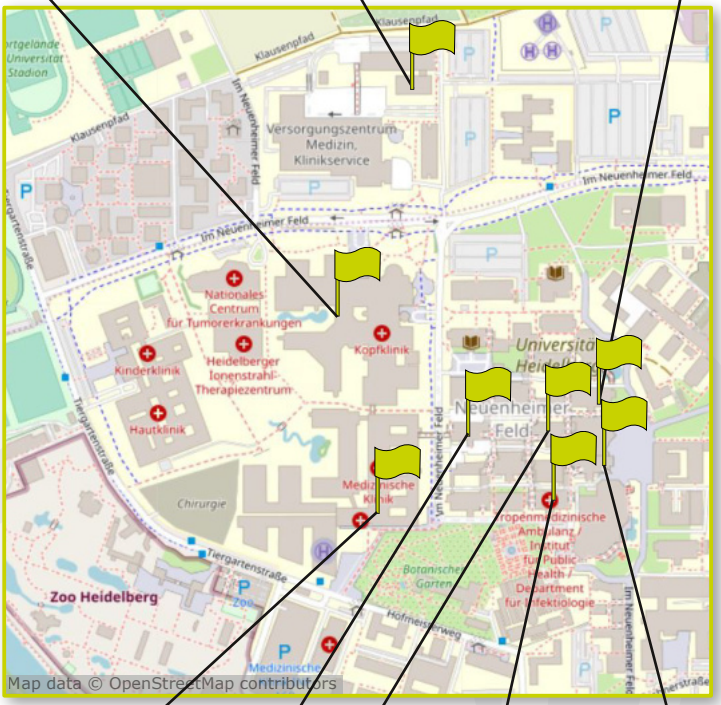
Universitätsklinikum und Medizinische Fakultät Heidelberg

AG Mier: S. 164

AG Thiel: S. 168

AG Ullrich: S. 170



AG Weiss: S. 172

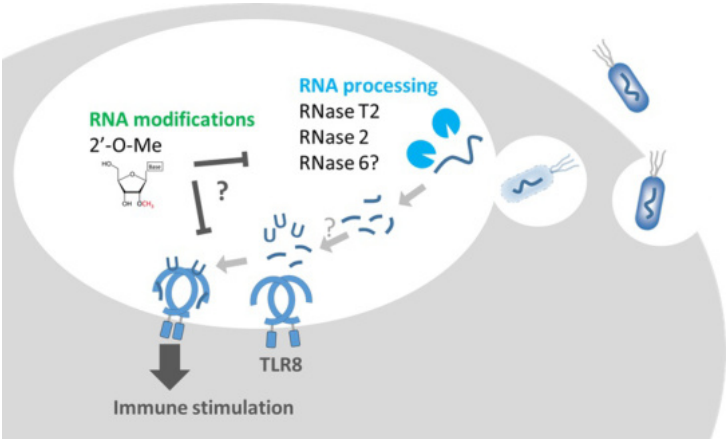
AG Laugsch: S. 162

AG Nakchbandi: S. 166

AG Dalpke: S. 154
AG Kubatzky: S. 160
AG Ingham: S. 158

AG Hecker: S. 156

Infection and Innate Immunity



Research focus

The focus of my research is infection and immunity. Recent work centers on two topics:

1. We are studying the recognition of microbial nucleic acids by pattern recognition receptors. We try to elucidate principles that enable Toll-like receptors to differentiate foreign, microbial from self nucleic acids. Specifically, we address the importance of RNA modifications and RNA degradation on immune stimulation. Moroever, we explore to what extent RNA sensing is of physiological importance for detection of bacterial infections.

2. A second project area studies polymicrobial infections by means of next generation sequencing. We focus on patients suffering from cystic fibrosis (CF) but also use this technique to explore microbiome changes in other diseases. In CF we aim to analyze microbiome alterations in early childhood as well as during exacerbation and focus on interactions of commensal and pathogenic bacteria. We also try to link microbiome changes to immunological alterations and we explore the interplay of commensal bacteria with lung pathogens.

Methods and specific features

- cell culture, primary cells
- organoids: precision cut lung slices
- Cell isolation, MACS
- qRT-PCR
- Flowcytometry
- NGS: amplicon sequencing, metagenomics, metatranscriptomics
- infection experiments *in vitro*
- gene manipulation, CRISPR

Opportunities in this group

Bachelor thesis: Yes, for interested students with knowledge in immunology.

Internship/Lab rotation: Yes, mostly for students of Master Mol. Biosciences, Major Infectious Diseases.

Master thesis: Yes, for students with very good knowledge in infections and immunity; intership advisable.

PhD: Upon announcment.

HiWi/Research assistant: Hiwi: teaching in microbio course in winter term.

Contact

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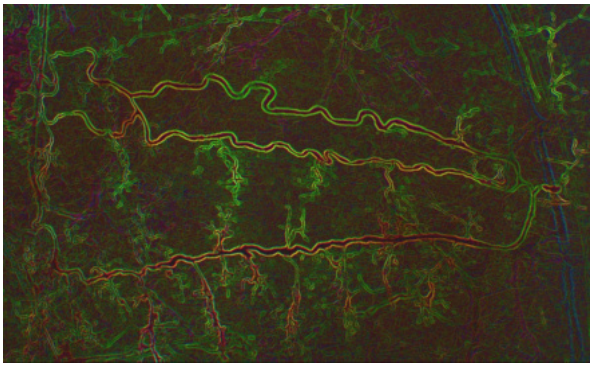
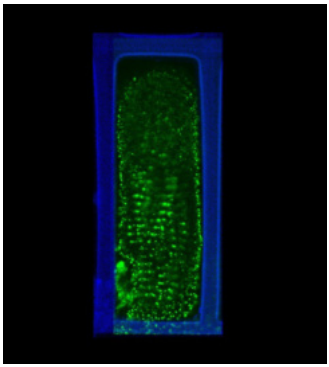
Klick me!

(Biomechanic) Signaling Pathways, Gene Regulation, Remodeling Processes, Electrophysiology and Stem Cell Differentiation in the Cardiovascular System





Research focus

Our department is active in basic biomedical research, using biochemistry, molecular biology, cell culture-, organ culture- and animal model-based approaches as well as human blood and tissue samples to investigate fundamental processes governing homeostatic regulation in the cardiovascular system. The knowledge gained hereby may serve as a basis for the development of novel molecular and cell biological therapies.

Research areas include

- cardiac and vascular gene regulation and remodeling triggered by biomechanical factors, e. g., during hypertension and atherosclerosis, at all levels of signal transduction, from focal adhesion-associated biomechanical transducers to transcription factors and epigenetic DNA modifications affecting gene expression
- development of nucleic acid-based therapeutics and their viral-based delivery and expression for the treatment of Marfan syndrome-associated vascular defects
- reactive oxygen species as signaling molecules in diabetes
- interaction of endothelial cells with leukocytes and platelets during chronic inflammatory diseases
- functional characterization of stem cell-derived cardiomyocytes, with special focus on ion channels and electric coupling, and their cultivation as 3D cell patches for regenerative medicine

Key publication

Remes A, Wagner AH, Schmiedel N, Heckmann M, Ruf T, Ding L, Jungmann A, Senger F, Katus HA, Ullrich ND, Frey N, Hecker M, Müller OJ. AAV-mediated expression of NFAT decoy oligonucleotides protects from cardiac hypertrophy and heart failure. Basic Res Cardiol. 2021 Jun 4;116(1):38.

Methods and specific features

- cell and organ culture (e.g. primary cells, cell lines, microwell co-cultures, cell cultivation in microfabricated 3D substrates, cultivation and experimental manipulation of blood vessels)
- animal models (e.g. transgenic mice, experimentally manipulated mouse models)
- molecular biology (e.g. standard and advanced analytical methods, transfection with plasmids and siRNA, AAV-based transduction)
- advanced light microscopy, immunocyto/histochemistry, confocal calcium imaging
- electrophysiology (e.g. patch clamp technique)

Opportunities in this group

Bachelor thesis: Yes; department head is co-opted member of Heidelberg University Faculty of Biosciences.

Internship/Lab rotation: Yes; within the framework of Heidelberg University Faculty of Biosciences' Master programs.

Master thesis: Yes, ideally following a Bachelor project or a practical lab course in our group, either for the experimental work only or, for specific programmes, supervised by the director of the department, who is co-opted member of Heidelberg University Faculty of Biosciences.

PhD: Yes, within the framework of the Heidelberg Biosciences International Graduate School.

HiWi/Research assistant: occasionally, please inquire.

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Klick me!

Insecticide Resistance and Parasite Development in Anopheles Mosquitoes

Research focus

Insecticide-based vector control tools are the most successful intervention at preventing malaria cases to date. Despite the success, the limited number of chemicals availabile for use in these programs has led to intense insecticide resistance in the mosquitoes that carry malaria. My group focuses on insecticide resistance to chemistries commonly used in malaria control programs. We determine novel mechanisms of resistance to insecticides and how insecticide resistance and/or exposure might directly impact the malaria parasite developing within the mosquito. We work on the interface between basic and translational biology, with the focus being on improving vector control strategies for use in national malaria control programs.

Key publication

A sensory appendage protein protects malaria vectors from pyrethroids. V A Ingham *et al*. Nature, 2019, 577:376–380.

Methods and specific features

We use molecular biology, bioinformatics and whole organism biology to determine how insecticides change mosquito biology and how this change impacts the vector competence. Amongst the most common techniques used in my lab are:

- RNAseq
- Whole genome sequencing
- Imaging
- RNAi
- qPCR
- PCR
- Plate read assays
- Cell culture
- Malaria infections
- Insecticide assays

Opportunities in this group

Bachelor thesis: Yes.

Internships/Lab rotation: Yes.

Master thesis: Yes.

PhD: Position dependent.

HiWi/Research Assistant: Occasionally.

Contact

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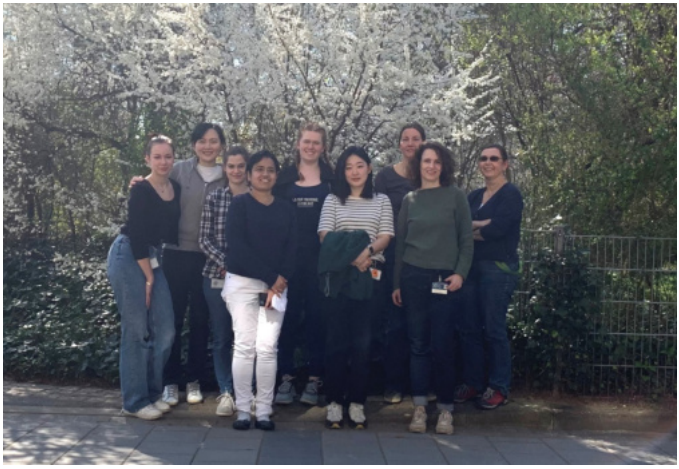
Klick me!

Physiological and Pathological Interactions between Bone and Immune Cells - Osteoimmunology



Research focus

We are interested in mechanisms of bacterial immune evasion in the context of bone infections. In mammalian cells, bone cells regulate the skeleton while the immune system deals with the detection and destruction of invading pathogens. Interestingly, there is a strong crosstalk between these two systems that led scientists to define the emerging field of osteoimmunology. During inflammatory conditions, especially when chronic, bone loss can be observed due to increased osteoclast formation and activity. Macrophage function as well as osteoclast differentiation are influenced by their metabolic activity. While pro-inflammatory M1 macrophages obtain their energy through glycolysis and fatty acid oxidation, anti-inflammatory M2 macrophages rely on oxidative phosphorylation. This change towards glycolytic energy production (Warburg effect) under inflammatory conditions allows the quick generation of energy needed for the induction of an efficient immune response. We use several model systems to investigate the metabolic activity of macrophages and osteoclasts:

- *Pasteurella multocida* Toxin: A bacterial protein toxin that triggers osteoclast differentiation through constitutive GPCR signalling.
- Staphylococci in bone infection: We aim to understand the crosstalk between bacteria and immune cells/osteoclasts.

- Plumbagin-mediated effects on bone cells: This phytochemical is a potent ROS inducer with (anti)osteoclastic properties.
- Immune-metabolism in bacterial infections: We investigate the ability of metabolic enzymes to modulate the plasticity of macrophages and their ability to become osteoclasts.

Key publication

Seebach E, Kubatzky KF. „Chronic Implant-Related Bone Infections-Can Immune Modulation be a Therapeutic Strategy?". Front Immunol, doi: 10.3389/fimmu.2019.01724 (2019)

Methods and specific features

- FACS analysis to look for immune cell activation or metabolic activity
- Western Blots to delineate signalling pathways
- qRT-PCR to study cell differentiation and activation, respectively
- Cell differentiation assays
- Metabolic assays
- Work with primary mouse cells and cell lines
- Retroviral and lentiviral transductions
- Generation of bacterial biofilms

Opportunities in this group

Bachelor thesis: Yes.
Internships/Lab rotation: Yes.
Master thesis: Yes, after prior internship.
PhD: Depends on funding situation.
HiWi/Research Assistant: No.

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Klick me!

Transcriptional Regulation and Non-coding Elements in Human Development and Congenital Diseases Using Various Human *in vitro* Cell Models

Research focus

Since many neurodevelopmental disorders are associated with craniofacial malformations, we explore the relationship between head (craniofacial) and brain development in health and disease. More exactly, we investigate the link between human neural crest (hNCC), which are forming the craniofacial structures, and neuronal cells (neural progenitors and neurons) that are shaping brain features. Our research focuses on developmental genes that require specific and dynamic regulation, e.g., by enhancers, to ensure the establishment of precise gene expression patterns during development. Alteration of this regulation can have pathological consequences and ultimately lead to disease.

Key publication

Laugsch M, Bartusel M, Rehimi R, Alirzayeva H, Karaolidou A, Crispatzu G, Zentis P, Nikolic M, Bleckwehl T, Kolovos P, van Ijcken WFJ, Šarić T, Koehler K, Frommolt P, Lachlan K, Baptista J, Rada-Iglesias A. Modeling the Pathological Long-Range Regulatory Effects of Human Structural Variation with Patient-Specific hiPSCs. Cell Stem Cell. 2019 May 2;24(5):736-752.e12.

Methods and specific features

To answer our biological questions, we use standard techniques such as RT-qPCR, immunofluorescence, Western blotting, etc. as well as state-of-the-art methods.

For this purpose, we differentiate healthy, patient-derived or CRISPR/Cas9 engineered induced pluripotent human stem cells (hiPSC) into the NCC, neural progenitors or neurones. Subsequently, we analyse them by various molecular and epigenetic techniques, e.g., ChIPseq, RNAseq and stateoftheart methods to capture 3D conformation of the genome and enhancergene interaction, such as 4Cseq and HiC.

Opportunities in this group

Bachelor thesis: Yes. Previous lab rotation in our group and basic expiernce in molecular biology are recommended.

Internships/Lab rotation: Yes. Please apply in advance. It will help us to tailor your experiments according to your individual and our needs.

Master thesis: Yes. Students with basics cell culture experience or bioinformatical background are particularly welcome. A prior internship in our group is perquisite for a master thesis.

PhD: Yes. Depending on our available resources, open positions are advertised on our homepage. Otherwise, we support excellent candidates to apply for a scholarship.

HiWi/Research Assistant: Yes. Occasionally available (for students with some experience in basic molecular biology methods).

Contact

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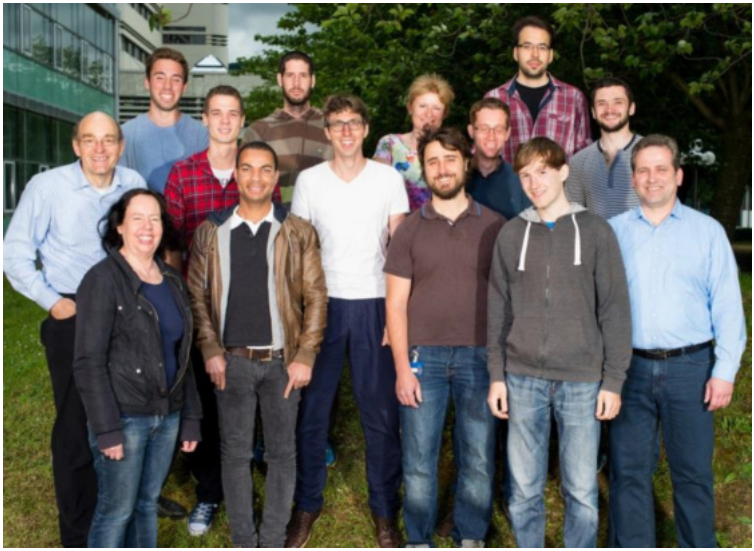
Klick me!

Radiopharmaceutical and Medicinal Chemistry



Research focus

Our research group "Radiopharmaceutical Chemistry" is working on the development of therapeutics. In particular, we are focusing on 4 main research areas:

- development of antibiotics-peptide variants for the treatment of antibiotic-resistant bacterial strains
- development of radioactively labelled tracers for diagnostics (molecular imaging) and therapy (endoradiotherapy) of solid tumors
- further development of Myrcludex B, a Hepatitis B entry inhibitor, in cooperation with Prof. Dr. Urban, Molecular Virology at UKH
- further development of antibody-drug-conjugates in cooperation with partners in the pharmaceutical industry

In this interdisciplinary research field, radiopharmaceutical chemistry allows chemical methods to be transferred to clinical application. Further, we are thoroughly evaluating the newly identified compounds *in vitro* and *in vivo.* Therefore, the range of methods applied in radiopharmacy can be ideally used to determine the pharmacokinetics of potential active ingredients. Promising compounds are then transferred into clinical trial.

Key publication

Umstätter et al. (2020). Vancomycin Resistance Is Overcome by Conjugation of Polycationic Peptides. Angew. Chem. Int. Ed. 59, 8823–8827.

Methods and specific features

- Peptide synthesis and bioconjugation
- Chemical synthesis and radio-labelling
- Biodistribution and toxicity studies
- Non-invasive small animal imaging (e.g. PET)
- Analytical methods: Chromatographie (HPLC), Mass Spectrometry (LC-MS)

Opportunities in this group

Bachelor thesis: Yes, for interested students with basic experience and interest in Chemistry.

Internship/Lab rotation: Yes, placement in diverse projects possible.

Master thesis: Yes, for excellent students with a laboratory experience and interest in our research topics.

PhD: Yes, depending on funding situation.

HiWi/Research assistant: Yes, occasionally.

Contact

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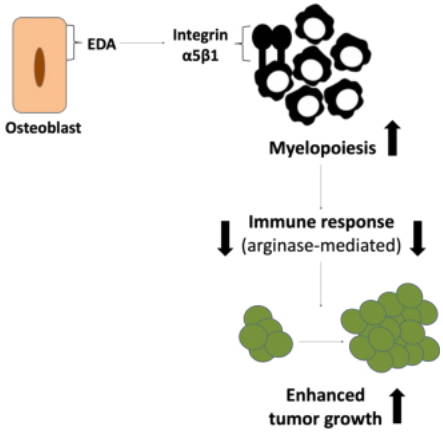
Klick me!

Untersuchung Klinisch Relevanter Fragen mit Hilfe Transgener Mausmodelle



Osteoblasts produce an isoform of fibronectin that is able to modulate myelopoiesis in the bone marrow. This exposure leads to a change in the immune response of myeloid cells and enhances cancer growth (Rossnagl et al. PLoS Biology).

Research focus

Unser Forschungsprogramm beinhaltet die Untersuchung der Funktionen der extrazellulären Matrix und die Rolle der daraus resultierenden Signalwege bei verschiedenen Erkrankungen (Krebs, Fibrose, Osteoporose). Wir verwenden ein breites Methodenspektrum, inklusive Protein-Biochemie, Primärzellisolation, zellulärer und molekularer Biologie, verschiedener Färbungsmethoden und -analysen sowie speziellerer Techniken, wie z. B. Biolumineszenz-Untersuchungen. Wir arbeiten an genetisch veränderten Mauslinien (wie z. B. konditionellen Knockout-Mäusen), führen aber auch Teile unserer Arbeiten an primären Zellen oder Zelllinien durch.
Siehe als Beispiel bitte:

A Subpopulation of Stromal Cells Controls Cancer Cell Homing to the Bone Marrow. Rossnagl S, Ghura H, Groth C, Altrock E, Jakob F, Schott S, Wimberger P, Link T, Kuhlmann JD, Stenzl A, Hennenlotter J, Todenhöfer T, Rojewski M, Bieback K, Nakchbandi IA. Cancer Res. 2018 Jan 1;78(1):129-142. Link: https://pubmed.ncbi.nlm.nih.gov/29066511/

EDA-Fibronectin Originating from Osteoblasts Inhibits the Immune Response against Cancer. Rossnagl S, Altrock E, Sens C, Kraft S, Rau K, Milsom MD, Giese T, Samstag Y, Nakchbandi IA. PLoS Biol. 2016 Sep 21;14(9):e1002562. Link: https://pubmed.ncbi.nlm.nih.gov/27653627/.

Key publication

Cdc42 in osterix-expressing cells alters osteoblast behavior and myeloid lineage commitment.
Wirth F, Huck K, Lubosch A, Zoeller C, Ghura H, Porubsky S, Nakchbandi IA. Bone. 2021 Dec;153:116150.

Methods and specific features

Protein-Biochemie, Primärzellisolation, zelluläre und molekulare Biologie, verschiedene Färbungsmethoden und -analysen sowie speziellere Techniken, wie z. B. Biolumineszenz-Untersuchungen. Wir arbeiten an genetisch veränderten Mauslinien (wie z.B. konditionellen Knockout-Mäusen), führen aber auch Teile unserer Arbeiten an primären Zellen oder Zelllinien durch.

Opportunities in this group

Bachelor thesis: Gelegentlich für Interessierte mit Laborerfahrung.
Internship/Lab rotation: Ja, für mindestens 3 Monate oder vor einer Masterarbeit.
Master thesis: Ja, für Interessierte mit der Bereitschaft, in einem "Maus-Labor" zu arbeiten.
PhD: Zurzeit eine Position offen. Bitte Kontakt aufnehmen.
HiWi/Research assistant: Ja. Bitte Kontakt aufnehmen.

Contact

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Wir sind auch mit dem MPI für medizinische Forschung (Jahnstr. 29, Heidelberg; Kein Einlass ohne Voranmeldung) und dem MPI für Biochemie (Martinsried/München) assoziiert

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Klick me!

Congenital Disorders of Glycosylation (CDG)

Research focus

Glycosylation is one of the most common protein modifications currently known. Defects in this complex metabolic pathway lead to the rapidly growing disease group "Congenital Disorders of Glycosylation" (CDG) with more than 150 monogenetic defects currently known. Patients suffer from a variety of symptoms including decreased cerebellar volume, seizures, reduced nerve conduction velocity, strabismus, facial and skeletal dysmorphisms, muscle weakness, liver and heart problems, fat distribution disorders and blood clotting problems. The focus of our group lies in the identification of so far unknown glycosylation deficiencies in human. In recent years our group identified several of the CDG-I and CDG-II index patients. Nevertheless, a lot of questions concerning e.g. the interplay of an affected protein with its sugar donor substrate or its neighbouring reaction partners are unsolved and the pathophysiological mechanisms underlying these defects are largely unknown. To find out, we apply a wide range of model systems which are also used to investigate new therapeutic approaches for different types of CDG.

Key publication

Feichtinger RG, Hüllen A, Koller A, Kotzot D, Grote V, Rapp E, Hofbauer P, Brugger K, Thiel C, Mayr JA, Wortmann SB. A spoonful of L-fucose-an efficient therapy for GFUS-CDG, a new glycosylation disorder. EMBO Mol Med. 2021 Sep 7;13(9):e14332.

Methods and specific features

We are applying a wide range of biochemical, genetic and cell biological techniques. We dispose methods like cloning, sequencing, qRT-PCR, enzyme and transporter activity measurements, metabolic labelling, analyses of lipid- and protein-linked oligosaccharides, glycan studies, SDS-PAGE, 2D electrophoresis, immunoprecipitation, Western and lectin blotting, HPLC, mass spectrometry, work with patient-derived fibroblasts, COS7, HEK293 and HeLa cells, transfection and viral infection (S2 Lab) as well as immunofluorescence.

Opportunities in this group

Bachelor thesis: Yes, for interested students with profound basics in biology/biochemistry.

Internship/Lab rotation: Yes.

Master thesis: Yes. Possible throughout the year for excellent students with emphasis on biochemistry.

PhD: Open positions are announced on the popular internet platforms. Please check.

HiWi/Research assistant: Occasionally. Please ask by email.

Contact

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Klick me!

Structural and Functional Maturation of Stem Cell-Derived Cardiomyocytes

Research focus

We are interested in the use of human iPSC-derived cardiomyocytes for the development of novel cell-based treatment options for heart failure patients, as disease models or for pharmacological tests of new compounds. Since these cells retain an immature phenotype after differentiation, they present significant structural and functional limitations in comparison to native adult cardiomyocytes. Therefore, the main focus of our research is to characterize the basic functional features of these cells in comparison with native cardiomyocytes and to develop new and innovative ways to improve cardiogenic maturation.

Our lab is specialized in three domains:

1.) Cardiac excitation-contraction coupling

2.) Structural and functional maturation

3.) Intercellular communication and electrical signal propagation

Key publication

Silbernagel N. et al., and Ullrich ND (2020) Shaping the heart: structural and functional maturation of iPSC-derived cardiomyocytes in 3D micro-scaffolds. Biomaterials, 227:119551. doi.org/10.1016/j.biomaterials.2019.119551

Methods and specific features

We work with induced pluripotent stem cell-derived cardiomyocytes from reprogrammed human fibroblasts (iPSC-cardiomyocytes) and apply special cell culture techniques to achieve stronger maturation in single iPSC-cardiomyocytes. Using a broad spectrum of electrophysiological and live-imaging techniques, we analyze the structural and functional properties of iPSC-cardiomyocytes in single cells, cell pairs and small multicellular preparations with special focus on ion channel function, calcium signaling, cell contraction and intercellular coupling of iPSC-cardiomyocytes. Molecular methods are used to genetically manipulate diverse intracellular signaling cascades to better understand the functional regulation of maturation processes.

Opportunities in this group

Bachelor thesis: No.

Internship/Lab rotation: Yes, within the scope of a Master Program with focus on Cell Biology, Biophysics, Optics, Cardiovascular Science or Neuroscience.

Master thesis: Yes, for excellent students with either a BSc in Biology or a prior internship in our group as starting point for a Master thesis.

PhD: Occasionally possible.

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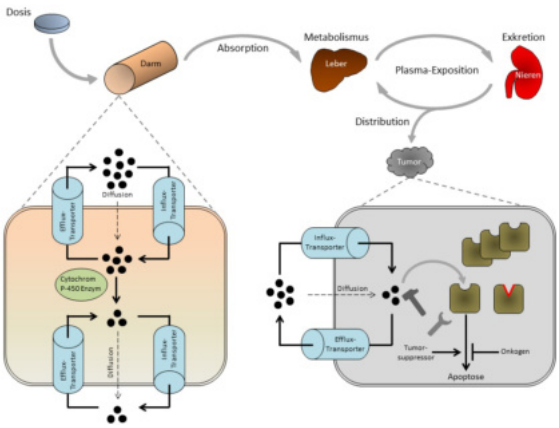
Klick me!

Experimentelle und Klinische Pharmakologie



Fokus der Forschung

Die Klinische Pharmakologie beschäftigt sich mit Fragen der Individualisierung von Arzneimitteltherapien, um deren Wirksamkeit und vor allem Sicherheit zu gewährleisten. Folgerichtig werden Modulatoren der Arzneimitteltherapiesicherheit erforscht, z.B. der Einfluss von Komedikation, Genetik oder Umweltfaktoren auf die Arzneistoffkinetik. Darüber hinaus werden die molekularen Wirkmechanismen von Pharmaka eingehend untersucht, um Rückschlüsse auf beobachtete klinische Wirkungen oder Nebenwirkungen ziehen zu können. Ein weiterer Schwerpunkt bildet die Entwicklung von Biomarkern. Im Detail:

- Arzneimittelinteraktionen durch Phase I-, Phase II-Enzyme oder Arzneistofftransporter.
- Zusammenhang zwischen extrazellulären/intrazellulären Wirkstoffkonzentrationen und Wirksamkeit von Arzneistoffen (zelluläre PK/PD).
- Pharmakogenetik pharmakokinetisch relevanter Gene.
- Etablierung und Validierung neuer pharmakodynamischer Biomarker.
- RNA Spezies als pharmakologische Zielstrukturen platinhaltiger Zytostatikar Zytostatika.

Schlüsselpublikation

Bajraktari G, Burhenne J, Bugert P, Haefeli WE, Weiss J. (2017). Cyclic guanosine monophosphate modulates accumulation of phosphodiesterase 5 inhibitors in human platelets. Biochem Pharmacol; 145:54-63.

Methoden

- Kultur etablierter Zelllinien (Tumorzelllinien, primäre Zellen)
- Blut-Hirnschranken-Sphäroidmodell
- Proliferationsassays
- Zytotoxizitätsassays
- Transkriptionsanalyse (qRT-PCR)
- Proteinanalyse (Western Blot, Immunfluoreszenz, Immunhistochemie, ELISA, Co-Immunoprezipitation, Durchflusszytometrie)
- Lumineszenz-basierte Reportergen-Assays für nukleäre Rezeptoren
- Funktionsassays für Arzneistoff metabolisierende oder transportierende Proteine
- Transfektionen für Knock-in oder Knock-down
- Uptake Assays für Arzneistoffe
- Isolation von Exosomen
- Intrazelluläre Arzneistoffquantifizierungen mittels UPLC-MS/MS

Möglichkeiten in dieser Gruppe

Bachelor thesis: Ja, für Studierende biowissenschaftlicher Studiengänge. Pharmakologisches Vorwissen nicht zwingend nötig.

Internship/Lab rotation: Ja, für Studierende biowissenschaftlicher Studiengänge mit einer Mindestlaufzeit von sechs Wochen. Pharmakologisches Vorwissen nicht zwingend nötig.

Master thesis: Ja, für Studierende biowissenschaftlicher Studiengänge. Ein vorangehendes Praktikum erscheint sinnvoll. Pharmakologisches Vorwissen nicht zwingend nötig.

PhD: Bei gesicherter externer Finanzierung (z.B. Stipendium) freuen wir uns über Ihre Bewerbung.

HiWi/Research assistant: z.Z. kein Bedarf.

Kontakt

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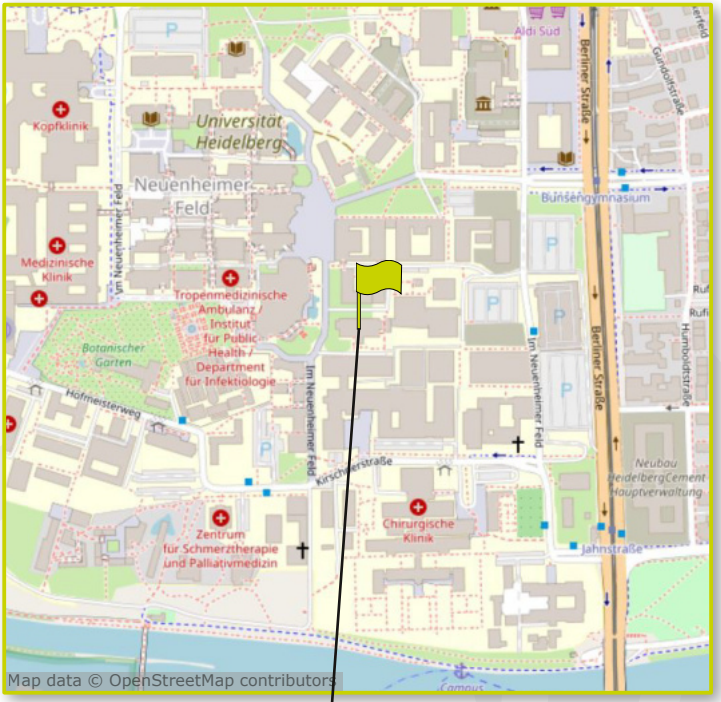
ZMBH

Zentrum für Molekulare Biologie der Universität Heidelberg



AG Bukau: S. 176
AG Kaessmann: S. 178
AG Mayer: S. 180
AG Pfeffer: S. 182

Protein Folding and Repair in Health and Disease

Research focus

Our research aims at understanding the intricate network of cellular protein quality control machineries that promotes the folding of newly synthesized proteins and the repair of misfolded proteins. We are dissecting the mechanisms of major folding processes such as the folding and assembly of newly synthesized proteins, the organized sequestration and refolding of aggregates of misfolded proteins, and the solubilization of amyloid fibrils. Our particular interest is on the mechanisms of chaperone machines. We furthermore investigate processes perturbing protein homeostasis in disease, cellular stress states and aging, and cellular responses to these challenges. Elucidation of these mechanisms is fundamental to understanding of how protein quality control contributes to human health and diseases such as neurodegeneration and cancer.

Key publication

Wentink AS, Nillegoda NB, Feufel J, Ubartaitė G, Schneider CP, De Los Rios P, Hennig J, Barducci A, Bukau B. Molecular dissection of amyloid disaggregation by human HSP70. Nature. 2020 Nov;587(7834):483-488. doi: 10.1038/s41586-020-2904-6. Epub 2020 Nov 11. PMID: 33177717

Methods and specific features

We are employing multi-disciplinary approaches ranging from genetics and molecular biology to protein biochemistry. These include ribosome profiling, generation of site-specific mutations, CRISPR/Cas9 technology, fluorescence microscopy incl. super resolution and single molecule FISH technology, protein purifications, folding assays, protein interaction analysis using fluorescence anisotropy, etc. We are employing a variety of model organisms including *E. coli*, yeast, mammalian cells, *C. elegans*.

Opportunities in this group

Bachelor thesis: No.
Internships/Lab rotation: Yes, within the Master program of the faculty of Biosciences or Chemistry.
Master thesis: Yes, for excellent and ambitious students with a background in biochemistry or molecular biology or biotechnology.
PhD: Temporarily possible.
Hiwi/Research Assistant: No.

Contact

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Consultation hour: Please contact secretariat (Jutta Rami)
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Klick me!

Functional Evolution of Mammalian Genomes

Research focus

A central goal in evolutionary biology is to understand the molecular changes responsible for phenotypic differences between species. Our group has been interested in a range of topics related to the functional evolution of genomes from mammals and other vertebrates. We previously elucidated gene expression evolution across adult and developing mammals based on extensive RNA-seq data for various organs. Topics of the projects that were based on these data include the origins and/or functional evolution of protein-coding genes, alternative splicing, long noncoding RNAs, microRNAs, and sex chromosomes.

In the current generation of projects developed in our lab, we are interested in the question of how new organs originate and evolve. This is fundamental to understanding the evolution of complex multicellular life forms, such as vertebrates. Among other topics, we aim to shed light on the emergence of new brain structures (e.g. telencephalon and cerebellum) in vertebrates and the placenta in mammals.

The advent of high-throughput single-cell genomics technologies now allows detailed investigations of the evolutionary "birth" of organs and constituent tissues and cell types. Our group produces large amounts of single-cell transcriptomic, epigenomic, and spatial transcriptomic data for a unique collection of tissues from representative vertebrates and performs integrated bioinformatics analyses to elucidate the molecular mechanisms that underlie the emergence of new organs and diversification of cell types in evolution.

Key publication

Wang, Z.Y., Leushkin, E., Liechti, A., Ovchinnikova, S., Mößinger, K., Brüning, T., Rummel, C., Grützner, F., Cardoso-Moreira, M., Janich, P., Gatfield, D., Diagouraga, B., de Massy, B., Gill, M.E., Peters, A.H.F.M., Anders, S., and Kaessmann, H. (2020) Transcriptome and translatome co-evolution in mammals. Nature 588: 642-647.

Methods and specific features

- next generation sequencing
- single-cell/single-nucleus RNA-seq
- single-cell ATAC-seq
  (Assay for Transposase-Accessible Chromatin using sequencing)
- single-molecule RNA-FISH
- spatial transcriptomics
- analysis of high throughput (single-cell) sequencing data
- application and development of comparative genomics approaches

Opportunities in this group

Bachelor thesis: Yes.
Internships/Lab rotation: Yes.
Master thesis: Yes.
PhD: Yes.
Hiwi/Research Assistant: Yes.

Contact

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https://twitter.com/kaessmannlab

Klick me!

Controlling Protein Conformation and Dynamics

Research focus

Proteins are highly complex metastable entities that need to assume precise tridimensional arrangements of their amino acids to perform their activity and that are often dynamic and alternate between different conformations in a functional cycle. Our research aims to understand how protein conformation and dynamics that are the basis for their functionality are controlled. The focus of our lab is on molecular chaperones of the Hsp70 and Hsp90 families that assist folding, maturation and conformational dynamics of client proteins throughout their lifespan from the beginning at the ribosome to the end at the proteasome or in lysosomes. We investigate on a molecular mechanistic level how these chaperone machines work, how their conformational changes and dynamics are regulated by cochaperones and posttranslational modifications, and how they affect their client proteins. We are especially interested in how the chaperones refold their client proteins out of a stress denature misfolded state or how the chaperones regulate their clients' conformation as part of the clients' activity cycle. One of the clients is the heat shock transcription factor Hsf1, the central regulator of the heat shock response in all eukaryotic cells. The heat shock response is an ancient transcriptional program to cope with adverse extrinsic and intrinsic conditions, such as elevated temperatures, oxidative stress and heavy metals, but also developmental processes and pathologies like cancer, neurodegeneration and infections.

We try to unravel the molecular mechanism of how the chaperones regulate Hsf1 in a negative feedback loop and how a multitude of different inputs are integrated.

Key publication

Kmiecik, SW, Le Breton, L, & Mayer, MP (2020) Feedback regulation of heat shock factor 1 (Hsf1) activity by Hsp70-mediated trimer unzipping and dissociation from DNA. EMBO J. 81, e50839-22, doi: 10.15252/embj.2019104096

Methods and specific features

We take a multidisciplinary approach to our research questions including biochemistry, molecular biology, cell biology and biophysics. We use reconstituted systems with purified components and analyze them with biochemical assays, fluorescence spectroscopy and hydrogen exchange mass spectrometry. We also use yeast and mammalian cell culture to validate our findings in cellular models using reporter assays and flow cytometry.

Opportunities in this group

Bachelor thesis: Yes, for students interested in protein purification, but places are limited.

Internships/Lab rotation: Yes, within the Master programs of the Faculty of Biosciences. External internships upon request. Basic skills in biochemistry are required.

Master thesis: Yes, for excellent and ambitious students with a background in Biochemistry, Molecular Biology or Biotechnology; a prior intership in our group is prerequisite for a master thesis.

PhD: Yes, pending on funding.

Hiwi/Research Assistant: Occationally, according to demand.

Contact

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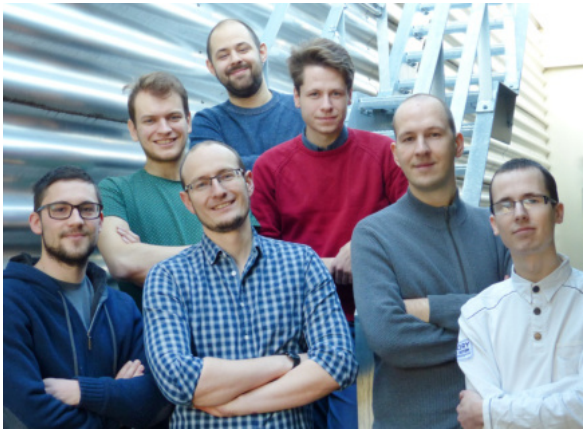
Cryo-electron microscopy of macromolecular complexes



Research focus

Macromolecular complexes are pivotal for all cellular processes and their function is often tightly coupled to their structure and conformational plasticity. Our group uses cryo-electron microscopy (cryo-EM) as a key technology to study the structural basis for two central cellular processes, protein biogenesis and regulated nucleation of microtubules.

The first focus of our group is to dissect how molecular chaperones and processing enzymes associate with the ribosome to act on growing nascent proteins and how these individual events are coordinated on a higher organizational level in the context of compact ordered polyribosomes. We also want to understand from a structural perspective how ribosomes that stall during the process can be recognized and how the incomplete nascent protein arising from the stalling event can be eliminated.

The second focus of our group is to elucidate the structural basis for microtubule nucleation. We want to understand how γ-tubulin complexes template de novo microtubule formation and how this reaction can be controlled by conformational activity regulation of the complex. We furthermore aim to dissect how compositional and structural differences of γ-tubulin complexes in yeast and human impact on the mechanism and regulation of the microtubule nucleation reaction.

Key publication

Filbeck, S.*, Cerullo, F.*, Paternoga, H., Tsaprailis, G., Joazeiro, C.A.P.#, Pfeffer, S.# (2021). Mimicry of canonical translation elongation underlies alanine tail synthesis in RQC. Mol Cell 81, 104-114.

* equal contribution # co-corresponding authors

Methods and specific features

To directly visualize and characterize biological processes at molecular resolution, we are pursuing a multi-modal approach using different cutting-edge cryo-electron microcopy techniques, which provide highly complementary information:

1) Cryo-electron microscopy and single particle analysis provide near-atomic resolution structures of purified complexes that are suitable for atomic modelling and interpretation on amino acid side chain level.

2) Cryo-electron tomography and subtomogram averaging allow for visualization and characterization of complexes in a physiological environment at intermediate resolution and thus perfectly complement high-resolution structures from isolated components. To access the native cellular context for imaging in cryo-electron tomography, we prepare thin sections from frozen-hydrated prokaryotic and eukaryotic cells using cryo-Focused Ion Beam milling.

We have regular access to high-end cryo-electron microscopy instruments on Campus, including a 300kV Titan Krios TEM, a 200kV Glacios TEM, an Aquilos cryo-FIB and a Vitrobot for semi-automated sample preparation.

Opportunities in this group

Internships/Lab rotation: Yes, for excellent students of Master programs at campus with an interest in structural and/or computational biology.

Master thesis: Yes, for excellent students with a background in structural biology.

PhD: Yes, for excellent students with a strong interest and potentially already some experience in structural biology methods.

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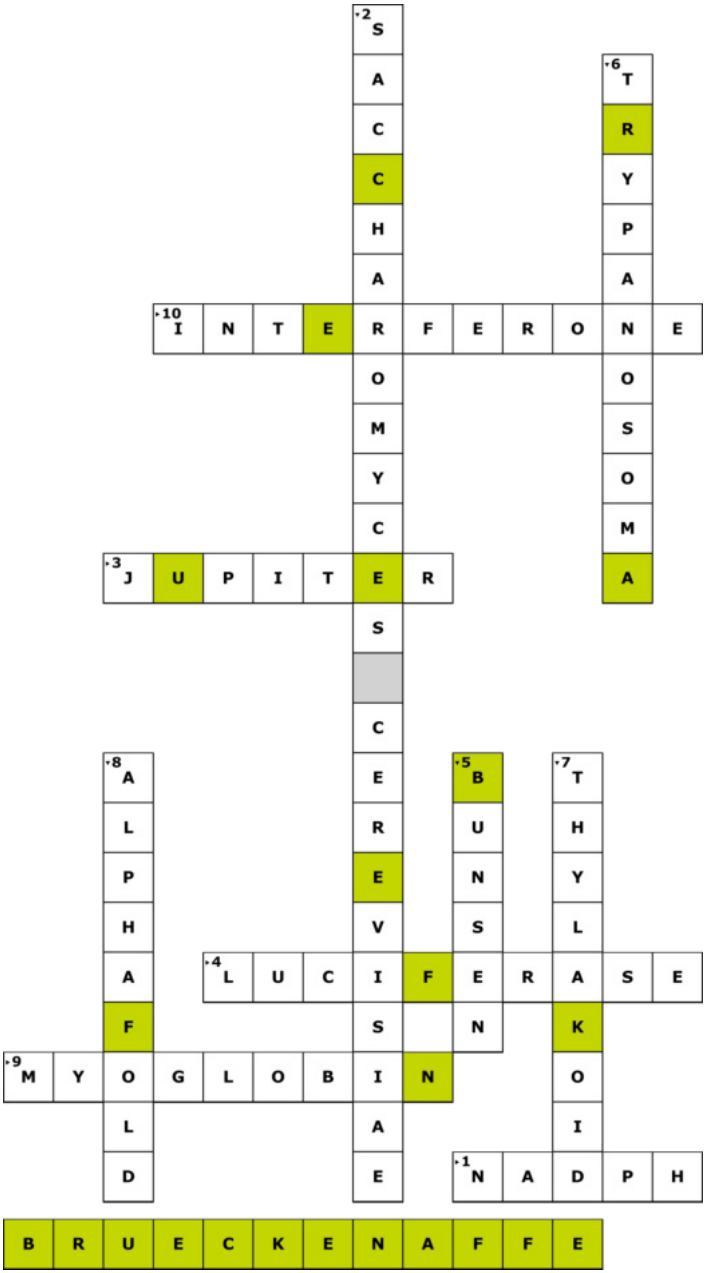
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Der ScieGuide hat sich als Lehrstuhlbroschüre bereits an mehreren Universitätsstandorten wie Berlin, Münster, Frankfurt, Jena und Göttingen etabliert. Damit unterstützen wir Studierende aus den verschiedensten Univeritätsstädten, ihre Traumthemen für ihre Abschlussarbeiten, Forschungspraktika und Promotionen in interessanten und passenden Arbeitsgruppen zu finden. Die Online-Versionen des ScieGuides Heidelberg sowie der anderen Standorte sind auf den Webseiten der jeweiligen Geschäftsstellen zu finden:

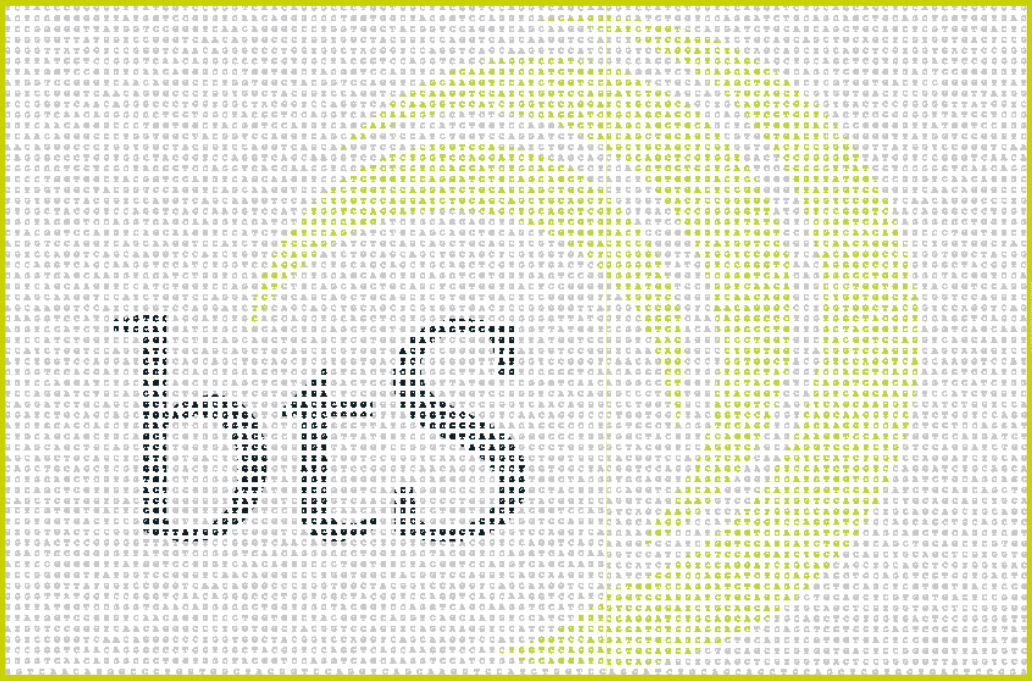
https://bts-ev.de/

Dieses Jahr ist die 5. Ausgabe des ScieGuides Heidelberg erschienen. Sie möchten auch Ihre Arbeitsgruppe im ScieGuide präsentieren? Im nächsten Jahr wird voraussichtlich zum Wintersemester wieder ein ScieGuide von der btS Heidelberg veröffentlicht. Wir freuen uns, wenn die Lehrstuhlbroschüre von Jahr zu Jahr vollständiger wird.

Ihre Vorteile

- Erhöhung der Sichtbarkeit Ihrer Arbeitsgruppe mit relevanten, von Ihnen bestimmten Informationen
- Einfacher Weg, sich einer breiten studentischen Zielgruppe zu präsentieren
- Aktuelle und gepflegte Informationen
- Verteilung und Organisation wird vollständig von uns übernommen
- Kostenlos für Sie, kostenlos für die Studierenden
- Kontaktieren Sie uns gerne unter:

ScieGuide.Heidelberg@btS-eV.de



Genkonstrukt für künstliches Spinnenseidenprotein; PubMed: DQ837297

Du bist auf der Suche nach einem passenden Berufsbild, einem Praktikum, einem Job oder willst einfach nur potentielle Arbeitgeber:innen in den Life Sciences kennenlernen?

Dann haben wir genau das Richtige für Dich:

ScieMatch

Das Karriere-Portal der btS!

Nutze unser Unternehmensmatching und...

- **entdecke unterschiedliche Unternehmen der Life Sciences Branche**
- **finde Firmen, die Deinen Bedürfnissen gerecht werden**
- **nimm direkt Kontakt mit Deinen Wunscharbeitgerber:innen auf**

Nutze unser Berufsbildmatching und...

- **lerne unzählige Jobprofile in den Life Sciences kennen**
- **matche Dich anhand Deiner Fähigkeiten mit Berufsbildern**
- **erfahre, welche Kenntnisse Dir für Deinen Traumberuf noch fehlen**

Haben wir Dein Interesse geweckt?

Registriere Dich kostenlos und finde Deinen Weg in den Life Sciences!

Scanne den QR-Code oder schau auf https://sciematch.bts-sciecon.de/ vorbei!

Das ScieGuide-Team dankt allen Helfer:innen, die zum Gelingen dieser Broschüre beigetragen haben!

Wir bedanken uns herzlich beim Vorstandsteam der btS Heidelberg:

- Vera Heesch
- Michelle Sommer

... und natürlich bei allen btS-Mitgliedern, die uns bei der Umsetzung dieser Ausgabe des ScieGuides unterstützt haben.

Wir danken außerdem unserem lokalen Kooperationspartner, der Techniker Krankenkasse, und vor allem Frau Tammy Bieth als lokale Ansprechpartnerin für die Unterstützung und die Ermöglichung des Drucks.

Vielen Dank auch an alle Arbeitsgruppen für das Interesse und die Teilnahme am ScieGuide Heidelberg 2022/23.

Auflage	5. Auflage, September 2022, Heidelberg
Herausgeber	btS – Life Sciences Studierendeninitiative e.V. Jacobsenweg 61 13509 Berlin +49 30 26492121 http://www.btS-eV.de Registereintragung: VR36222B (Amtsgericht Berlin Charlottenburg)
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Feedback und Wünsche

Wie hat Euch der ScieGuide gefallen? Gibt es etwas, was Du im ScieGuide vermisst hast? Hast Du Ideen für die nächste Auflage? Was können wir noch besser machen? Willst Du selbst an der Erstellung der nächsten ScieGuide-Auflage aus Heidelberg mitwirken? Eure Meinungen und Anregungen sind uns wichtig!

Schreibt uns gerne unter ScieGuide.Heidelberg@btS-eV.de oder kommt einfach selbst zu unserem nächsten Geschäftsstellentreffen vorbei.

Die Techniker

Wir sitzen gleich neben Ihnen

Unsere Hochschulberater finden Sie da, wo es am meisten Sinn macht: direkt an Ihrem Campus.

Dort stehen wir Ihnen rund um alle Fragen zu Ihrer Krankenversicherung vor, während und nach dem Studium zur Verfügung. Gerne treffen wir uns wo Sie wollen, Anruf oder E-Mail genügt.

Ich berate Sie gern:
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Unterstützt von: