

TRR179 Newsletter

10/2021

Information & News of the TRR179

In this issue

- Letter of the speaker
- Organs of the TRR179
- Events
- News and Accomplishments
- Publications
- IRTG Immunovirology
- Central Support

Dear TRR179 members,

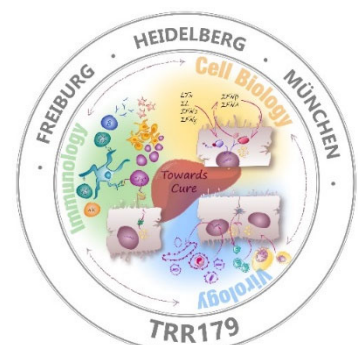
We are happy to present you the next newsletter of our TRR179. The aim of this newsletter is to bring everybody to the same level of information on recent developments and results obtained within the TRR179, the work of the IRTG "Immunology" and of the executive board as well as administrative issues.

Although we are still in a pandemic situation, for most of us kind of normal life and lab work possible again and we can focus again on our TRR179s most prior goal, i.e. a cure for chronic viral hepatitis.

We very much enjoyed meeting you all in person during our retreat on July, 18./19.th, 2021 at Forum Hohenwart. For many of us, especially, for our youngsters and new members of the IRTG it was essential to get to know each other in person. We had many fruitful discussions, some of them even leading to new cooperative projects within the TRR179. Furthermore, we could see that all of our projects are in good shape. In consideration of the pandemic situation of the last year this cannot be taken for granted and is a great achievement we can be proud of.

However – as you know "after the appraisal is before the appraisal" and we therefore ask you all to further work intensely on our overall and specific project research aims that we have promised in our application.

For now, we hope that you will enjoy this newsletter and find it of help for your collaborative efforts.



Organs of the TRR179

Executive Board

Speaker: Prof. Ralf Bartenschlager, Heidelberg

Co-Speaker: Prof. Robert Thimme, Freiburg and Prof. Ulrike Protzer, München

Representative for...

Equal Opportunity: Prof. Ursula Klingmüller, Heidelberg

IRTG: Prof. Hartmut Hengel, Freiburg

Junior Group: Prof. Sabrina Schreiner, München

Students: Matthias Reinscheid, Freiburg

Board of the IRTG

Speaker: Prof. Hartmut Hengel, Freiburg

Co-Speakers: Prof. Volker Lohmann, Heidelberg; Prof. S. Schreiner, München

Students´ Speaker: Matthias Reinscheid, Freiburg

Co-Speakers: Kira Leitl, Munich; Philipp Ralfs, Heidelberg

*We are looking forward
to further successful
board meetings*

Events

Retreat 2021

We keep good memories from the meeting and having the IRTG retreat attached to it seemed for most of us as an agreeable and favorable proceeding. Instead of a general retreat in 2022, we all will meet in person at the international conference in Freiburg in May:



TRR179 - International Conference 2022

"Viral hepatitis and beyond: from basic science to cure"

The planning for the international TRR179 symposium has started. It will take place on **Monday, May, 30th 2022** the whole day and **Tuesday, May, 31st 2022** till early afternoon. The colleagues in **Freiburg** found with the "Kollegiengebäude" a nice venue downtown for roundabout 300 participants, also close to the train station. We are planning a hybrid event with presence (which counts for all of the TRR179 members) and the possibility for remote attendance. We have the opportunity to display solely one poster per project which can be discussed during breaks. Instead of traditional poster session we reserved a slot of talks during the conference for our young scientists to present their work.

Please, block this date in your calendars!!

Project reviewing meeting 2022

In order to prepare the next application round we will meet with all PIs in November 2022. We keep you informed about the precise date and location.

The TRR179 offers Gerok stipends in Munich and Freiburg

News

Gerok stipends

Dr. Carolin Mogler (Munich) and Dr. Annegrit Decker (Freiburg) started to dedicate their Gerok positions to the TRR179 from July 2021 on for one year. We will surely get further results of their projects during the conference in May 2022.

MD-Stipends

A new MD scholarship could be awarded to David Reeg (TP01), who started in October working on his project "Interplay of subset diversification and functional adaption of HBV- and HCV-specific CD8+ T cells in chronically infected patients". Moreover, due to the Corona situation, three further scholarship awards could be extended until December 2021.

The IRTG would like to take the opportunity to inform the PIs of the TRR179, that **two 12-months fellowships for MD students will be available from January 2022 on**. The awardees are expected to suspend their curricular studies for one year and to devote their full time to their research project. Allocation of MD fellowships will be strictly guided by the individual excellence of the candidates. Moreover, each of the TRR sites is asked to provide one additional MD fellowship from institutional sources. For more information, please contact Dr. Eva Schnober.

Cooperations

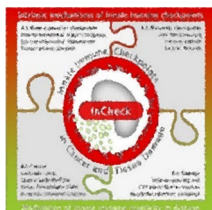
GRK2727

We congratulate our member Adelheid Cerwenka (TP07) for the approval of the DFG funded graduate school GRK 2727 "Innate Immune Checkpoints in Cancer and Tissue Damage" starting on January 1st, 2022. We are looking forward to future cooperations with TRR179.

CanHepC

Our longstanding cooperation with the research Consortium CanHepC in Canada has been reactivated. Since the borders are now open again between Canada and Germany for vaccinated people, CanHepC and TRR179 networks are pleased to announce that the possibility to apply for an exchange program is now open.

As already announced via email, the deadline to submit applications is **January 16th, 2022**, and the exchange should take place any time during 2022. For further details, please check our or CanHepC's homepage ([TRR179 Determinants and dynamics of elimination versus persistence of hepatitis virus infection | News](#))



Project news

Steeve Boulant, project leader of subproject TP22 (Boulant/Dao Thi), has successfully negotiated for a professorship at Florida University. He will leave Heidelberg and therewith also the TRR179 on December 31st, 2021. We are wishing him and his family all the best for his future career. From January 1st on, Viet Loan Dao Thi will take over his project part. The TRR179 will therefore. We are glad we could fill the gap successfully and in agreement with the DFG.

Accomplishments

We are happy to announce that **Stephan Urban**, project leader of TP15, received the Distinguished Award in Hepatitis B Research 2021.

For her research on depleted immune cells, **Maike Hofmann** (TP20) has been awarded this year's Adolf Kußmaul Prize of the Southwest German Society of Gastroenterology. The prize, endowed with 5,000 euros, was presented virtually to her on the occasion of the annual meeting of the Southwest German Society of Gastroenterology on June 25th, 2021. She was honored for her research on the role of special immune cells, so-called virus-specific CD8+ T cells, in chronic hepatitis C virus infection.

We congratulate Stephan and Maike for the recognition and wish them all the best for their future work.



TRR179 Homepage www.trr179.de

If you have any ideas and suggestions or think there is something missing on the homepage, please do not hesitate to contact us. We do appreciate all of your comments.

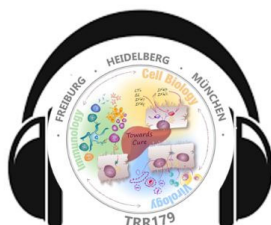
And it's worth checking the homepage from time to time in order to find information about the latest news, events, job offers and publications of the TRR179 which are frequently posted there.



Twitter

We are also on twitter and looking forward to many followers **@trr179_2**.

Please like and follow us! Furthermore, we are more than happy about every inspiration for tweets.



Podcasts

By now we already published the second and third issue of our Podcast. We hope you enjoy listening every now and then and stay tuned.

Our podcasts cover the following topics:

- 1. Podcast:** Latest research findings on "Memory-like HCV-specific CD8+ T cells retain a molecular scar after cure of chronic HCV infection": T. Boettler together with R. Bartenschlager, R. Thimme, and M. Hofmann.
- 2. Podcast:** TRR179 and SARS-CoV-2": We highlight how members of our research network applied their specific expertise to study SARS-CoV-2 in order to support the fight against the pandemic.
- 3. Podcast:** "Hepcludex": Tobias in conversation with S. Urban, who invented the first direct-targeting medication to treat chronic hepatitis D.

Seminar series

Topic-specific lectures by TRR179 PIs ensure a high level of broad knowledge in the fields of immunology and virology, irrespective of the students' background and the focus of his/her individual PhD or MD project. Several of these talks are available as video lectures and accessible via the secured IRTG website! Each lecture contains 5 questions which must be answered in written form and approved by the supervising PI in order to be accepted by the IRTG as curricular activity.

Most recent lectures:

- 05/07/2021** **Dr. Paola Fiscaro:** "From transcriptomic to functional characterization of virus-specific CD8 T cells in chronic hepatitis B to identify novel molecular targets for therapeutic T cell reconstitution strategies".
- 20/09/2021** **Dr. Kerstin Brinkmann:** "Determining the essential functions of distinct pro-survival BCL-2 family members by using gene-swap mice"
- 21/09/2021** **Dr. Konstantin Sparrer:** "SARS-CoV-2 vs. Innate Immunity"

We keep you posted on upcoming seminars via email announcement.

Publications

This is a short list of the most recent publications of our TRR179:

Oberhardt, V., Luxenburger, H., Kemming, J. et al. Rapid and stable mobilization of CD8+ T cells by SARS-CoV-2 mRNA vaccine. **Nature** (2021). doi.org/10.1038/s41586-021-03841-4 (TP01, TP02, TP04, TP20, TP21)

Schulien, I., Kemming, J., Oberhardt, V. et al. Characterization of pre-existing and induced SARS-CoV-2-specific CD8+ T cells. **Nat Med** 27, 78–85 (2021). doi.org/10.1038/s41591-020-01143-2. (TP01, TP02, TP04, TP20, TP21)

Delphin M, Desmares M, Schuehle S, **Heikenwalder M**, Durantel D, Faure-Dupuy S. How to get away with liver innate immunity? A viruses' tale. **Liver Int.** 2021 Nov;41(11):2547-2559. doi: 10.1111/liv.15054. (TP06)

Quitt O, Luo S, Meyer M, Xie Z, Golsaz-Shirazi F, Loffredo-Verde E, Festag J, Bockmann JH, Zhao L, Stadler D, Chou WM, Tedjokusumo R, Wettengel JM, Ko C, Noebner E, Bulbuc N, Shokri F, Lüttgau S, **Heikenwälder M**, Bohne F, Moldenhauer G, Momburg F, **Protzer U**. T-cell engager antibodies enable T cells to control HBV infection and to target HBsAg-positive hepatoma in mice. **J Hepatol.** 2021 Nov;75(5):1058-1071. doi: 10.1016/j.jhep.2021.06.022.

Salimi Alizei E, **Hofmann M**, **Thimme R**, **Neumann-Haefelin C**. Mutational escape from cellular immunity in viral hepatitis: variations on a theme. **Curr Opin Virol.** 2021 Oct;50:110-118. doi: 10.1016/j.coviro.2021.08.002. (TP01, TP02, TP20)

Oswald A, Chakraborty A, Ni Y, Wettengel JM, **Urban S**, **Protzer U**. Concentration of Na⁺-taurocholate-cotransporting polypeptide expressed after in vitro-transcribed mRNA transfection determines susceptibility of hepatoma cells for hepatitis B virus. **Sci Rep.** 2021 Oct 5;11(1):19799. doi: 10.1038/s41598-021-99263-3. (TP14, TP15)



Keep yourself informed
about the latest
research results which
can also be found on
our website
www.trr179.de

And even more publications

Zoldan K, Ehrlich S, Killmer S, Wild K, Smits M, Russ M, Globig AM, **Hofmann M, Thimme R, Boettler T**. Th1-Biased Hepatitis C Virus-Specific Follicular T Helper-Like Cells Effectively Support B Cells After Antiviral Therapy. *Front Immunol*. 2021 Sep 30;12:742061. doi: 10.3389/fimmu.2021.742061 (TP01, TP04, TP20)

Urban S, Neumann-Haefelin C, Lampertico P. Hepatitis D virus in 2021: virology, immunology and new treatment approaches for a difficult-to-treat disease. *Gut*. 2021 Sep;70(9):1782-1794. doi: 10.1136/gutjnl-2020-323888. (TP02, TP15)

Koch J, Uckeley ZM, Doldan P, Stanifer M, **Boulant S**, Lozach PY. TMPRSS2 expression dictates the entry route used by SARS-CoV-2 to infect host cells. *EMBO J*. 2021 Aug 16;40(16):e107821. doi: 10.15252/embj.2021107821. (TP22)

Chen Q, Coto-Llerena M, Suslov A, Teixeira RD, Fofana I, Nuciforo S, **Hofmann M, Thimme R**, Hensel N, **Lohmann V**, Ng CKY, Rosenberger G, Wieland S, Heim MH. Interferon lambda 4 impairs hepatitis C viral antigen presentation and attenuates T cell responses. *Nat Commun*. 2021 Aug 12;12(1):4882. doi: 10.1038/s41467-021-25218-x. (TP01, TP17, TP20)

Rappez L, Stadler M, Triana S, Gathungu RM, Ovchinnikova K, Phapale P, **Heikenwalder M**, Alexandrov T. SpaceM reveals metabolic states of single cells. *Nat Methods*. 2021 Jul;18(7):799-805. doi: 10.1038/s41592-021-01198-0. (TP06)

Rennert C, Tauber C, Fehrenbach P, Heim K, Bettinger D, Sogukpinar Ö, Schuch A, Zecher BF, **Bengsch B**, Lang SA, Bronsert P, Björkström NK, Fichtner-Feigl S, Schultheiss M, **Thimme R, Hofmann M**. Adaptive Subsets Limit the Anti-Tumoral NK-Cell Activity in Hepatocellular Carcinoma. *Cells*. 2021 Jun 2;10(6):1369. doi: 10.3390/cells10061369. (TP01, TP20, TP21)

Stukalov, A., Girault, V., Grass, V. et al. Multilevel proteomics reveals host perturbations by SARS-CoV-2 and SARS-CoV. *Nature* 594, 246–252 (2021). <https://doi.org/10.1038/s41586-021-03493-4> (TP11, TP14, TP18)

Schwabenland M, Salié H, Tanevski J, Killmer S, Lago MS, Schlaak AE, Mayer L, Matschke J, Püschel K, Fitzek A, Ondruschka B, Mei HE, **Boettler T, Neumann-Haefelin C, Hofmann M**, Breithaupt A, Genc N, Stadelmann C, Saez-Rodríguez J, Bronsert P, Knobloch KP, Blank T, Thimme R, Glatzel M, Prinz M, **Thimme R, Bengsch B**. Deep spatial profiling of human COVID-19 brains reveals neuroinflammation with distinct microanatomical microglia-T cell interactions. *Immunity*. 2021 Jul 13;54(7):1594-1610.e11. doi: 10.1016/j.immuni.2021.06.002. (TP01, TP02, TP04, TP20, TP21).

Deczkowska A, David E, Ramadori P, Pfister D, Safran M, At The B, Giladi A, Jaitin DA, Barbooy O, Cohen M, Yofe I, Gur C, Shlomi-Loubaton S, Henri S, Suhail Y, Qiu M, Kam S, Hermon H, Lahat E, Ben Yakov G, Cohen-Ezra O, Davidov Y, Likhter M, Goitein D, Roth S, Weber A, Malissen B, Weiner A, Ben-Ari Z, **Heikenwälder M**, Elinav E, Amit I. XCR1+ type 1 conventional dendritic cells drive liver pathology in non-alcoholic steatohepatitis. *Nat Med*. 2021 Jun;27(6):1043-1054. doi: 10.1038/s41591-021-01344-3 (TP06)

Stadler D, Kächele M, Jones AN, Hess J, Urban C, Schneider J, Xia Y, Oswald A, Nebioglu F, Bester R, Lasitschka F, Ringelhan M, Ko C, Chou WM, Geerlof A, van de Klundert MA, Wettengel JM, Schirmacher P, **Heikenwälder M, Schreiner S, Bartenschlager R, Pichlmair A**, Sattler M, Unger K, **Protzer U**. Interferon-induced degradation of the persistent hepatitis B virus cccDNA form depends on ISG20. *EMBO Rep*. 2021 Jun 4;22(6):e49568. doi: 10.15252/embr.201949568. (TP06, TP09, TP11, TP14, TP16)

Riedl T, Faure-Dupuy S, Rolland M, Schuehle S, Hizir Z, Calderazzo S, Zhuang X, Wettengel J, Lopez MA, Barnault R, Mirakaj V, Prokosch S, Heide D, Leuchtenberg C, Schneider M, Heßling B, Stottmeier B, Wessbecher IM, Schirmacher P, McKeating JA, **Protzer U**, Durantel D, Lucifora J, Dejardin E, **Heikenwalder M**. HIF1 α -mediated RelB/APOBEC3B downregulation allows Hepatitis B Virus persistence. *Hepatology*. 2021 May 15. doi: 10.1002/hep.31902.(TP06, TP14)

Dudek M, Pfister D, Donakonda S, Filpe P, Schneider A, Laschinger M, Hartmann D, Hüser N, Meiser P, Bayerl F, Inverso D, Wigger J, Sebode M, Öllinger R, Rad R, Hegenbarth S, Anton M, Guillot A, Bowman A, Heide D, Müller F, Ramadori P, Leone V, Garcia-Caceres C, Gruber T, Seifert G, Kabat AM, Malm JP, Reider S, Effenberger M, Roth S, Billeter AT, Müller-Stich B, Pearce EJ, Koch-Nolte F, Käser R, Tilg H, **Thimme R, Böttler T**, Tacke F, Dufour JF, Haller D, Murray PJ, Heeren R, Zehn D, Böttcher JP, **Heikenwälder M, Knolle PA**. „Auto-aggressive CXCR6+ CD8 T cells cause liver immune pathology in NASH.“ *Nature*. 2021 Apr;592(7854):444-449. doi: 10.1038/s41586-021-03233-8. (TP01, TP04, TP05, TP06)

A. Stukalov, V. Girault, V. Grass, O. Karayel, V. Bergant, C. Urban, D. A. Haas, Y. Huang, L. Oubraham, A. Wang, M. S. Hamad, A. Piras, F. M. Hansen, M. C. Tanzer, I. Paron, L. Zinzula, T. Engleitner, M. Reinecke, T. M. Lavacca, R. Ehmann, R. Wölfel, J. Jores, B. Kuster, U. **Protzer**, R. Rad, J. Ziebuhr, V. Thiel, P. Scaturro, M. Mann & **A. Pichlmair**. Multilevel proteomics reveals host perturbations by SARS-CoV-2 and SARS-CoV. *Nature* (2021). DOI: 10.1038/s41586-021-03493-4 (TP14, TP11)

Pfister, D., Núñez, N.G., Pinyol, R., ... **Knolle P, ... Heikenwalder M** (2021) NASH limits anti-tumour surveillance in immunotherapy-treated HCC. *Nature* (2021). <https://doi.org/10.1038/s41586-021-03362-0> (TP05, TP06)

Hofmann S, Stubbe M, Mai J, **Schreiner S**. Double-edged role of PML nuclear bodies during human adenovirus infection. *Virus Res*. 2021 Apr 2;295:198280. doi: 10.1016/j.virusres.2020.198280. (TP16).

The aim of the graduate school is to train PhD and MD students to meet the challenges of interdisciplinary research.



IRTG „Immunovirology“

New IRTG student speakers

The IRTG-students elected a new student representative during the IRTG-retreat on July 21st, 2021 in Forum Hohenwart. We congratulate Matthias Reinscheid (TP01) on his election. Together with the Co-student speakers, Kira Leitl (TP23) and Philipp Ralfs (TP17) Matthias will join the IRTG management and TRR 179 executive board teams.

“Doktoranden-Café”

This event serves to exchange amongst each other, present latest research results, and get insights into different professional careers of invited speakers or Alumni of the TRR179.

The next IRTG-Café with Prof. Ulrike Protzer will take place on November 5th, 2021 at 1.00 p.m. In a relaxed atmosphere she will talk about career paths and more. All interested IRTG members are invited to participate.

Lunch Lectures

The TRR179 Thursday Lunch lecture series has started after a summer break in October 2021. As before, the TRR179 Thursday Lunch Lectures take place every first Thursday of each month at 12.00 – 1.00 pm.

Prof. Sabrina Schreiner (TP16) gave a lecture on the „Role of SUMOylation and PML bodies for viral infection“ on October 7th, 2021. The next lecture will be held on November, 4th, 2021. Dr. Maïke Hofmann (TP 20) will speak about „COVID-19 and CD8+ T cells“. We would like to take the opportunity to invite also the PIs of the TRR179 to attend the lecture. All lectures will be recorded and stored on the IRTG server.

Workshops

Due to the positive feedback and the high demand for the R-course, we would like to announce, that the second R-workshop, organized by Dr. Carl Herrmann and Dr. Carlos Ramirez, TRR179 (TP23) will take place on December 8./9.th 2021.

Furthermore, we are currently conducting a survey to find out which workshop topics are prioritized by the IRTG-students.

Applications can be sent any time!!

Secondments

In case you would like to go to one of the laboratories within our TRR for learning novel techniques, gaining novel expertise or other, you can apply for funds to do so. Eva Schnober and Katrin Woll will support you in realizing the secondments. **If you are interested, please send us your expression of interest for the exchange program latest on October 31st, of the respective year.**

*There are no
problems, only
challenges!*

Central Support

Travel Expenses

According to the grant approved by the DFG and the decision of the steering committee of the TRR179, every **project leader (PI)** of the TRR179 can be supported with up to 1.500 € travel expenses each year. This amount of money can also be spent by anyone working within the PIs' project. Please submit the travel proposals **prior** to the journey to Katrin Woll and for reimbursement please send **all original** documents, together with the reimbursement-form of the University Hospital Heidelberg to Katrin Woll.

NOTE: Registration fees for online conferences can also be reimbursed. The procedure is the same.

Publication Expenses and reference to TRR179

Expenses for publications within the TRR179 will be supported, but only if the first author is supported by the TRR179 and the TRR179 is cited in the acknowledgement. Please note that we must cite according to DFG guidelines: „Gefördert durch die Deutsche Forschungsgemeinschaft (DFG) - Projektnummer 272983813 – TRR 179“ or “Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) - Project-ID 272983813 - TRR 179“, respectively.

For funding please agree with the publisher on a bill with the billing address of the TRR179. If you have any questions, please ask Katrin Woll.

Gender measures

If you are a female scientist who wants to be supported in career development or a young researcher in TRR, who needs (financial) support in compatibility of job and family, please let us know. We get specific funding from the DFG which can for example be spent on childcare during the events organized by the TRR179, for financing a "mobile educator" or a baby sitter service (only for times outside the usual childcare hours, which are justified by the time necessities of the project or for special occasions such as illness). Also for child care during holidays, for setting up and operating a home office or setting up parent/child rooms, basically for everything that helps you to facilitate reconciliation of work and family or that supports especially women in research. In 2021 we already dedicated a vast amount of the money to support young male and female PIs who are parents of young children to allow them more flexible working hours. This is enormously important and helpful, especially in times of pandemic, and can be facilitated by the support of HiWis financed by the TRR179.

Furthermore, we provided funds for the seminar of Vera Strauch "Female leadership".



Contacts

IRTG

Dr. Eva Schnober, Freiburg;
phone: +49 761 203-6572;
email: eva.schnober@uniklinik-freiburg.de

TRR179

Dr. Katrin Woll, Heidelberg;
phone: +49 6221 56 34078;
email: katrin.woll@med.uni-heidelberg.de