



SFB/TR 209 LIVER CANCER

New mechanistic and therapeutic concepts in a solid tumor model

Dear SFB/TR 209 - colleagues,

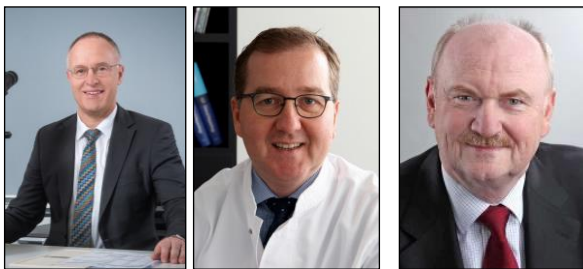
We are facing difficult times. Currently, the Corona-virus pandemic is not only challenging our medical system to the maximum and thus also many of our PIs, but also biomedical research and thus our SFB/TR209. We are experiencing tremendous restrictions due to shutdown of research facilities and draining of resources. This is especially painful as we are in a highly productive period of our SFB/TR209 and looking ahead to our grant renewal proposal.

Currently it seems highly unlikely that our conference scheduled in early July will take place in its originally intended international format. This is very sad as we have received very positive feedback from keynote speakers and applicants around the world. If no unexpected changes occur, we will inform all non-SFB participants and speakers about cancellation beginning of April.

Nevertheless, we ask all SFB participants/Pis/applicants to keep July, 7th /8th on their calendar to give us the possibility for internal discussions of ongoing and further projects, planning of the grant renewal process and all necessary internal decisions on these two days. We will keep you informed about the possible and intended formats.

We wish you all good luck and health and hope to send you the next newsletter under better circumstances.

Yours,



P. Schirmacher

N. Malek

M. P. Manns

CALL FOR DOCUMENTATION OF RESEARCH RESTRICTIONS

In this difficult situation we are asking for your support and activity to maintain function as good as possible. The SFB/TR209 infrastructures are still fully functional and please make use of them. Each individual project is asked to evaluate how to maintain its research as good as possible either by maintaining long term experiments or using the non-lab time for planning and writing of publications. We ask all projects to precisely document existing and upcoming restrictions and to transmit this information to our SFB/TR209 office (Dr. Woll). This is essential for further planning and discussion with the DFG. Please keep us informed about any other news relevant for the SFB/TR209.

HCC CONFERENCE 2020

As intended and applied for, we are still organizing an international HCC conference in the third year of our **SFB/TR 209**. The conference should take place **on July 6-8th, 2020** at the DKFZ conference center in Heidelberg.

In the last few days we have been asked frequently and justified whether our international HCC conference can and will take place in July.

Therefore, we would like to provide you all with the same up-to-date information:

We realistically assume that we can NOT count on the international speakers and guests, but we still hope to be able to hold the conference - if possible - on a national level. We are trying to postpone the decision as long as possible, possibly until April 20th, 2020 as we still have some hope for an improvement of the current restrictions at that time.

If the conference as such cannot take place, we would still ask you to keep the date blocked at least for July 7th /8th, 2020 and also to have the posters ready so that we can at least use the date for an SFB-internal exchange (retreat replacement) with viewing and discussion of the projects for the follow-up application and discussion of the further strategy. If necessary, we will check if there are possibilities to realize parts of the meeting at least via internet.

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GEROK STIPENDS

Gerok stipends are in place at all three sites according to the regulations. The SFB-Gerok stipend is now located in Heidelberg. Since April 2020 we will have Dr. S. Thomann working on his project "YAP orchestrates heterotypic endothelial cell communication via HGF/c-MET signaling in liver tumorigenesis" related to the project B03 (Breuhahn).

MD-STIPENDIARIES

We are happy to introduce our two new MD stipendiaries who joined the SFB/TR 209 in April 1st, 2020: Mrs E. Dreher will work for her experimental MD thesis on the project "Identification of functional tumor suppressors in liver tumors", related to the project B01 (Rössler) and Mrs. M. Wesener on "Identification of the YAP/TAZ interactome in HCC cells" related to the project B03 (Breuhahn).

Please look out for further potential candidates for our SFB/TR 209 MD stipend program.

HOMEPAGE

The homepage of the SFB/TR 209 is available under www.livercancer.de. Please let us know your ideas and suggestions and keep us informed about any changes and announcements concerning your project on the homepage. The logo can be downloaded from the site. Please use it wherever possible.

SERVICE PROJECTS

INF-Data analysis: Access to TCGA data only for applying sites (TÜ and MHH) available; in HD the Institute of Pathology and DKFZ have access to raw data of TCGA; SOPs for application to access will be provided; contact to the HiGHmed consortium could be beneficial.

INF-Cell lines: The list of available cell lines can be downloaded from the internal area of the SFB/TR 209 homepage or requested from K. Woll.

UPCOMING CONFERENCES

SFB/TR 209 HCC-Conference: 06.-08.07.2020, Heidelberg (see above)

Currently all conferenced are postponed/rescheduled some of the dates seem to be unrealistic and we will keep you informed as the situation changes

RECENT TOP PUBLICATIONS

Mahak Singhal#, Nicolas Gengenbacher#, Silvia La Porta#, Stephanie Gehrs, Jingjing Shi, Miki Kamiyama, Diane M Bodenmiller, Anthony Fischl, Benjamin Schieb, Eva Besemfelder, Sudhakar Chintharlapalli, Hellmut G Augustin (#, equally contributing first authors) Preclinical validation of a novel metastasis-inhibiting Tie1 function-blocking antibody EMBO Mol Med (accepted for publication) (C03)

Heike Bantel, Franziska Wandrer, Stephanie Liebig, Silke Marhenke, Arndt Vogel, Michael Peter Manns, Andreas Teufel, Timo Itzel, Thomas Longrich, Olaf Maier, Roman Fischer, Roland Kontermann, Klaus Pfizenmaier, Klaus Schulze-Osthoff, Katharina John TNF-Receptor-1 Inhibition Reduces Liver Steatosis, Hepatocellular Injury and Fibrosis in NAFLD Mice. Cell Death & Disease (in press) (A06, B08)

Zhang XJ, Olsavszky V, Yin Y, Wang B, Engleitner T, Öllinger R, Schledzewski K, Koch PS, Rad R, Schmid RM, Friess H, Goerdt S, Hüser N, Géraud C, von Figura G, Hartmann D. Angiocrine Hepatocyte Growth Factor Signaling Controls Physiological Organ and Body Size and Dynamic Hepatocyte Proliferation to Prevent Liver Damage during Regeneration. Am J Pathol. 2020 Feb;190(2):358-371. (C03)

Luiken S, Fraas A, Bieg M, Sugiyanto R, Goeppert B, Singer S, Ploeger C, Warsaw G, Marquardt JU, Sticht C, De La Torre C, Pusch S, Mehrabi A, Gretz N, Schlesner M, Eils R, Schirmacher P, Longrich T, Roessler S. NOTCH target gene HES5 mediates oncogenic and tumor suppressive functions in hepatocarcinogenesis. Oncogene. 2020 Feb 13. doi: 10.1038/s41388-020-1198-3. (B01)

Ewels PA, Peltzer A, Fillinger S, Patel H, Alneberg J, Wilm A, Garcia MU, Di Tommaso P, Nahnsen S. The nf-core framework for community-curated bioinformatics pipelines. Nat Biotechnol. 2020 Mar;38(3):276-278. (INF-Tü)

Hirsova P, Bohm F, Dohnalkova E, Nozickova B, Heikenwalder M, Gores GJ, Weber A. Hepatocyte apoptosis is tumor promoting in murine nonalcoholic steatohepatitis. Cell Death Dis. 2020 Feb 3;11(2):80. (A04)

Namineni S, O'Connor T, Faure-Dupuy S, Johansen P, Riedl T, Liu K, Xu H, Singh I, Shinde P, Li F, Pandya A,

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Sharma P, Ringelhan M, Muschaweckh A, Borst K, Blank P, Lampl S, Durantel D, Farhat R, Weber A, Lenggenhager D, Kündig TM, Staeheli P, Protzer U, Wohlleber D, Holzmann B, Binder M, Breuhahn K, Assmus LM, Nattermann J, Abdullah Z, Rolland M, Dejardin E, Lang PA, Lang KS, Karin M, Lucifora J, Kalinke U, Knolle PA, Heikenwalder M. A dual role for hepatocyte-intrinsic canonical NF- κ B signaling in virus control. *J Hepatol*. 2020 Jan 15. pii: S0168-8278(20)30010-6. (A04)

Winkler I, Bitter C, Winkler S, Weichenhan D, Thavamani A, Hengstler JG, Borkham-Kamphorst E, Kohlbacher O, Plass C, Geffers R, Weiskirchen R, Nordheim A. Identification of Ppar γ -modulated miRNA hubs that target the fibrotic tumor microenvironment. *Proc Natl Acad Sci U S A*. 2020 Jan 7;117(1):454-463. (B02)

Drucker E, Holzer K, Pusch S, Winkler J, Calvisi DF, Eiteneuer E, Herpel E, Goepfert B, Roessler S, Ori A, Schirmacher P, Breuhahn K, Singer S. Karyopherin α 2-dependent import of E2F1 and TFDP1 maintains protumorigenic stathmin expression in liver cancer. *Cell Commun Signal*. 2019 Nov 29;17(1):159. (B04)

Niemann J, Woller N, Brooks J, Fleischmann-Mundt B, Martin NT, Kloos A, Knocke S, Ernst AM, Manns MP, Kubicka S, Wirth TC, Gerardy-Schahn R, Kühnel F. Molecular retargeting of antibodies converts immune defense against oncolytic viruses into cancer immunotherapy. *Nat Commun*. 2019 Jul 19;10(1):3236. (C06)

Holzer K, Ori A, Cooke A, Dauch D, Drucker E, Riemenschneider P, Andres-Pons A, DiGuilio AL, Mackmull MT, Baßler J, Roessler S, Breuhahn K, Zender L, Glavy JS, Dombrowski F, Hurt E, Schirmacher P, Beck M, Singer S. Nucleoporin Nup155 is part of the p53 network in liver cancer. *Nat Commun*. 2019 May 14;10(1):2147. (B04)

Weiler SME, Lutz T, Bissinger M, Sticht C, Knaub M, Gretz N, Schirmacher P, Breuhahn K. TAZ target gene ITGAV regulates invasion and feeds back positively on YAP and TAZ in liver cancer cells. *Cancer Lett*. 2020 Jan 2. S0304-3835(19)30666-4. (B03)

NEWS AND ACCOMPLISHMENTS

P. Schirmacher was appointed as Co-editor of the first fascicle of the new 5th edition of the WHO classification of tumors and section editor for tumors of the liver and intrahepatic bile ducts as well as tumors of the gallbladder and extrahepatic bile ducts (Digestive System tumors, WHO Classification of tumors, 5th Edition, Volume 1 (WHO Classification of tumors Editorial Board; ISBN-13 (Print Book):978-92-832-4499-8))

R. Bartschlagler researching at the University Hospital of Heidelberg and the German Cancer Research Centre, received the Thai Prince Mahidol Award in January 2020 for his research work on the hepatitis C virus in the field of medicine.

The German guideline on carcinoma of the liver and biliary tract is ongoing under coordination of N. Malek (M. Bitzer, P. Schirmacher, A. Vogel are members of the steering committee).

The ESMO clinical Practice Guidelines is finished and published "Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up." *Ann Oncol*. 2019 May 1;30(5):871-873 (Coordination: A. Vogel).



The publication "Nuclear Translocation of RELB Is Increased in Diseased Human Liver and Promotes Ductular Reaction and Biliary Fibrosis in Mice" (*Gastroenterology*, November 2018) was awarded with the prize of the German Liver Foundation 2019. Dr. Bruno C. Köhler (Gerok stipendiary) from the University Hospital of Heidelberg (UKHD) and the National Centre for Tumour Diseases (NCT) in Heidelberg received the prize money of 7.500 €.

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FINANCIAL ISSUES

Travel grants

According to the application and granting each project has 2.000 € /year travel allowance for travel costs related to scientific issues of the respective SFB/TR 209 project. For reimbursement of your travel expenses please complete the form which can be downloaded from the internal area of our homepage or provided by K. Woll and send the original receipts together with the signed form to K. Woll.

In addition, we ask you to provide us with information to which conferences you have contributed by presentation and represented the SFB/TR 209 for announcement in the newsletters and on our homepage.

Publication funds

We have a common pool to support publications if the work published is related to the SFB/TR 209. Therefore, please always use the following phrase in your publications:

„Gefördert durch die Deutsche Forschungsgemeinschaft (DFG) - **SFB/TRR 209- 314905040**“. In fremdsprachigen Veröffentlichungen kann eine Übersetzung der DFG in die Zielsprache ergänzt werden (z.B. im Englischen: „funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) - SFB/TRR 209 - 314905040“.

Please also here keep us updated about the latest publications also in advance for announcement in the newsletter and on our homepage.

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