iCANx Minisymposium

(iCANx: Cancer – Lung (Disease) Crosstalk: Tumor and Organ Microenvironment)

11th May 2023; 14:30 – 17:30

BFS Seminar Room 17.1 and 17.2,
Schubertstr. 81, Gießen

14:30 ***Welcome***

14:35 **Sebastian Kobold**
(University Hospital Munich, Germany)
How T cells drive metastatic spread in lung cancer and beyond

15:15 **Meike J. Saul**
(Technical University of Darmstadt, Germany)
The role of miR-574-5p in inflammation and cancer

15:55 ***Coffee break***

16:10 **Markus E. Diefenbacher**
(Julius-Maximilians-University Würzburg, Germany)
Exploiting tumour intrinsic vulnerabilities via the ubiquitin system

16:50 **Manuel Kaulich**
(Goethe University Frankfurt, Germany)
Assigning function to genes by unbiased 2D and 3D CRISPR screens

17:30

Organizers: T. Acker | T. Stiewe | R. Savai | S. S. Pullamsetti | F. Grimminger | N. Salik | M. Cekay | N. Ritschel

LOEWE Exzellente Forschung für Hessens Zukunft
JUSTUS-LIEBIG-UNIVERSITÄT GIESSEN
Philipps Universität Marburg
Max-Planck-Institute for Heart and Lung Research W.G. Kerckhoff-Institute
DZL Deutsches Zentrum für Lungenforschung
CARDIO PULMONARY INSTITUTE

Biosketches of the speakers at the 5th iCANx Minisymposium

Prof. Dr. med. Sebastian Kobold (University Hospital Munich, Germany)

„How T cells drive metastatic spread in lung cancer and beyond.“

Prof. Dr. med. Sebastian Kobold is professor for experimental immunooncology, head of the immunopharmacology group and deputy director of the division of clinical pharmacology at the university hospital in Munich. He has received, among many other awards, the Cancer Research Award 2022 of the Berlin-Brandenburg Academy of Sciences.

Focusing on tumor immunology, Prof. Kobold is especially interested in developing and testing novel strategies to treat cancer using the immune system. His goal is to translate his findings into the clinics in order to improve therapies for cancer patients.

In the field of lung cancer, Prof. Kobold's group recently uncovered an immunosuppressive circuit that is activated by T cell-derived IL-22 that ultimately is promoting lung metastasis.

Selected recent literature (3 selected publications):

1. Briukhovetska D, Suarez-Gosalvez J, Voigt C, Markota A, Giannou A D, Schubel M, ... **Kobold S**. T cell-derived interleukin-22 drives the expression of CD155 by cancer cells to suppress NK cell function and promote metastasis. ***Immunity***. 2023.
2. Gottschlich A, Thomas M, Grunmeier R, Lesch S, Rohrbacher L, Igl V, ... **Kobold S**. Single-cell transcriptomic atlas-guided development of CAR-T cells for the treatment of acute myeloid leukemia. ***Nat Biotechnol***. 2023.
3. Lesch S, Blumenberg V, Stoiber S, Gottschlich A, Ogonek J, Cadilha B L, ... **Kobold S**. T cells armed with C-X-C chemokine receptor type 6 enhance adoptive cell therapy for pancreatic tumours. ***Nat Biomed Eng***. 2021.

Dr. Meike J. Saul (Technical University of Darmstadt, Germany)

„*The role of miR-574-5p in inflammation and cancer.*“

Dr. Meike Saul is group leader at the technical university in Darmstadt. She has received, among other awards, the Dr. Hans Messer Stiftungspreis in 2021.

Dr. Saul's main research focus are small extracellular vesicles (sEV) that are important for intercellular communication, for example via components such as microRNAs. Her studies aim at understanding miRNA functions in health and disease and to transfer these findings into novel treatment strategies against various diseases.

Recently, Dr. Saul's group reported a novel function of miR-574-5p: In lung adenocarcinoma cells, prostaglandin E_2 (PGE_2) regulates the sorting of miR-574-5p into sEV. Arriving in recipient cells, sEV-derived miR-574-5p activates Toll-like receptors (TLR) 7/8, resulting in decreased PGE_2 levels and hence reduced sorting of miR-574-5p into sEVs.

Selected recent literature (3 selected publications):

1. Donzelli J, Proestler E, Riedel A, Nevermann S, Hertel B, Guenther A, ... **Saul M J**. Small extracellular vesicle-derived miR-574-5p regulates PGE2-biosynthesis via TLR7/8 in lung cancer. ***J Extracell Vesicles***. 2021.
2. Breitwieser K, Koch L F, Tertel T, Proestler E, Burgers L D, Lipps C,... **Saul M J**. Detailed Characterization of Small Extracellular Vesicles from Different Cell Types Based on Tetraspanin Composition by ExoView R100 Platform***. Int J Mol Sci***. 2022.
3. Hegewald A B, Breitwieser K, Ottinger S M, Mobarrez F, Korotkova M, Rethi B, ... **Saul M J**. Extracellular miR-574-5p Induces Osteoclast Differentiation via TLR 7/8 in Rheumatoid Arthritis. ***Front Immunol***. 2020.

Dr. Markus E. Diefenbacher (Julius Maximilians University Würzburg, Germany)

„Exploiting tumour intrinsic vulnerabilities via the ubiquitin system.“

Dr. Markus Elomar Diefenbacher is group leader at the Biocenter of the Julius Maximilians University in Würzburg and the Comprehensive Cancer Centre Mainfranken. He was awarded the IZKF Research Award in 2017.

Dr. Diefenbacher's work focuses on the deregulation of protein turnover as a central driver in tumourigenesis. By utilising *in vitro* and *in vivo* models, his lab aims to understand the role of key components of the ubiquitylation machinery in order to find ways to counteract deregulation of protein stability as a therapeutic approach.

Current work in Dr. Diefenbacher's group addresses the role of the deubiquitylase USP28 in oncogenic transformation of respiratory cells and especially in squamous cell carcinomas (SCC). Recently, his group discovered a novel mechanism by which SCC cells that express ΔNp63 – a transcription factor that is essential for the survival of SCC - can be targeted to overcome chemotherapy resistance.

Selected recent literature (3 selected publications):

1. Prieto-Garcia C, Hartmann O, Reissland M, Fischer T, Maier C R, Rosenfeldt M, ... **Diefenbacher M E**. Inhibition of USP28 overcomes Cisplatin-resistance of squamous tumors by suppression of the Fanconi anemia pathway. ***Cell Death Differ***. 2022.
2. Prieto-Garcia C, Hartmann O, Reissland M, Braun F, Bozkurt S, Pahor N, ... **Diefenbacher M E**. USP28 enables oncogenic transformation of respiratory cells, and its inhibition potentiates molecular therapy targeting mutant EGFR, BRAF and PI3K. ***Mol Oncol***. 2022.
3. Hartmann O, Reissland M, Maier C R, Fischer T, Prieto-Garcia C, Baluapuri A, ... **Diefenbacher M E**. Implementation of CRISPR/Cas9 Genome Editing to Generate Murine Lung Cancer Models That Depict the Mutational Landscape of Human Disease. ***Front Cell Dev Biol***. 2021.

Prof. Dr. Manuel Kaulich (Goethe University Frankfurt, Germany)

„Assigning function to genes by unbiased 2D and 3D CRISPR screens.“

Prof. Dr. Manuel Kaulich is LOEWE-FCI (Frankfurt Cancer Institute) Professor, independent group leader at the Institute of Biochemistry II and head of the Frankfurt CRISPR/Cas9 Screening Center (FCSC) at the Goethe University Frankfurt. Very recently, he was selected as an Henriette Herz Scout for the Alexander von Humboldt foundation.

Prof. Kaulich's laboratory develops gene editing technologies and applies them to understand cellular transformation, autophagy and drug resistance. Importantly, his group engineered the covalently-closed-circular-synthesized (3Cs) CRISPR/Cas gRNA system for preparing highly diverse and uniformly distributed (combinatorial) CRISPR libraries. This platform was recently used to identify genetic interactions in autophagy. There, 3Cs multiplexing was proven to be a powerful tool for genetic interaction screens at scale.

Selected recent literature (3 selected publications):

1. Diehl V, Wegner M, Grumati P, Husnjak K, Schaubeck S, Gubas A, ... **Kaulich M**. Minimized combinatorial CRISPR screens identify genetic interactions in autophagy. ***Nucleic Acids Res***. 2021.
2. Wegner M, Diehl V, Bittl V, de Bruyn R, Wiechmann S, Matthess Y, ... **Kaulich M**. Circular synthesized CRISPR/Cas gRNAs for functional interrogations in the coding and noncoding genome. ***Elife***. 2019.
3. **Kaulich M**, Lee YJ, Lönn P, Springer AD, Meade BR, Dowdy SF. Efficient CRISPR-rAAV engineering of endogenous genes to study protein function by allele-specific RNAi. ***Nucleic Acids Res***. 2015.