

NEWS letter

M_HH
Medizinische Hochschule
Hannover



Graduate School of Excellence

OKTOBER
2024
Alumni

NEWSletter

Save the date: 25 years of structured PhD programs at MHH: November 7th/8th, 2025



Dear HBRS Alumni,

We proudly present our **19th HBRS Alumni newsletter**.

MHH is currently still in a phase of transition, meaning for example that due to a retirement wave many department heads have recently been replaced. HBRS, of course, is happy to continue in supporting numerous international PhD students in all departments/institutes of MHH and partners.

In this newsletter, we report our current activities as well as news from your fellow Alumni. Thanks for your warm support and interest!

Reinhold Förster, Acting Dean of HBRS

Current status of HBRS and news

HBRS currently comprises six international (MD)/PhD programs ("Molecular Medicine", "Infection Biology / DEWIN", "Regenerative Sciences", "Auditory Sciences", "Epidemiology" and "Biomedical Data Science"). So called DFG "Graduiertenkollegs" are associated to HBRS. There are meanwhile altogether three structured doctoral programs for medical students to receive the Dr.med. degree (StrucMed; KlinStrucMed and DigiStrucMed). Three HBRS-associated **Master** programs "Biomedicine", "Biochemistry" and "Biomedical Data Science" are established.

Currently, the various programs of HBRS host ~260 PhD students. In addition, 30 medical students were accepted for StrucMed, 14 for KlinStrucMed and 10 for DigiStrucMed this year. About 80 new Master students (in three programs) are enrolled. About 60% of our PhD students are international and around 10% have a medical background. About 50% are women.

Since 2023, HBRS has been embedded in the newly established Deanship of Academic Career Development lead by Prof. Dr. Anette Melk.

Fritz Hartmann Lecture

Opening of study year, October 2023



Josef Penninger, Scientific Director of Helmholtz Centre for Infection Research Braunschweig; Professor for Personalized Medicine, Medical University Vienna, Austria

prestigious Emmy Noether program for his research on blood stem cells and leukemia

- Caroline Perner (Neuroimmunology) received the 250.000 Euro Memorial stipend by Else-Kröner Fresenius Foundation.
- Hildegard Büning (Experimental Hematology) and MHH receive about 1 million Euro from the EU consortium MAGIC. She will research on AAV (adeno-associated virus) vectors for gene therapies.
- From July 2024, Aiden Haghikia is the new head of the MHH Neurology department.
- Verena Scheper (Otorhinolaryngology) will receive 770.000 Euro from the Institute of Biomedical Translation (IBT) for her hearing loss and implant research.



from professors and supervisors:

- Amar Sharma (Gastroenterology) is now a prestigious DFG Heisenberg professor.
- Laura Hinze was awarded the Max-Eder Nachwuchsgruppe and receives 742.00 Euro for her research.
- Tobias Welte (Pneumology) sadly passed away on March 10th, 2024
- Lars Dölken is now head of Virology (succession of Thomas Schulz).
- Florian Perner (Hematology) received 2.2 million Euro in the

Guided tour through Hannover,

October 2023



Weekend workshop in Berlin

Susanne Kruse and 20 international HBRS students travelled to Berlin from May 31st–June 2nd, 2024. Students from 11 different countries formed part of the group. In the mornings, the trainer Grit Kümmele discussed various aspects of integration into the German thinking and way of life as well as conflict management. The cultural program in the afternoons and evenings included a guided bus tour, a guided tour through the “Tränenpalast”, the Reichstag, as well as a walking tour to Eastside Gallery. The DAAD kindly supported a weekend workshop for specialists from third world countries on the topic “Understanding the Germans – Intercultural aspects”. The weekend was a great success. The workshop will certainly be repeated :-).



News from MHH

Overall MHH received the record sum of 109.4 million Euro of third-party funds in 2023.

According to the ranking “world’s best hospitals”, MHH is German wide on rank 5. In the American “Newsweek” ranking MHH is overall number 39 of the top 250 clinics.

MHH and Andre Bleich (Central Animal Facility) received 1.6 million Euro from the DFG supported research group FOR 2591, which was extended for another two years.

CAIMed, the new virtual Lower Saxony research center for artificial intelligence and causal methods in medicine was inaugurated in March 2024.

In March 2024, the Danish company Novo Nordisk bought the MHH spin-off Cardior Pharmaceuticals (Thomas Thum) for 1.025 billion Euro.

The EU supports the research network RESOLVE with 8 million Euro. Researchers will look for “gold standards” of leukemia treatments.

DFG supports the research group TARGET-MPN, head Florian Heidel from Hematology/ Hemostaseology/ Oncology/ StemCell Transplantation, with altogether 5.1 million Euro (1.5 million for MHH) in the coming 4 years.

The new building of the Centre for Individualized Medicine (CiiM) recently celebrated the roofing ceremony.

MHH has submitted the applications for the Excellence Clusters R-CUBE (new), RESIST and Hearing4All.

The Comprehensive Cancer Center (CCC-N), a cooperation between MHH and UMG Göttingen will continue and will receive 4.8 million Euro for the coming 4 years.

In addition, the research institute of CCC-N, the so-called IZKf, will receive 4.5 million Euro of Lower Saxony and Volkswagenstiftung for the coming 5 years.

The MHH children’s hospital celebrated its 50th anniversary on August 30th, 2024.

ZIB Retreat 2024

The ZIB Retreat 2024, held at the Twincore Centre for Experimental and Clinical Infection Research, brought together PhD students and experts from the fields of immunology, virology, and microbiology, fostering a spirit of collaboration and innovation. This annual event, meticulously planned over a year by a dedicated team of PhD students, provided important opportunities for students to present their research, engage with leading experts, and receive valuable feedback.

The planning began with an enthusiastic brainstorming session, where the organizing committee, comprised of students from various disciplines, collaborated to shape the retreat. Responsibilities were divided, with team members focusing on tasks such as inviting speakers, securing sponsorships, creating the event booklet, and managing logistics.

The retreat opened with a ceremony that underscored the importance of collaboration and personal growth. The first keynote speaker, Dr. Hannah Burgess, presented her latest research on viral co-option of RNA modification and decay pathways. This was followed by presentations from virology PhD students, who shared new insights on topics ranging from human cytomegalovirus to SARS-CoV-2. The second keynote speaker, Gianni Panagiotou led us into the field of microbiology, delivering an engaging talk on the intricate interplay between gut bacteria and human health. The day concluded with a dinner attended by guest speakers and the organizing committee, fostering networking and collaboration in a relaxed atmosphere.



organization committee

The second day began with a keynote by Dr. Johanna Strobl, who offered insights into Skin-resident memory T-cells. This was followed by presentations from immunology students, who covered a wide range of topics, enriching the academic exchange. It was followed by the first poster session giving an inside view into the PhD work of the first and second year virology students. The afternoon was dedicated to a career session with industry representatives, offering insights into various career paths and allowing students to explore opportunities beyond academia. Simultaneously, younger PhD students presented

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their research through posters, sparking lively discussions and potential collaborations.

The retreat ended with a social event centered around a lively barbecue that brought everyone together. Amid the aroma of grilled delicacies, participants enjoyed a joyful get-together, exchanging stories and laughter. Highlights of the evening included the honoring of the best poster presentations in the fields of microbiology, virology, and immunology, as well as the recognition of the best talk, celebrating outstanding contributions to the scientific community.

The ZIB Retreat 2024 was a resounding success, characterized by rich scientific dialogue, networking opportunities, and a sense of community among participants. The event not only highlighted the latest research but also inspired future collaborations, reinforcing the value of interdisciplinary engagement. As the organizing committee reflects on the retreat's achievements, they look forward to next year's event, eager to continue this tradition of fostering innovation and connection across disciplines.

The organizing committee

News in Research

In this section, we will regularly publish short reviews of important and recent achievements in selected research fields, or useful tips! Everybody is welcome to contribute.

The role of interleukin-2 receptor subunits in recombinant interleukin-2-induced skin rash

by Charline Sommer, Fraunhofer Institute ITEM

Hello everyone!



Alumnus of MD/PhD program
Molecular Medicine; now Postdoc

My name is Charline Sommer, and I recently completed my PhD in the Molecular Medicine Program at the Fraunhofer ITEM in Hannover under the supervision of Prof. Armin Braun and Dr. Katherina Sewald. Our team, known for its expertise in toxicology, is involved in the imSAVAR project (<https://imsavar.eu/>), which is focused on understanding how immune therapies can lead to immunotoxic side effects. Specifically, we investigated skin rashes that often occur during

therapies with biologicals like interleukin-2 (IL-2), which was commonly used in treating cancers and is now increasingly being explored for treating autoimmune and inflammatory diseases. Despite its potential, IL-2 therapy is still limited by these side effects.

During my research, we found that the side effects triggered by IL-2, particularly skin rashes, seemed similar to pathologies observed in patients with mutations affecting the IL-2 receptor (IL-2R) β subunit. This notion led us to explore whether similar mechanisms (i.e. reduced IL-2R β expression on immune cells) might be at play in both conditions.

To address these points, we isolated PBMCs from healthy donors, stimulated them with varying concentrations of therapeutic IL-2 (al-

leukin) for up to 7 days, and analyzed expression of IL-2R β . Interestingly, after only 15 min of IL-2 stimulation, IL-2R β surface expression was basically absent on CD4⁺ effector T (Teff) and regulatory T (Treg) cells upon stimulation with high IL-2 concentrations (<1% IL-2R β +), while expression on NK cells, CD8⁺ T cells and other T cell subsets was not significantly affected (Figure 1A). When we extended the IL-2 stimulation to up to 7 days, the reduction in IL-2R β surface expression became more pronounced, especially in T cell subsets, while NK cells maintained relatively high levels of IL-2R β (>55% IL-2R β +) (Figure 1B) – mirroring what has been reported for patients with IL2RB mutations.

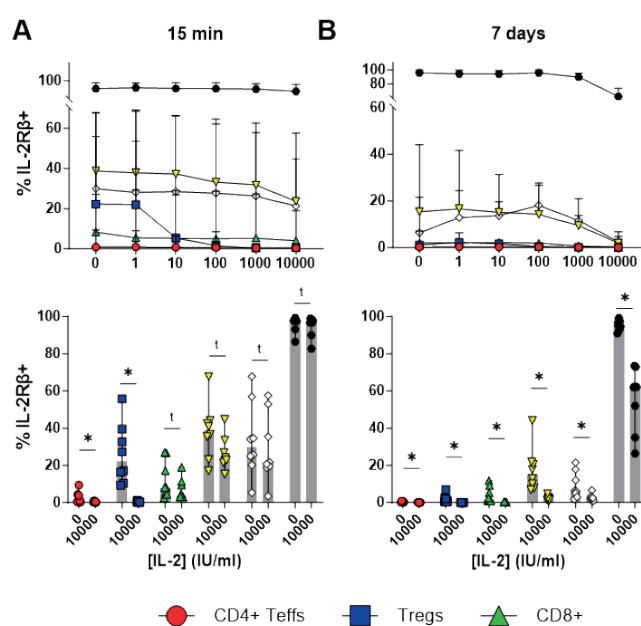


Figure 1 Continuous hIL-2 stimulation reduces IL-2R β surface expression on lymphocytes. Human PBMCs were stimulated with increasing IL-2 doses for up to 7 days prior to analysis of CD4⁺ T effs, CD4⁺ Tregs, CD8⁺ T cells, $\gamma\delta$ T cells (GDs), NKT cells, and NK cells. Mean frequencies of IL-2R β ⁺ cells after 15 min (A) or 7 days (B) of IL-2 stimulation. Bar graphs (lower panel) highlight mean frequencies of IL-2R β ⁺ lymphocytes as shown above. n = 8 donors, two independent experiments. * p < 0.05, all other conditions non-significant (t < 0.1), analyzed by multiple paired t-test (Holm-Šidák method).

In a next step, we wanted to understand how these changes impacted the functionality of the cells. Therefore, we re-stimulated the IL-2-treated cells with a high dose of IL-2 and measured the resulting phosphorylation of STAT5 (pSTAT5) as part of the downstream IL-2 signaling pathway. After just 18 hours, we noticed a slight decrease in pSTAT5 in T cells, with CD4⁺ T cells showing a more significant reduction than CD8⁺ T cells (Figure 2A). Over the full 7-day period, this decrease in pSTAT5 became more pronounced in T cells, particularly in Tregs, but not in NK cells. This suggests that continuous IL-2 stimulation leads to a decreased signaling capacity in T cells, especially Tregs (Figure 2B), potentially impacting their role in maintaining immune balance.

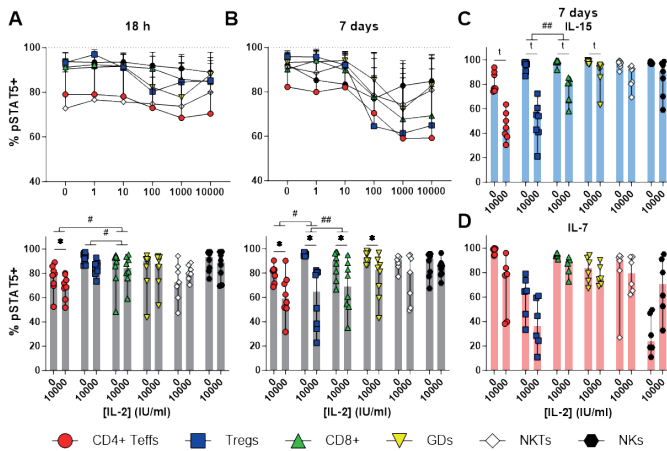


Figure 2 IL-2R signaling capacity is reduced in cells with previous high-dose IL-2 stimulation. Human PBMCs were stimulated with IL-2 and re-stimulated with high-dose IL-2 (10,000 IU/ml), IL-15, or IL-7 for 15 min. **A+B** Mean frequencies of pSTAT5+ cells after 18 h (A) or 7 days (B) of IL-2 stimulation after re-stimulation with IL-2. Bar graphs (lower panel) highlight mean frequencies of pSTAT5+ lymphocytes as shown above. **C+D** Mean frequencies of pSTAT5+ cells after 7 days with or without IL-2 and subsequent re-stimulation with IL-15 (C) or IL-7 (D). $n = 6-8$ donors, two independent experiments, mean \pm SD. * $p < 0.05$, ** $p < 0.01$, all other conditions non-significant ($t < 0.1$), analyzed by multiple paired t -test (Holm-Šidák method).

Moreover, we found that this decrease in signaling was not limited to IL-2 but extended to other cytokines known for their role in homeostasis of lymphocytes in tissues: We also observed reduced signaling in response to IL-15, another cytokine that shares the IL-2R β subunit, particularly in Tregs (Figure 2C). Interestingly, IL-7 signaling, which uses a different receptor component (IL-2R γ), was not significantly altered, although there was a trend towards decreased signaling in CD4+ T cells, especially Tregs (Figure 2D).

To add another layer to our findings, we performed a correlation analysis and discovered that higher baseline expression of the IL-2R α subunit – necessary to form the high-affinity IL-2R – was linked to more pronounced reductions in pSTAT5 signaling upon IL-2 re-stimulation of $\alpha\beta$ T cells (Figure 3A-C). This suggests that cells with higher IL-2R α expression might have increased IL-2R turnover, leading to greater reductions in IL-2R β and subsequently in IL-2R signaling capacity. This finding could help explain why some patients are more susceptible to IL-2-induced side effects, particularly those with higher IL-2R β expression.

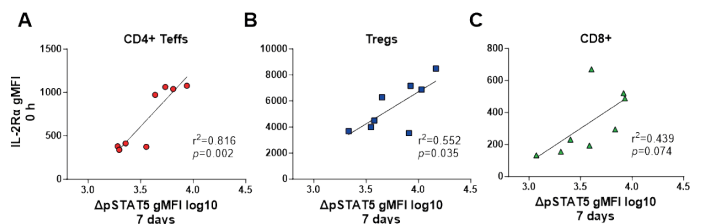


Figure 3 IL-2R α expression correlates with decreases in IL-2 signaling capacity of high-dose IL-2-stimulated T cells. Donor-dependent correlation of baseline IL-2R α gMFI on CD4+ T effs (A), CD4+ Tregs (B), and CD8+ T cells (C) with differences in pSTAT5 signal on day 7. Δ pSTAT5 is calculated as the difference in pSTAT5 gMFI of unstimulated cells and gMFI of IL-2-stimulated cells upon re-stimulation with IL-2 (as shown in Figure 4B). The common logarithm (log₁₀) of Δ pSTAT5 is shown. $N = 8$ donors, two independent experiments. r^2 and p -values determined using simple linear regression.

In summary, our research highlights the complex and cell-specific effects of continuous high-dose IL-2 therapy. The similarities we observed between IL-2-stimulated cells and cells from patients with IL-2R β defects suggest that IL-2R signaling could be a valuable biomarker for predicting and managing adverse effects during IL-2 therapy. While IL-2 remains a promising treatment option, our findings underline the need for a better understanding of its long-term impact on immune function to minimize side effects and improve patient outcomes.

If you want to know more about our research, you can check out the publication online at Clinical Immunology (doi.org/10.1016/j.clim.2024.110288)!

NEWSletter

View from abroad

By Jovana Markovic

In this section, we will regularly publish short reports of experiences of our Alumni students as Postdocs etc. abroad! Everybody is welcome to contribute.



Jovana Markovic

MD/PhD program "Molecular Medicine"; final exam November 2021; currently GMP Project Manager, ViruSure GmbH, Vienna

consistently challenged me to surpass expectations, provided me with invaluable support as well. My resilience and multitasking skills, in addition to my development as a researcher, were all molded by the entire experience.

When I finished my PhD, I wanted to apply my knowledge in industry. Even though I initially accepted a position as a scientist in a Vienna-based company that performs cell and gene therapy, at that point I only knew how to be a scientist. I therefore desired to broaden my knowledge and experiment in a different area. I currently work for a company that performs biosafety testing for products in the (pre-)clinical stages as a GMP Project Manager. I've never had a job quite like this one, and it's very interesting. Project management, quality assurance, and regulatory compliance are my main areas of expertise. Also, I still get to apply my scientific knowledge.

Life in Austria is quite different from Germany. Even though the language is the same (but not the Hannover's Hochdeutsch), Austrians have a touch of Balkan and Italian passion, that makes me feel at home. Vienna is a very international, sunny and stunning city, incredibly organized, with beautiful vineyards and ski resorts nearby. Interestingly, I met a lot of Germans from Lower Saxony here.

I am grateful for my PhD journey at HBRS and mentorship I received. I was able to learn about some alumni's career paths and the companies they work for by getting in touch with them thanks to the program. Moreover, I made lifelong friends there. For those PhD students who are close to finishing, I encourage you to consider other opportunities outside of academic world and research. Challenge yourself, explore, see what fits when you go out of your comfort zone. You have the necessary skill set for it. If you want to know more about my professional journey, feel free to contact me on LinkedIn.

Final exams

In November 2023, and June 2024, twenty students of the MD/PhD program "Molecular Medicine" successfully passed their final exams (Naisam Abbas, Franziska Baatz, Alexandra Bogomolova, Sachin K. Singh Chauhan, Sarah Cushman, Jenni Fleischauer, Leonie Hoffmeis-

Hello from Vienna, Austria

I finished my PhD in Molecular Biology in November 2021, almost 3 years ago in the group of Prof. Dr. Amar Deep Sharma. I wanted to pursue a PhD in Germany, but since I'm from a place with lots of sunshine, adjusting to rainy, overcast Hannover was difficult. Nevertheless, the PhD program was a great experience for me. I was enthusiastic about my projects, which, in my opinion, is essential if you plan to spend long hours in the lab. My supervisor, a remarkable scientist who

ter, Nurul Khalida B. Ibrahim, Malte Juchem, Ona Marija Kalesnykaite, Jonathan Lühmann, Philip Mausberg, Greta Meyer, Gema Morillas Ramos, Philipp Joel Mroch, Larissa Nassauer, Olga Oleshko, Kevin Schmidt, Anton Shaverskyi, Charline Sommer). The next exams are expected for November 5th/8th, 2024.

The final exams in the PhD programs "Infection Biology" and "DEWIN" took place on January 19th, 2024 (Belén Carriqui Madroñal, Nicoletta Schwermann, Anna Rebecca Siemes, Katja Steppich and Tao Yang), followed by the next ones on June 14th, 2024 (Angela Aringo, Sarah Beyer, Safaa Bouheraroua, Sven Cleeves, Sabrina Clever, Dilfuza Djamalova, Rajendra Khanal, Carolina Mastella Botelho, Pia Peppermüller-Rindler, Rebecca Pospich, Isita Sagar and Melanie Urbanek-Quaing). The next final exams are scheduled for January 31st, 2025.

Award of PhD Prizes

PhD Infection Biology/DEWIN, June 2024

Sabrina Clever, Virology, TiHo



On January 12th, 2024, Marjan Kheirmand-Parizi and On-Chung Ian Shum and on January 19th, 2024, Philippe Alexandre Vollmer Barbosa geb. Dänzer Barbosa of the PhD program "Regenerative Sciences" successfully passed their final exams. On February 28th, 2024, Aynaz Kianmehr defended her thesis.

On June 3rd, 2024, 8 students of the PhD program "Regenerative Sciences" successfully passed their final exams: Shifaa Abdin, Tamari Askurava, Miriana Dardano, Kelsey Lolatte, Zulaikha Malik, Rajesh Vivekanandan, Laura von Schledorn, and Yankai Xiao.

Basil Kaburi (November 2023) and Christin Walter (February 2024) had their final exams in the PhD program "Epidemiology".

Tomas Jozef Gajecki Somervail, Daniel Kipping (geb. Daniel Alrutz), and Brilliant from the PhD program Auditory Sciences successfully passed their final exams.

Hanan Bengali (5.3.2024), Martijn Vincent Zoodma (5.4.2024), Wen-chao Li (20.6.2024) and Zhaoli Liu (28.8.2024) from PhD program BIOMEDAS passed their final exams.

*„Everything is theoretically impossible,
until it is done“*

Robert A. Heinlein (1907-1988), Engineer/Author

Announcements



Marriages: Many of our students have married recently. We know of Matthias Bruhn, Praeploy Pongpamorn. Congratulations!



Children: There are new "HBRS babies" by Celina Genschel; Jana van Luttikhuisen (MolMed)/ Giacomo Castoro (IB), Patricia Morán Losada (IB); Laura Ospina (IB)/ Andres Vasquez (RegSci), Adele Mucci (RegSci). Congratulations!

Prizes and grants

Some Alumni students were awarded important prizes for their research achievements or received grants:

Matthias Bruhn: HZI Promotionspreis

What is....doing?

I have finally moved back to India and to my hometown Chennai. Hurraayyy

My current position:

Associate Director, Translational Immunogenomics Unit, Centre for Advanced Biomedical sciences, Indian Institute of Technology - Madras (Chennai), India.

I am really excited about HBRS 2025 and hopefully would be present in person for the festivities.

Hari Balaji (Alumni MD/PhD)

If you would like to get in touch with anybody from the huge Alumni list, please contact the HBRS office. We will be happy to assist you!

There is also a HBRS LinkedIn group:

<https://www.linkedin.com/groups/2354739>

and a LinkedIn ZIB Alumni group:

<https://www.linkedin.com/in/alumni-zib-46756a16b/>

As well as a PhD RegSci LinkedIn group:

<https://www.linkedin.com/groups/9084167/>

Impressum and contact:

HBRS office, OE 9117

Dr. Susanne Kruse

Carl-Neuberg-Str. 1, D-30625 Hannover

Tel. +49-(0)511-532-6011; Fax. -2611

HBRS@mh-hannover.de

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