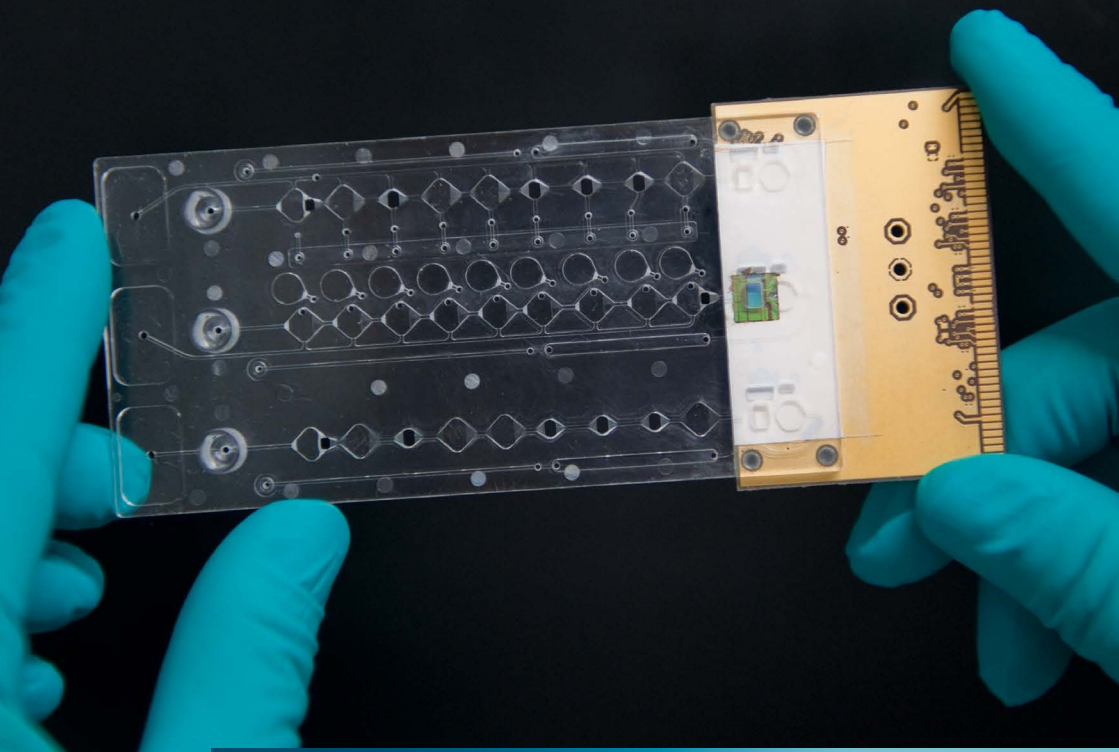
Fraunhofer IZI

Fraunhofer Institute for Cell Therapy and Immunology IZI



Competence atlas

Diagnostics

Interdisciplinary competences and partnership for future projects

Medical therapy is difficult to imagine without excellent diagnostics. The SARS-CoV-2 pandemic alone has shown us how diagnostic tests can save lives and make it easier for society to return to normality. But also in the case of oncological, cardio-metabolic, rare or neurological diseases, treating physicians need a well-founded diagnosis.

The Fraunhofer Institute for Cell Therapy and Immunology offers these diagnostic solutions that go far beyond a traditional assay development. With this brochure, we want to show you innovative technologies and diagnostic procedures that address future trends in this important area of research and development.

We would like to offer you our inter-disciplinary competences and partnership for future projects – from biomarker research to complete diagnostic devices. Our team is passionate about science and diagnostics, so please feel invited to get in touch with the experts at the institute and to discuss new projects. We look forward to you and your challenges, because we are convinced that solutions like application-oriented, innovative and sophisticated diagnostics have a major benefit on human health. After all, it is through diagnostics that therapy becomes effective and life-saving.

Cell and gene therapy development

Analytics and quality controls

Research topics

- Generation and functionality testing of cell and gene therapeutics (in vitro & in vivo models)
- GMP process & quality control development for cell and gene therapeutics, proteins and viral vector production

Competences

- Molecular phenotyping (e.g. qPCR, ddPCR, Western blot)
- Cellular phenotyping (fluorescence microscopy, flow cytometry, histology)
- Development of cytotoxicity and potency assays
- Automated analytics and quality controls
- Under GMP compliance

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Bioassays und lyophilization

Tools for diagnostics and therapy

Research topics

- Lyophilization
- Bioluminescence / luminescent bioassays
- Sample preparation
- Sustainability of POCT

Competences

- Developing adapted lyophilization processes and verify lyophilized product regarding certain parameters
- Validating and experimenting with assays based on bioluminescence
- Developing sample preparation technologies and handling e.g. whole blood filtration via membranes
- Finding more sustainable materials for POCT and verifying them with practical assays

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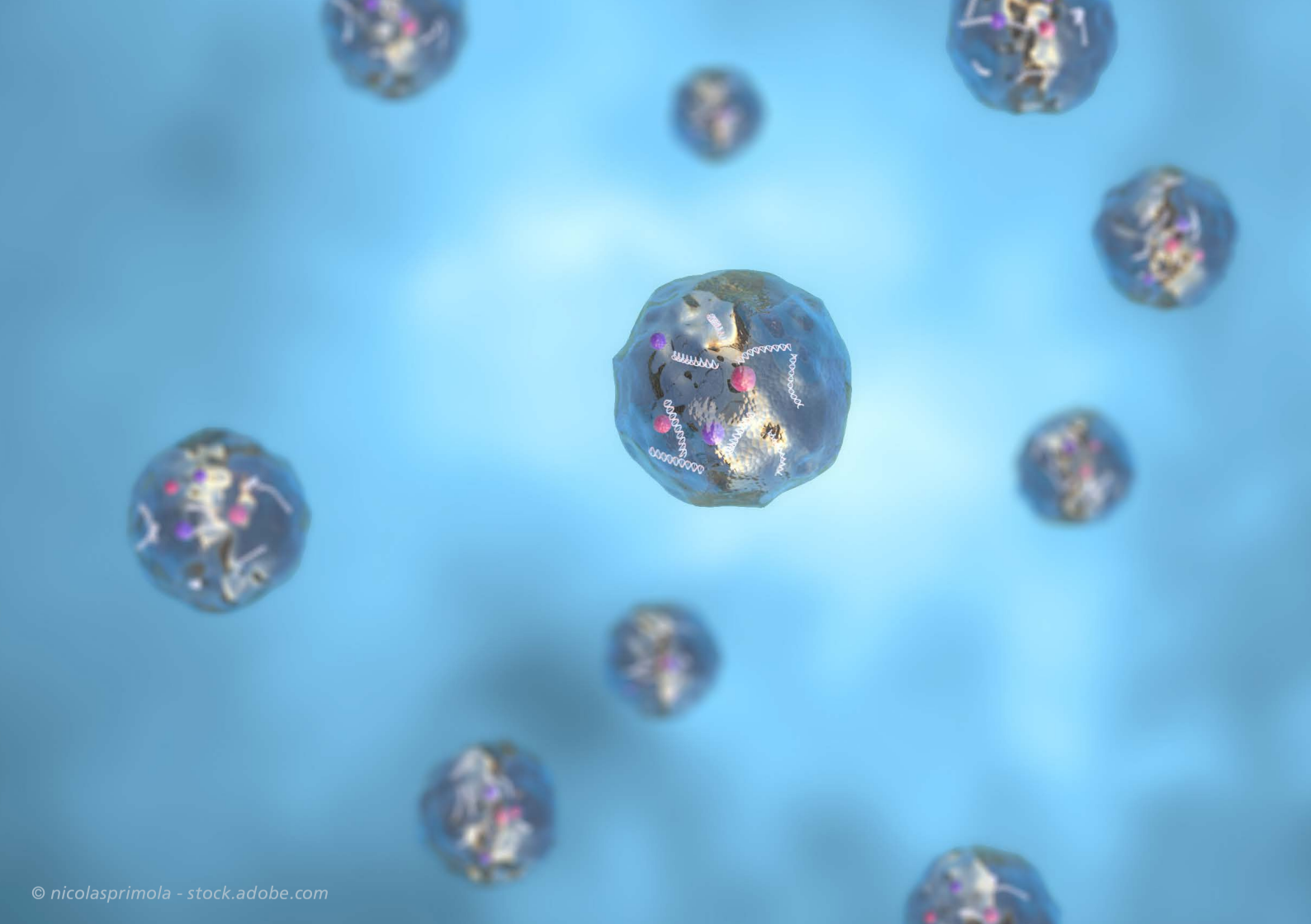

Liquid biopsy

Tools for diagnostics and therapy

Research topics

- Extracellular vesicles and their use in diagnostics and therapy
- Detection of cytokine release syndrome

Competences

- Total and specific isolation of extracellular vesicles from cell culture supernatant, blood plasma and urine
- Characterization of extracellular vesicles
- Antibody-microarray
- Homogeneous immunoassays
- Assay integration in microfluidic devices

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coagulation 9 NCS ml
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Sample preparation

Solutions for preanalytical phase in diagnostics

Research topics

- Integrated diagnostics & Point-of-care tests
- Medical diagnostics
- Environmental, food & beverage analytics

Competences

- Target isolation & enrichment
- Lysis techniques for cells and viruses
- Inactivation of inhibitors
- Strategies for rare targets
- Technical integration of sample preparation into test systems

Selected publications

- Sandetskaya N, Engelmann B, Brandenburg K, Kuhlmeier D. **Application of immobilized synthetic anti-lipopolysaccharide peptides for the isolation and detection of bacteria.** Eur J Clin Microbiol Infect Dis. 2015 Aug;34(8):1639-45. doi: 10.1007/s10096-015-2399-5
- Sandetskaya N, Naumann A, Hennig K, Kuhlmeier D. **Specific enrichment of prokaryotic DNA using a recombinant DNA-binding protein.** Anal Bioanal Chem. 2014 Jun;406(15):3755-62. doi: 10.1007/s00216-014-7787-7

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Microfluidics

Tools for diagnostics and research

Research topics

- Integrated diagnostics & Point-of-care devices
- Organs-on-chip
- Microfluidic design

Competences

- Design, development and testing of microfluidic structures
- Hot-embossing for rapid prototyping of microfluidics and optical structures
- Process development and optimization in manufacturing technology

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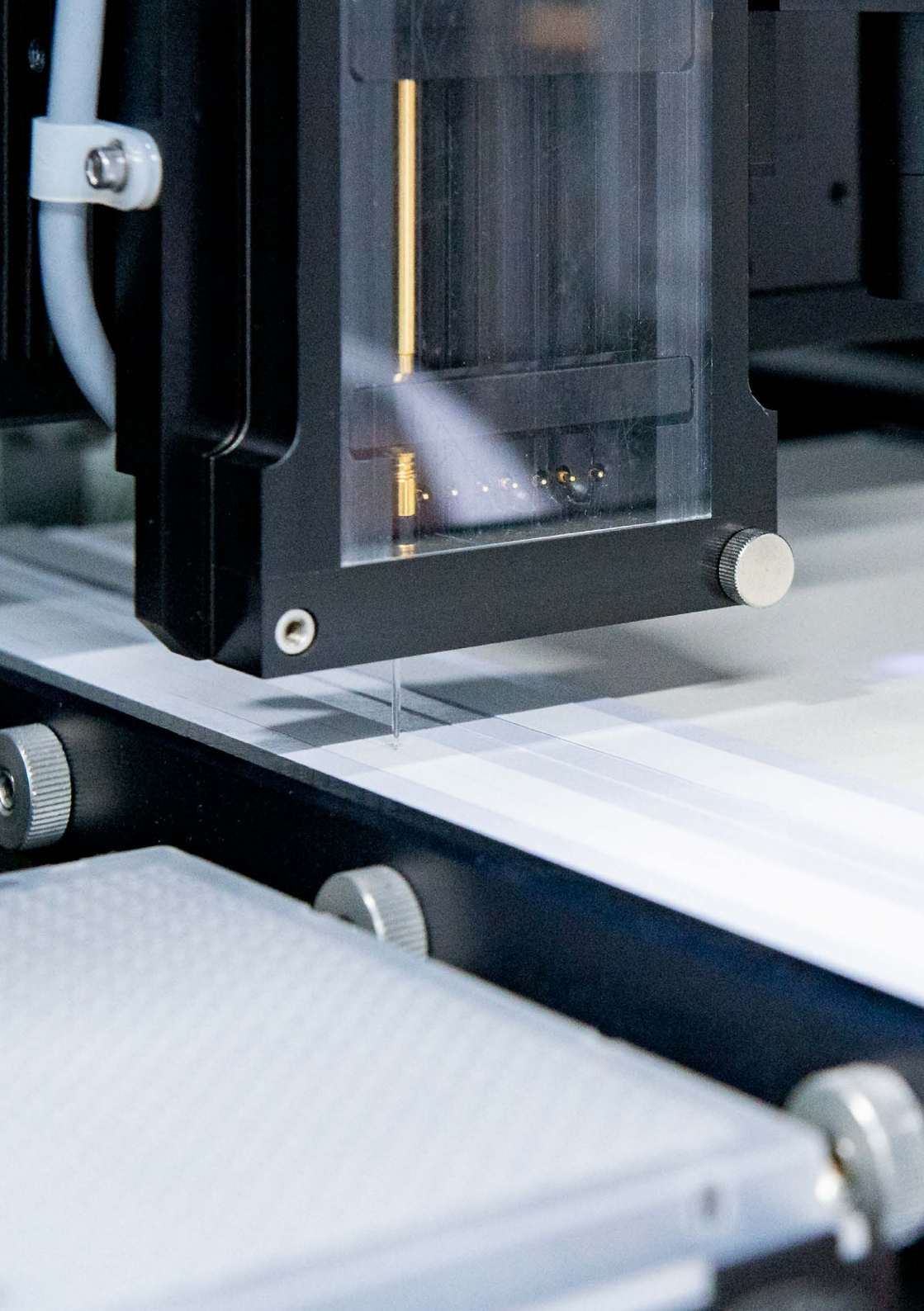

MicroArray and lateral flow test

Tools for diagnostics and therapy

Research topics

- MicroArrays and lateral flow tests are multi-purpose tools in diagnostics
- Antibody-, peptide-, oligonucleotide- or artificial molecule-based assays for the detection of pathogens and biomarkers
- Visible- or fluorescence-based read-out

Competences

- Design, development and testing of MicroArrays and innovative lateral flow assays
- Interdisciplinary exchange for assay development
- Integration into microfluidic structures

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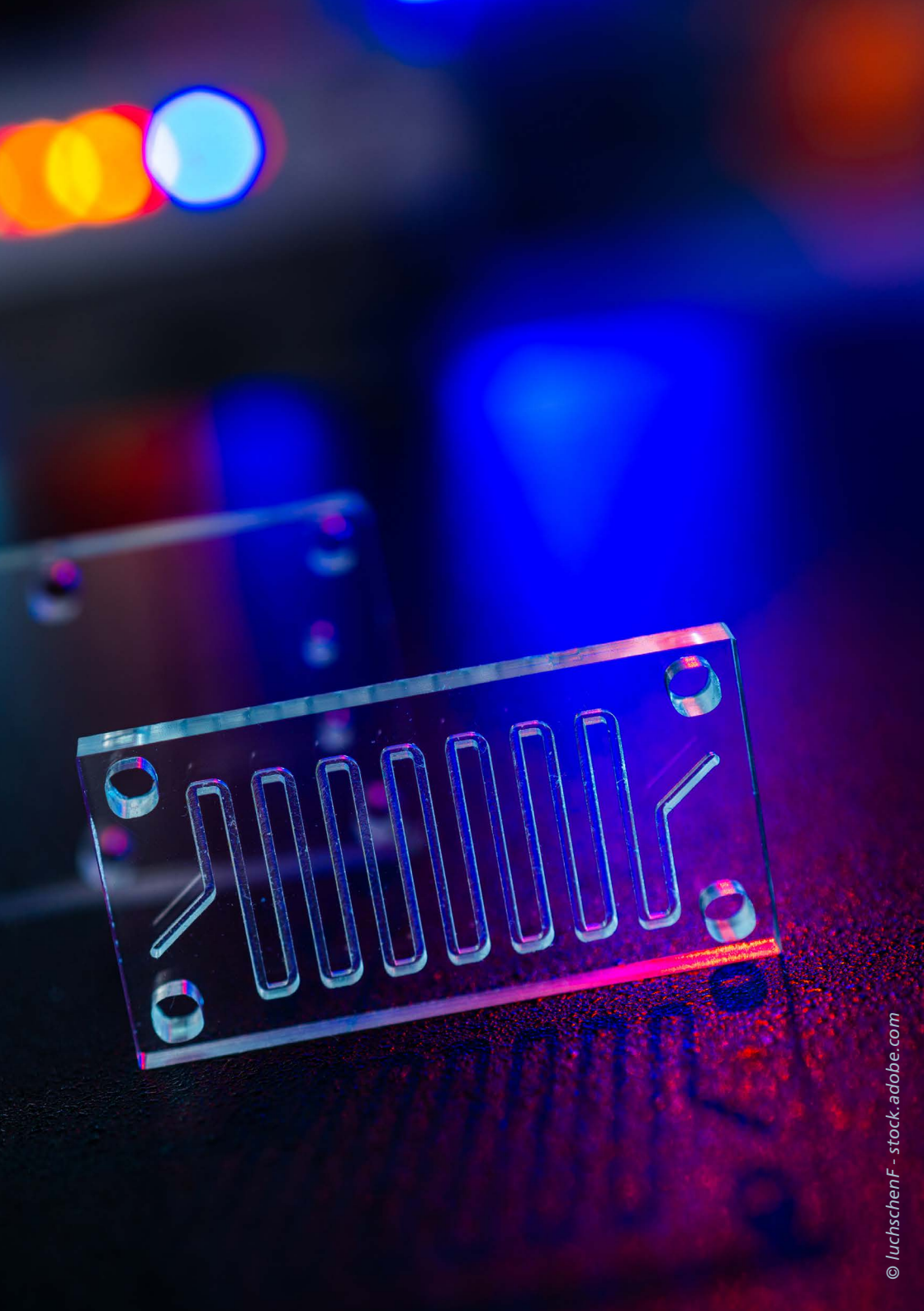

Microphysiological systems

Designing advanced human-based model systems

Research topics

- Organ-on-chip and organoids
- Disease modelling
- Drug screening

Competences

- 2D and 3D cell culture (hiPSCs, primary cells, immortalized cell lines)
- Developing engineering solutions to generate artificial tissues (micro patterning, PDMS device fabrication, microfluidics, biomaterials)
- Designing and validating quantitative, cell-based assays (cellular and molecular phenotyping, force measurements, optogenetics, gene and protein expression)
- Advanced microscopy and image analysis
- Drug screening (cell viability, biomarker expression, drug efficacy, cytotoxicity)

Selected publications

- Hennig K, Hardman D, Barata DM, Martins II, Bernabeu MO, Gomes ER, Roman W. **Generating fast-twitch myotubes in vitro with an optogenetic-based, quantitative contractility assay.** Life Sci Alliance. 2023 Aug 7;6(10):e202302227. doi: 10.26508/lsa.202302227

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Next-Generation Biomarkers
Transcript-omics & Genomics
ISO 9001
NGS as a service
R&D in personalized medicine

Next-generation diagnostics

Genomics & transcriptomics for diagnostics and research

Research topics

- Genomics & Transcriptomics for clinical and non-clinical research e.g. in oncology and immuno-oncology
- Biomarker discovery and validation using next-generation sequencing and PCR-based methods

Competences

- Advanced NGS methods: Single-cell multi-omics (scRNA-seq, TCR/BCR-seq, CITE-seq); Spatial transcriptomics (Visium Spatial Gene expression for FF or FFPE, Visium HD Spatial)
- Classical NGS methods: Whole transcriptome sequencing (mRNA and total RNA); Whole genome and exome sequencing; Small genome and 16S sequencing

Selected publications

- Rade M, Kreuz M, Borkowetz A, Sommer U, Blumert C, Füssel S, Bertram C, Löffler D, Otto DJ, Wöller LA, Schimmelpfennig C, Köhl U, Gottschling AC, Hönscheid P, Baretton GB, Wirth M, Thomas C, Horn F, Reiche K. **A reliable transcriptomic risk-score applicable to formalin-fixed paraffin-embedded biopsies improves outcome prediction in localized prostate cancer.** Mol Med. 2024 Feb 1; 30(1):19. doi: 10.1186/s10020-024-00789-9
- Rade M, Böhlen S, Neuhaus V, Löffler D, Blumert C, Merz M, Köhl U, Dehmel S, Sewald K, Reiche K. **A time-resolved meta-analysis of consensus gene expression profiles during human T-cell activation.** Genome Biol. 2023 Dec 14;24(1):287. doi: 10.1186/s13059-023-03120-7

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IEC 62304
Next-Generation Biomarkers
Omics Technologies
Data Science
Computing Resources
ISO 14971
ISO 9001

Medical bioinformatics for precision medicine

Research topics

- Computational biomedicine in oncology and immuno-oncology
- Software development for software components in / as in vitro diagnostic devices (IVDs)
- Biomarker discovery and validation
- Computational RNA biology & functional genomics

Competences

- Tailored data processing tools to detect and characterize engineered immune cells in single cell multi-omics and spatial transcriptomics
- Machine learning and multi-omics: Machine learning and AI for deep molecular data; multi-modal data science; statistical learning; integrative bioinformatics; pipeline development
- Virtual Twins in cellular immunotherapies
- Software components for IVDs: Development of algorithms and software components for medical devices in particular in vitro diagnostic devices (IVDs) and lab developed tests

Selected publications

- Rade M, Grieb N et al. **Single-cell multiomic dissection of response and resistance to chimeric antigen receptor T cells against BCMA in relapsed multiple myeloma.** Nat Cancer. 2024 Sep;5(9):1318-1333. doi: 10.1038/s43018-024-00763-8
- Derraz B, Breda G et al. **New regulatory thinking is needed for AI-based personalised drug and cell therapies in precision oncology.** NPJ Precis Oncol. 2024 Jan 30;8(1):23. doi: 10.1038/s41698-024-00517-w

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FUJITSU

Statistical consulting

Competences

- Support of applications for animal experiments (TVV/TVA) including case number planning and joint preparation of the biometrics section for the application text, advice in experimental design for the trial, determination of strategy and appropriate statistical methods for the subsequent evaluation
- Support for the biometric planning of other experiments, e.g. case number planning in the context of third-party funding applications
- Support in statistical planning for students and PhD students

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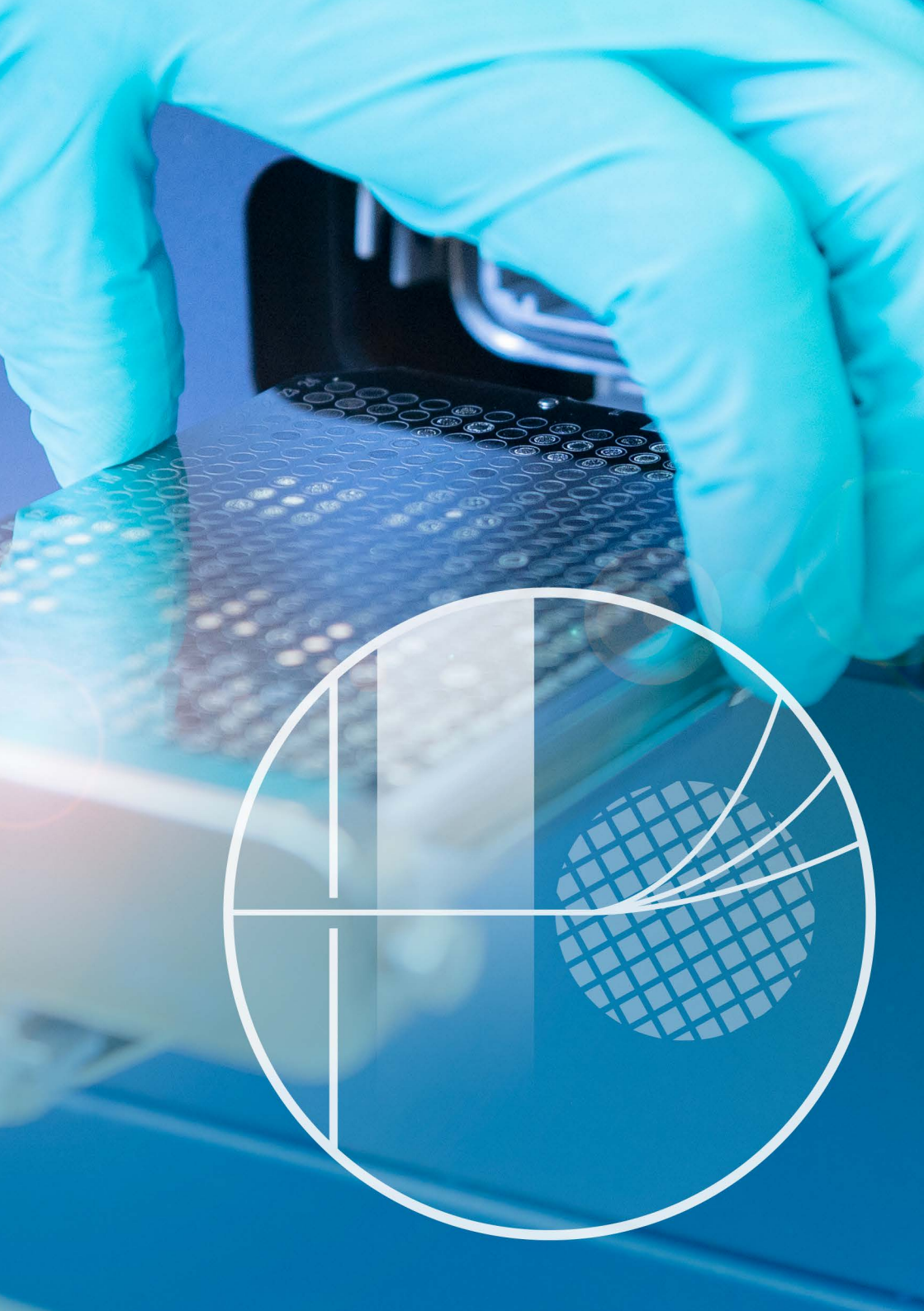

Chromatography & mass spectrometry

Competences

- Preparative chromatographic separations (RP, SEC, IC)
- Identity determination of isolated proteins by peptide mass fingerprinting (PMF) and MS/MS analyses
- MS-based elucidation and detection of protein modifications and protein interactions
- Consulting, sample preparation, performance and evaluation of proteomics studies
- Determination of toxins and metabolites in biofluids by Multiple Reaction Monitoring (MRM)
- Analysis of active substances and their degradation products by MRM
- Characterization of ssDNA and ssDNA conjugates

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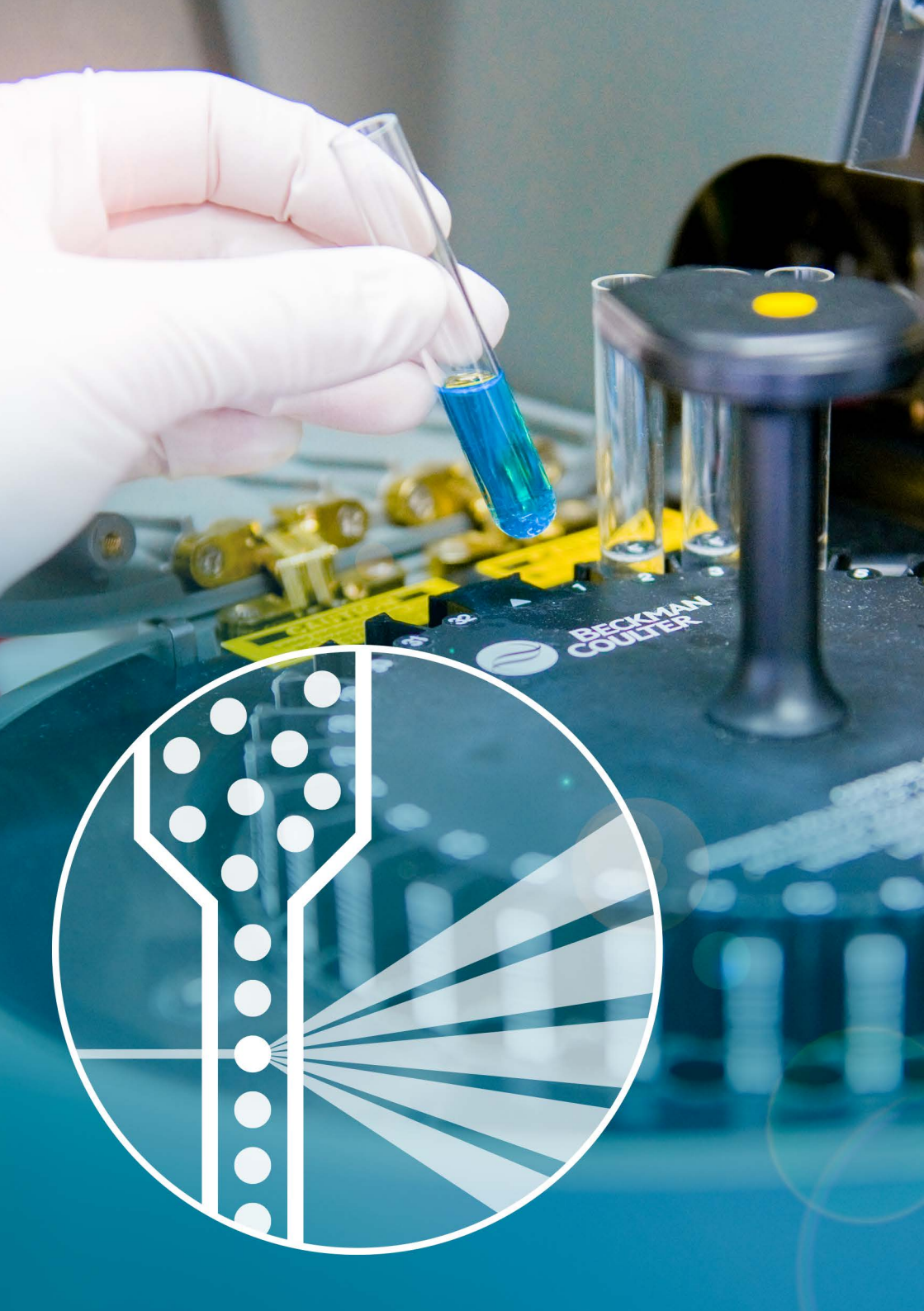
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COULTER

Flow cytometry and FACS

Competences

- Cell-based assays (immunophenotyping, apoptosis, internalization, proliferation / cell cycle, migration, degranulation)
- Cell sorting
- Advice on set-up of experiments, evaluation and other flow cytometry-related topics

Equipment

- Beckman Coulter: Navios Ex TM 10/3, CytoFlex
- Merck/Luminex: ImageStream-X MarkII, FLEXMAP 3D
- BD: Influx Cell Sorter
- Sartorius: IntelliCyt ique Gen 2
- Miltenyi: MACSQuant X

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Microscopy and image analysis

Core Unit Imaging

Competences

- Acquisition and evaluation of various (also correlative) image data
- Brightfield, live cell, fluorescence and confocal laser scanning microscopy
- Slide scanning services
- In vivo imaging via magnetic resonance imaging (MRI), computed tomography (CT) and optical imaging (BLI/FLI) for small animals
- Microscopy training of users and technical support

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Emerging Microbes & Infections (2017) 6, e99; doi:10.1038/emi.2017.87
www.nature.com/emi

OPEN

ORIGINAL ARTICLE

Specific detection of dengue and Zika virus antibodies using envelope proteins with mutations in the conserved fusion loop

Alexandra Rockstroh[1], Beyene Moges[1], Luisa Barzon[2], Alessandro Sinigaglia[2], Giorgio Palù[2], Widuranga Kumbukgolla[3], Jonas Schmidt-Chanasit[4,5], Manoel Sarno[6,7], Carlos Brites[6], Andres Moreira-Soto[8,9], Jan Felix Drexler[8,9], Orlando C Ferreira[10] and Sebastian Ulbert[1]

EMi
Taylor & Francis
Taylor & Francis Group

Emerging Microbes & Infections
2021, VOL. 10
https://doi.org/10.1080/22221751.2021.1913973

Correlation of humoral immune responses to different SARS-CoV-2 antigens with virus neutralizing antibodies and symptomatic severity in a German COVID-19 cohort

Alexandra Rockstroh [a], Johannes Wolf [b,c], Jasmin Fertey [a], Sven Kalbitz[d], Stefanie Schroth[d], Christoph Lübbert [d,e,f], Sebastian Ulbert [a,*] and Stephan Borte[b,c,*]

MDPI
viruses

Article

Pathogens Inactivated by Low-Energy-Electron Irradiation Maintain Antigenic Properties and Induce Protective Immune Responses

Jasmin Fertey [1], Lea Bayer [1], Thomas Grunwald [1], Alexandra Pohl [2], Jana Beckmann [2], Gaby Gotzmann [2], Javier Portillo Casado [2], Jessy Schönfelder [2], Frank-Holm Rögner [2], Christiane Wetzel [2], Martin Thoma [3], Susanne M. Bailer [4,5], Ekkehard Hiller [4], Steffen Rupp [4] and Sebastian Ulbert [1,*]

Native and recombinant antigens

Tools for serological diagnosis of infections

Research topics

- Antibody detection with high specificity and sensitivity
- Viral and bacterial pathogens
- Zoonoses and (re-)emerging infections

Competences

- Inactivation of pathogens by low-energy irradiation to yield intact native antigens (patent)
- Mutant recombinant proteins to increase specificity by reduction of cross-reactive antibody binding (patent)
- Serum neutralization assays up to BSL-3 to test for protective antibodies

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Expression
Diagnostics
ProteinSequence
Regulation
Surface
PosttranslationalModification
ModeOfAction
Structure
Proteomics
Signalling
Quantification
Phosphorylation
SurfaceProteome
DrugTargets
Interactome

Proteomics

Biomarkers and understanding disease

Research topics

- Identification and validation of proteins to be used as diagnostic biomarkers or representing therapeutic targets
- Mode of Action of drugs and biomaterials
- Role of exosomes in diseases

Competences

- Quantitative Proteomics
- Protein/Protein/Ligand-Interaction
- Signaling analysis

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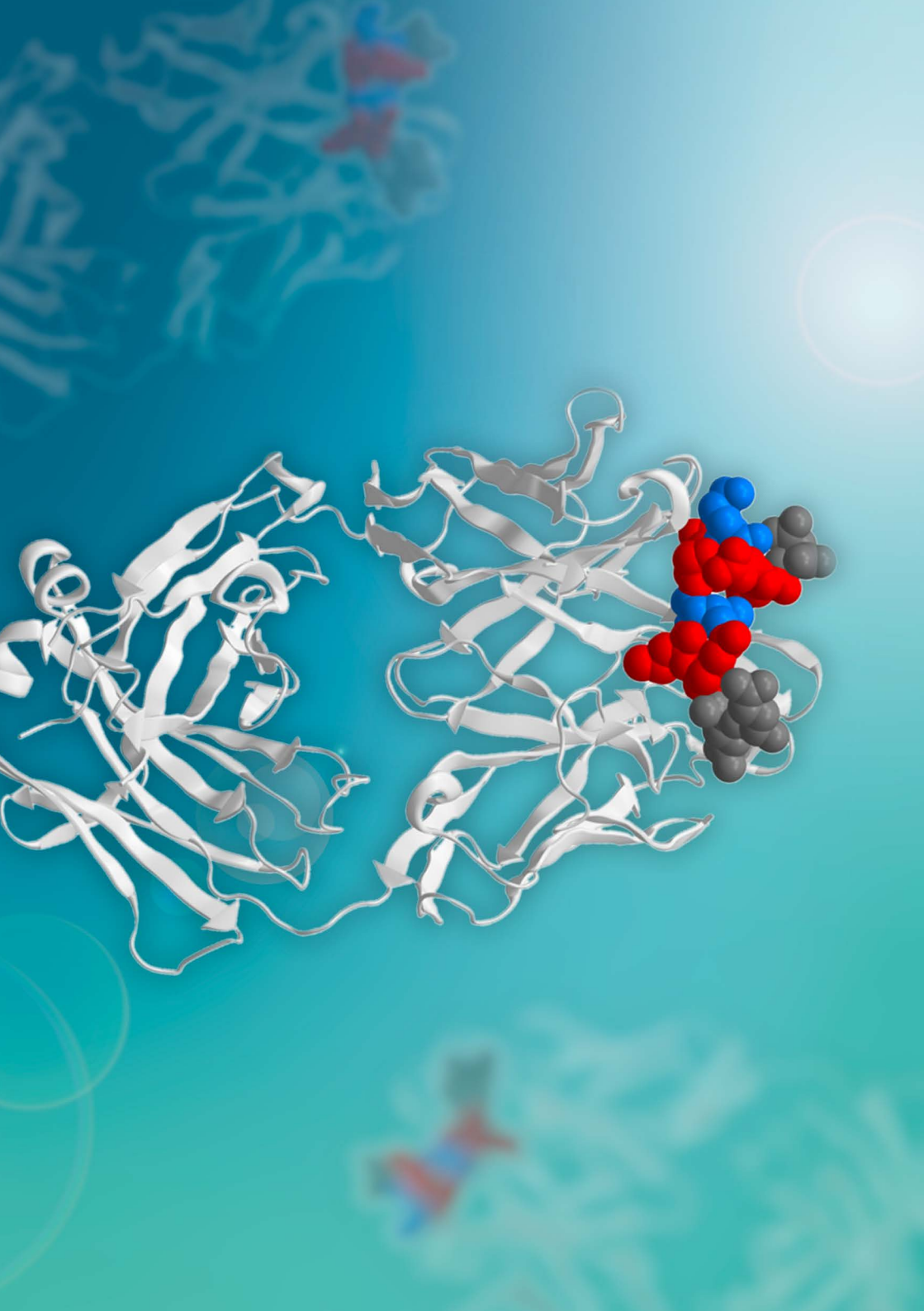

Antibody epitopes

Understanding antibody characteristics

Research topics

- Antibody epitope mapping
- Specificity of polyclonal sera
- Validation for diagnostic and therapeutic applications

Competences

- Antibody epitope fingerprinting from µg amounts of antibody
- Epitopes at amino acid resolution
- Mapping multiple antibodies in parallel

Selected publications

- de Maat S, Clark CC, Barendrecht AD, Smits S, van Kleef ND, El Otmani H, Waning M, van Moorsel M, Szardenings M, Delaroque N, Vercruysse K, Urbanus RT, Sebastian S, Lenting PJ, Hagemeyer CE, Renné T, Vanhoorelbeke K, Tersteeg C, Maas C. **Microlyse: a thrombolytic agent that targets VWF for clearance of microvascular thrombosis.** Blood. 2022 Jan 27;139(4):597-607. doi: 10.1182/blood.2021011776
- Treudler R, Delaroque N, Puder M, Simon JC, Szardenings M. **Dupilumab-induced serum sickness-like reaction: an unusual adverse effect in a patient with atopic eczema.** J Eur Acad Dermatol Venereol. 2021 Jan;35(1):e30-e32. doi: 10.1111/jdv.16782

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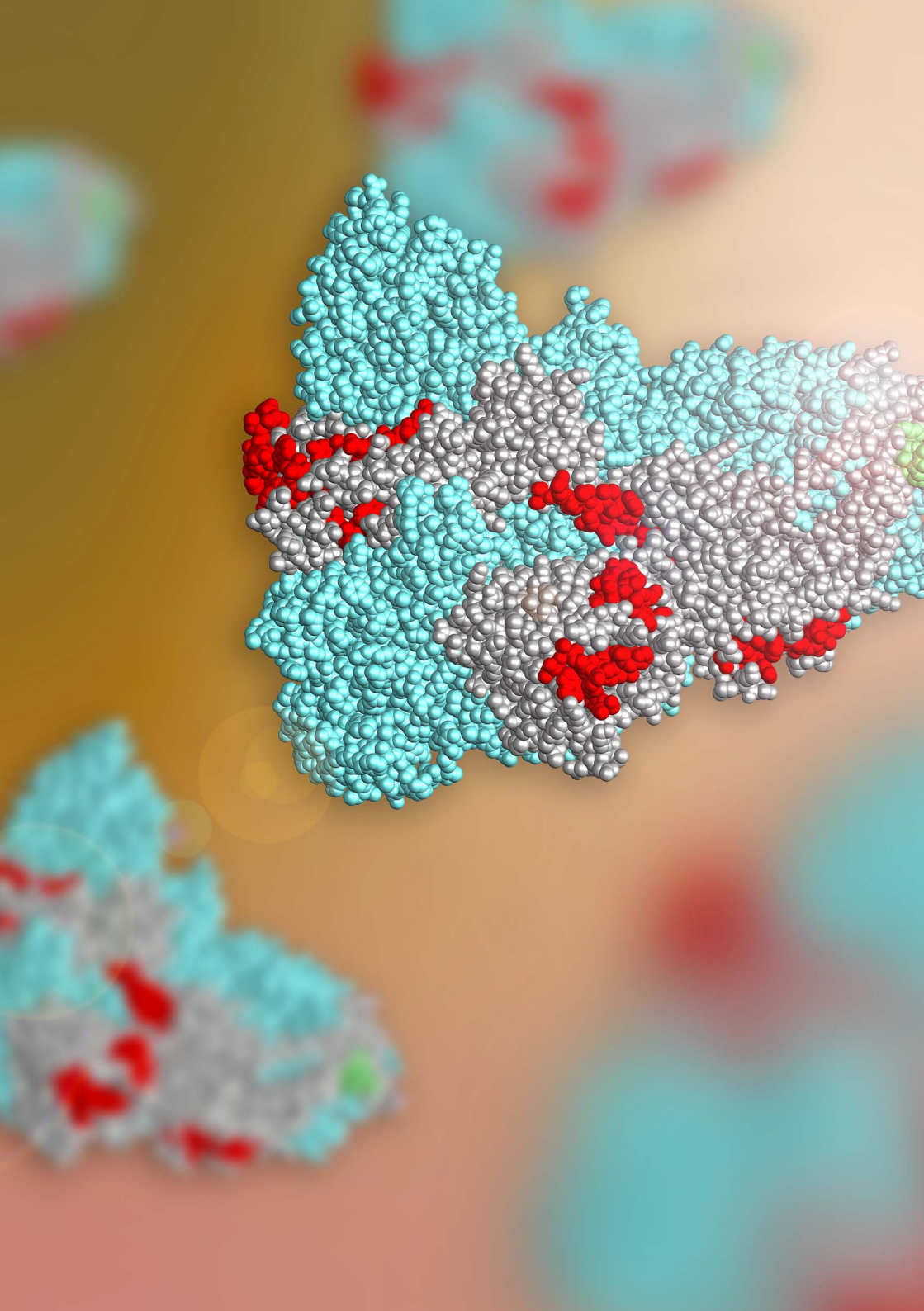


Epitope mapping of the immunome

Immune reactions to disease and vaccination

Research topics

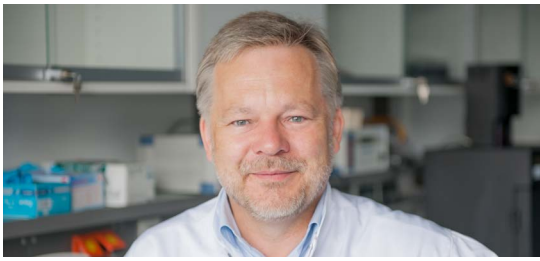
- Mapping the individual immune response
- Identifying and comparing epitopes on (auto-)antigens
- Applications: Allergies, auto-immune disease, vaccines, etc.

Competences

- Immune disease related peptide epitopes for diagnostics
- Comparing immunomes from a larger number of patients
- Anti-drug antibodies
- Resource saving: 100 µl serum are sufficient
- In silico analyses of data allows for follow-up studies

Selected publications

- Szardenings M, Delaroque N, Kern K, Ramirez-Caballero L, Puder M, Ehrentreich-Förster E, Beige J, Zürner S, Popp G, Wolf J, Borte S. **Detection of Antibodies against Endemic and SARS-CoV-2 Coronaviruses with Short Peptide Epitopes.** Vaccines (Basel). 2023 Aug 23;11(9):1403. doi: 10.3390/vaccines11091403



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Clinical relevance of peptides recognition at EoT
GL15 (epitope) TFLEDGETKF
IgE: Decrease of LOAEL$_{obj}$ at EoT
IgG: Increase of LOAEL$_{subj}$ at EoT
GL14 (mimotope) KVLEDGEYVH
IgG: Decrease Cor a 1-spec. IgE conc. at EoT
IgG: Increase intensity lip swelling at EoT
Bet v 1 ISFPEGFPFKYV
Gly m 4 ITFLEDGETKFV
Cor a 1.01 ITFGEGSRYKYV
Cor a 1.04 ITFAEGNEFKYM
Api g 1 ITLPDGGPITTM
57
67
GL12 (mimotope) CNGLGHYGDAEPC
IgE: Increase of Bet v 1-, Gly m 4-spec. IgE at EoT
IgE: Decrease of LOAEL$_{obj}$ at EoT
IgG: Increase of LOAEL$_{subj}$ at EoT
Bet v 1 KYHTKGDHEVKAE
Gly m 4 KYETKGDAEPNQD
Cor a 1.01 KFHAKGDHEINAE
Cor a 1.04 KYHTKGNASINEE
Api g 1 IFHTKGDAVVPEE
127
139
HU4 (mimotope) SSKSVEVPFDY
IgG: Decrease of number of subj. symp. at EoT
IgG: Decrease of LOAEL$_{subj}$ at EoT
Bet v 1 FPKVAPQAISSVENIEGN
Gly m 4 IPKAL-DSFKSVENVEGN
Cor a 1.01 IPKVAPQAITSVENVEGN
Cor a 1.04 IPKVAPQHFTSAENLEGN
Api g 1 LPKAAPGAYKSVE-IKGD
30
46
GL2 (epitope) LGFIESIENH
IgG: Decrease Cor a 1-spec. IgE conc. at EoT
IgG: Decrease intensity oral itching/tingling
Bet v 1 IGDTLEKISNEIKIV
Gly m 4 LPDTAEKITFDSALV
Cor a 1.01 LGDKLEKVCHELKIV
Cor a 1.04 LGHTLEKISYEIKMA
Api g 1 LLGFIESIFNHVVLV
96
110
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Food allergy diagnostics

Cross reactivity and relevance of food allergens

Research topics

- Improving diagnosis of food allergies
- Cross reactivity between food allergens
- Identification of allergy related peptide epitopes
- Immune response to allergy treatments

Competences

- Allergy related peptide epitopes for diagnostics
- Large biobank and data sets from hundreds of patients ready to use
- Peptide epitope arrays
- In silico analyses of data allows for follow-up studies

Selected publications

- Kern K, Havenith H, Delaroque N, Rautenberger P, Lehmann J, Fischer M, Spiegel H, Schillberg S, Ehrentreich-Foerster E, Aurich S, Treudler R, Szardenings M. **The immunome of soy bean allergy: Comprehensive identification and characterization of epitopes.** Clin Exp Allergy. 2019 Feb;49(2):239-251. doi: 10.1111/cea.13285

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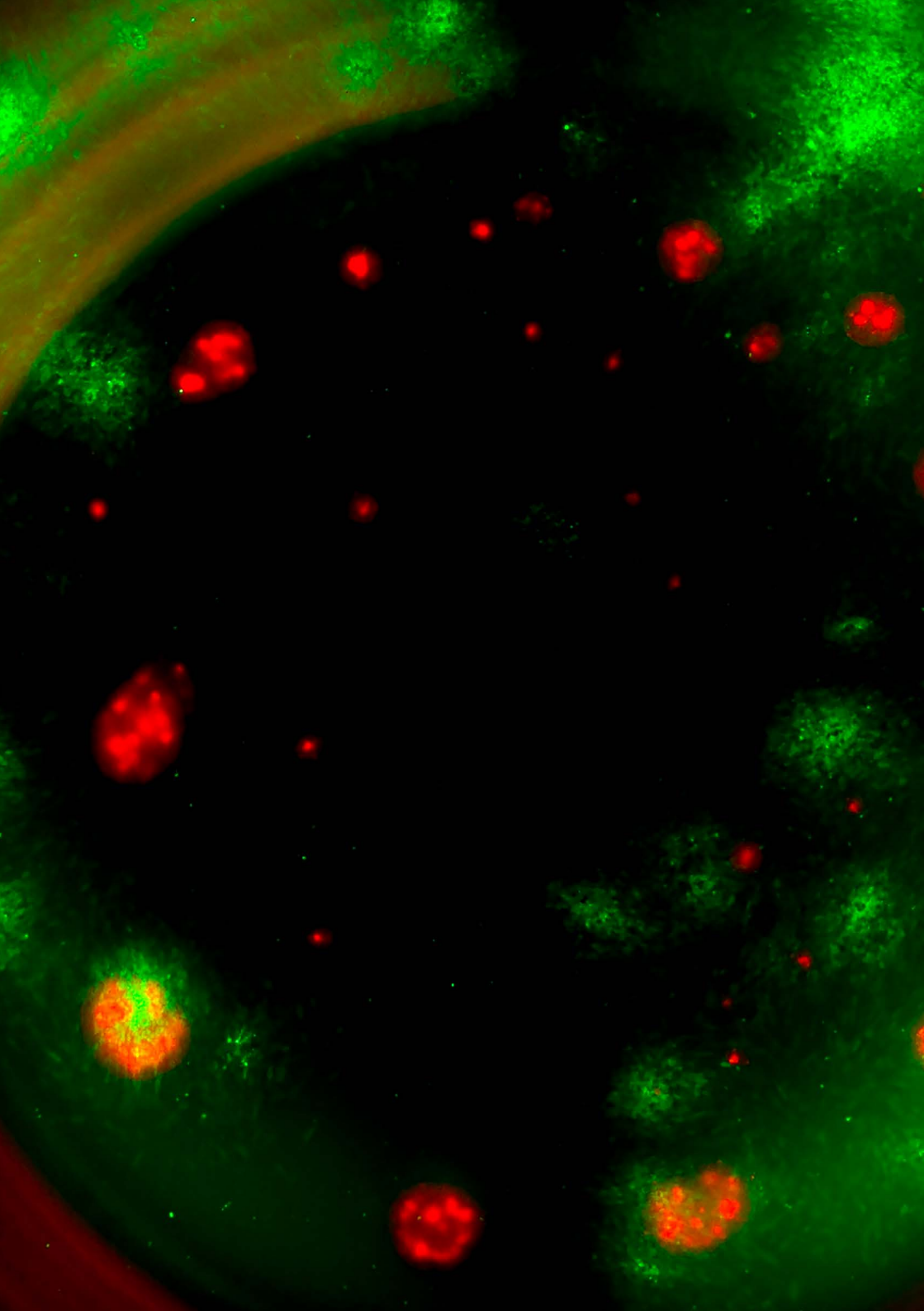


Tissue and cell targeting peptides

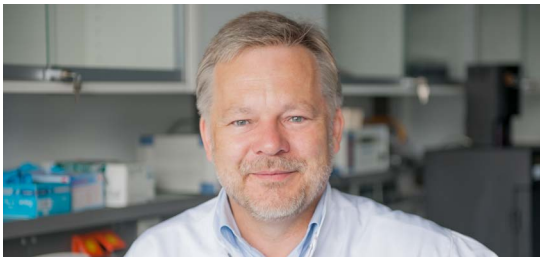
Tools for diagnostics and therapy

Research topics

- Specific binding to (cancer-)tissue or cell types
- Drug delivery
- Imaging
- Diagnostics

Competences

- Successful selection of short peptides binding to cells and/or tumor tissues
- Differential selection methods
- Databases for different tumor tissues



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Non-invasive diagnostics

Tools for diagnostics and therapy accompaniment

Research topics

- Detection of infections and other diseases, including antibiotic resistance
- Analysis of volatile organic compounds (VOCs)
- Breath analysis and other non-invasive specimens, including cultures

Competences

- Ion mobility spectrometry of gaseous samples
- Method development for lab samples and clinical studies
- Data analysis of IMS spectra

Publication

- Steppert I, Schönfelder J, Schultz C, Kuhlmeier D. **Rapid in vitro differentiation of bacteria by ion mobility spectrometry.** Appl Microbiol Biotechnol. 2021 May;105(10):4297-4307. doi: 10.1007/s00253-021-11315-w

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Active traces
Signal
Aux
Program
Protein
Conjugate 1
Conjugate 2
DNA
off
on
Cancel
Traces
Conjugate 1
Valve 16Port16Pos - Position
Valve 6Port 2Pos - Position
ynamic
BIOSENSORS

DNA Nanodevices group

Competences

- Synthesis, characterization & application of DNA-based nanostructures for diagnostic approaches
- Functionalization of DNA strands & nanostructures with (bio)molecules such as fluorophores, biotin, peptides, sugars, small molecules, etc.
- Antibody functionalization with fluorophores, small molecules, nucleotides, etc.
- Cell culture assays (e.g. proliferation, apoptosis, migration/invasion) and flow cytometry analyses
- Virus culture assays (e.g. infection inhibition assays, ELISA, dynamic light scattering (DLS) of viruses) and virus production
- Large-scale production of phage-derived scaffold DNA for DNA origami fabrication

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CardiOMICs Unit

Research topics

- Clinical studies on infectious diseases relevant to cardio- and prosthetic-surgery
- Identification of microorganisms and their virulence profiles in clinical samples
- Analysis of digitization in ambulant and clinical healthcare structures based on real patient pathways

Competences

- Processing of clinical and experimental studies
- Molecular and immune biological diagnostics based on proteomics, NGS and targeted PCR
- Histological and ultrastructural analysis of tissue
- Translation of diagnostic procedures into clinical routine

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