

ANNUAL REVIEW HIRI

2017-2020



ANNUAL REVIEW 2017

It all started in May 2017: The new Helmholtz Institute for RNA-based Infection Research became reality. The first research groups started their work in the fields “RNA-Biology of Bacterial Infections” and “Single Cell Analysis”. Our reputation reached several international scientists who will strengthen the institute with their research groups in the coming year.

FOUNDATION

With the “Helmholtz Institute for RNA-based Infection Research” (HIRI) in Würzburg, both parent institutions, the Helmholtz Centre for Infection Research (HZI) and the Julius-Maximilians-University of Würzburg (JMU), have established a research institution with an internationally unique orientation. The aim of HIRI is to combat infectious diseases by exploiting the potential of ribonucleic acid (RNA) as a diagnostic, target, and drug.

At the beginning of May 2017, the new Helmholtz Institute was officially presented to the Bavarian State Parliament. On May 24th, the founding agreement was approved by the stakeholders and the cooperation agreement between JMU and HZI was signed. The foundation of HIRI was then celebrated with a ceremony in the Würzburg Residence with representatives from politics, science, and industry.



Ilse Aigner (m.), Bavarian State Minister of Economic Affairs and Media, Energy and Technology, symbolically hands over the start-up financing for the HIRI provided by the State of Bavaria to HIRI Director Prof Jörg Vogel (l.) and Prof Dirk Heinz, Scientific Director of the HZI (r.) © Rudi Merkl

PERSONNEL



Dr Antoine-Emmanuel Saliba, head of the single cell analysis group at HIRI. © HIRI

HIRI director Prof Jörg Vogel and group leader Dr Antoine-Emmanuel Saliba established their research groups at the institute's foundation. The first HIRI doctoral students, Annika Schulz and Ehsan Vafadarnejad, started on July 1st, 2017. A two-day selection symposium was held in July in order to quickly staff other HIRI working groups. Subsequently, Prof Chase Beisel, North Carolina State University (USA), was appointed to a W2 professorship for RNA-based Infection Research, and four junior professorships for RNA-based Infection Research were offered to Dr Lars Barquist, JMU Würzburg, Dr Neva Caliskan, Max Planck Institute for Biophysical Chemistry Göttingen, Dr Redmond Smyth, Institut de Biologie Moléculaire et Cellulaire, Strasbourg (France) and Dr Alexander Westermann, JMU Würzburg. In addition to his appointment as W1 professor, Redmond Smyth has been selected for a Helmholtz Young Investigator Group by an independent review panel of the Helmholtz Association in Berlin on September 5th, 2017.

With Alice Hohn as head of administration and Dr Nina Littwin as scientific coordinator, the administration department quickly took its first steps and grew to a total of five employees in the course of the year. By year's end, the institute already had 12 employees (see next page).



ANNUAL REVIEW 2017



The HIRI team in the summer of 2017 (from left to right): HIRI director Prof Jörg Vogel, PhD student Ehsan Vafadarnejad, PhD student Annika Schulz, scientific coordinator Dr Nina Littwin, head of administration Alice Hohn, administrative assistant Christoph Kosche, facility technician Sebastian Stockmann, group leader Dr Antoine-Emmanuel Saliba, IT and laboratory manager Hilde Merkert. © HIRI / Monika Meece

NEW BUILDING



A new building will be constructed on the campus of the University Hospital Würzburg for HIRI, and will be home to more than 100 scientists in the future. The Free State of Bavaria is providing 30 million euros for the construction. Regular planning discussions between all parties involved in the construction started at the beginning of the year. The most important result of the third meeting in July 2017 was the definition of the construction site on the campus of the University Hospital of Würzburg. Afterwards, a planning competition for the architectural design of the new HIRI was launched. Until the new building is ready, HIRI will have 1,500 square meters of space at the JMU Würzburg at its disposal.

SEMINARS

HIRI scientists were integrated into the lecture series of the JMU. At the same time, the establishment of an RNA Faculty was initiated, which is intended to bring together leading scientists in the field of RNA research and infection biology in Würzburg. The RNA Faculty will be the central organ of the cross-institutional RNA seminar series planned by HIRI that will start in 2018.

INFRASTRUCTURE

High-throughput RNA sequencing is a core technology at HIRI. Therefore, one of the first acquisitions was an Illumina NovaSeq6000 system for about 1 million euros. The new system enables HIRI scientists and their colleagues at the HZI to share the analyses, which are up to four times faster and considerably more economical.

Shortly after the founding of the institute, the DropSeq Bio-Rad ddSEQ™ single cell sequencing system was introduced at HIRI in Würzburg. This microfluidic system analyzes nanoliter-sized droplets for single cell sequencing and enables monitoring of thousands of genes per cell, strengthening the important research area of single cell analysis at HIRI.



The installation of the Illumina NovaSeq6000 creates synergies between the new HIRI in Würzburg and its parent center HZI in Braunschweig. © HIRI / Illumina Inc.



ANNUAL REVIEW 2017

RESEARCH FUNDING

With the call for “HIRI Seed Grant Projects” starting July 1st, 2017, collaboration between HIRI scientists and the HZI, the JMU and the University Hospital of Würzburg (UKW) was accelerated. Joint research projects at the interface of RNA and infection research have been supported with up to 100,000 euros each. A total of 22 projects were selected, for which HIRI provided 1.9 million euros from its own budget. The first results of a joint seed grant project of HIRI, HZI and JMU was submitted to the journal *Frontiers in Immunology* under the title “Tolerogenic Transcriptional Signatures of Steady-State and Pathogen-Induced Dendritic Cells” by the end of the year.



In its first year of existence, HIRI was also engaged outside the Helmholtz Association. In January 2017, for example, Jörg Vogel took over the chairmanship of the German Research Foundation (DFG) Equipment Committee.

AWARDS AND POSITIONS



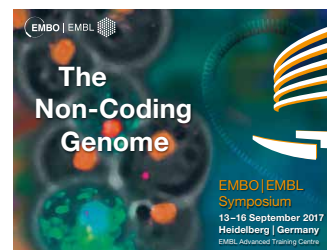
DFG President Prof. Peter Strohschneider hands over the certificate for the Gottfried Wilhelm Leibniz Prize to laureate Prof. Jörg Vogel.
© DFG / David Ausserhofer

Jörg Vogel was honored with the renowned Gottfried Wilhelm Leibniz Prize of the German Research Foundation (DFG). He received the award, endowed with 2.5 million euros in research funding, for his groundbreaking work on understanding regulatory RNA molecules in infection biology.

CONFERENCES

As member of the organizing committee, Antoine-Emmanuel Saliba co-hosted the two-day congress “Next Generation Sequencing & Single Cell Analysis”, which took place in London (UK) in November 2017. Together with Elisa Izaurralde, David Bartel and John Rinn, Jörg Vogel organized the EMBO|EMBL Symposium “The Non-Coding Genome” which took place in Heidelberg in September.

In total, HIRI group leaders represented the institute at 37 scientific events in 2017, 21 times as invited speakers.



PUBLICATIONS

24 publications appeared at the HIRI in 2017, seven of them in high impact journals.

Jörg Vogel and Stan Gorski, together with CRISPR researcher Jennifer Doudna, published a review article in *Nature Reviews Molecular Cell Biology* about a mechanism used by regulatory RNAs to recognize their target segments.



ANNUAL REVIEW 2017

Together with an international team of experts, Jörg Vogel described a novel approach to mapping the sites of a central cellular RNA cleavage enzyme (RNase E) in bacteria, published in *Molecular Cell*. His group also published the first mechanistic papers on the recently described global RNA binding protein ProQ in the *EMBO Journal*.

In their article “The primary transcriptome of *Neisseria meningitidis* and its interaction with the RNA chaperone Hfq” in the journal *Nucleic Acids Research*, colleagues from different institutes in Würzburg shed light on the complex RNA-based regulatory network of *Neisseria meningitidis*, a pathogen that can cause life-threatening meningitis and blood poisoning.

OUTREACH & EVENTS

The opportunities and risks of genome editing are an increasing focus of public discussion. In Leopoldina’s “Unterhausdebatte” in February, Jörg Vogel and other scientists answered questions on the topic “Specifically altering the genome - how far can genome surgery go?” for 28 invited journalists. In November, while being invited as a speaker in the Burkhardushaus of the Würzburg Cathedral School, he answered the question “What do you think about genome editing?” and in December he discussed this topic in front of the camera with representatives from science and society in the DFG’s talk series “Science On with Cécile Schortmann”.



Scientists discuss the topic of genome analysis with the press.
© Leopoldina / Christof Rieken

VISITS



Entrepreneur Baldwin Knauf during his visit at the HIRI.
© HIRI / Mario Schmitt

At the beginning of the year Ilse Aigner, Bavarian State Minister of Economic Affairs and Media, Energy and Technology, honored us with a visit. In summer, philanthropist Baldwin Knauf visited us and took part in the annual cross-institutional summer party.

The Scientific Director of the HIRI mother centre HZI, Professor Dirk Heinz, got a personal tour of the young Helmholtz Institute. Professor Dominic Grün from the Max Planck Institute of Immunobiology and Epigenetics (Freiburg) gave a talk for the interested staff of HIRI, the Institute of Molecular Infection Biology (IMIB) and surrounding research institutions. Shortly afterwards, we presented the new Helmholtz Institute in Würzburg to a delegation from the ruling Bavarian political party, the CSU, and explained what makes the research area of RNA-based infection research so unique and promising.

None of this would have been possible without the support of the wider scientific community. Our heartfelt thanks go to all those who have contributed to our success and to all those who are now actively shaping the new institute. Exciting times lie ahead!

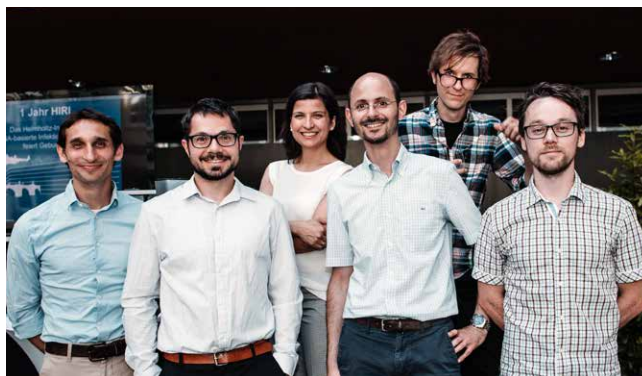


ANNUAL REVIEW 2018

In June 2018, HIRI celebrated its first birthday. Thanks to the additions of Neva Caliskan, Chase Beisel, Lars Barquist, Alexander Westermann and the Helmholtz Young Investigator Redmond Smyth, the institute grew to seven working groups. To promote young scientists, the HIRI launched the new graduate program "RNA & Infection". In addition, an excellent doctoral student at the HIRI was awarded a Dr Eckernkamp Fellowship. The new HIRI building on the campus of the Würzburg University Hospital also made progress: the architectural competition produced a great design whose implementation can soon begin.

PERSONNEL

On January 1st, 2018, Prof Chase Beisel (North Carolina State University, USA) joined the HIRI with his research group "RNA Synthetic Biology"; Dr Neva Caliskan (Max Planck Institute for Biophysical Chemistry, Göttingen) started to establish her research group "Recoding Mechanisms in Infections"; and Dr Lars Barquist expanded HIRI with his research group "Integrative Informatics for Infection Biology". On March 1st, the appointment of Dr Alexander Westermann and his research group "Host-Pathogen-Microbiota Interactions" followed. On May 1st, Dr Redmond Smyth (Université de Strasbourg, France) started as head of the Helmholtz Young Investigator Group "Genome Architecture and Evolution of RNA Viruses". All new group leaders were appointed as professors (W1, or W2 in the case of Chase Beisel) at the Medical Faculty of the University of Würzburg before the end of the year. This means that HIRI has grown to a total of seven research groups in its first year of existence. In addition, the Würzburg virologist Prof Lars Dölken and the holder of the chair of microbiology at the JMU, Prof Thomas Rudel, have been affiliated with HIRI. By the end of the year, the number of employees had reached almost 50.



The squad of young group leaders at HIRI (from left to right): Chase Beisel, Alexander Westermann, Neva Caliskan, Emmanuel Saliba, Lars Barquist and Redmond Smyth.
© HIRI / HZI

NEW BUILDING

The designated building site for the new HIRI building was formalized in March. The architectural competition for the building was officially announced and a jury of experts, users, and stakeholders met in Braunschweig on October 10th to evaluate concepts and select a winner. At a press conference on 12 October, doranth post architekten GmbH (Munich) was

announced as the winner of the architectural competition. Among the stakeholders present were representatives of the Bavarian State Ministry of Economic Affairs, Energy and Technology as well as representatives of the City of Würzburg, the JMU Würzburg, the Würzburg University Hospital, the jury, and the winners.



There is great interest in the model of the new HIRI building.
Image: Hilde Merkert, © HIRI / HZI

Following the press conference, the submissions were exhibited publicly for two weeks in the foyer of building D15 on the Medical Campus in Würzburg. In addition to cooperation partners, friends, and sponsors of HIRI, architecture students from the Würzburg Schweinfurt University of Applied Sciences were invited to the exhibition.



ANNUAL REVIEW 2018

SEMINARS

With the “RNA Seminar”, HIRI initiated its own lecture series together with the Institute for Molecular Infection Biology (IMIB), the Biocenter, and the Institute for Virology and Immunobiology of the University of Würzburg. The focus of the RNA Seminar is on science and technology centered on RNA, and thus covers a broad spectrum of topics. Top international scientists have come to Würzburg as speakers for the RNA Seminar to present their work and thus enter into dialogue with colleagues and students. The seminars on Tuesday evening are very well attended and rounded off by a subsequent reception. The official kick off of the RNA Seminar was held by Henrik Oerum, Founder and CSO of CiVi Biopharma and General Manager of the Roche Innovation Center Copenhagen with his presentation “RNA therapeutics - the long road to success”. Other invited speakers included Gilad Bachrach (The Hebrew University of Jerusalem), Susan Carpenter (University of California, Santa Cruz), Blake Wiedenheft (Montana State University), Birgitta Henriques Normark (Karolinska Institutet), Lingling Chen (Shanghai Institute of Biochemistry and Cell Biology), John D. MacMicking (Yale), and Fabian Theis (Helmholtz Zentrum München).

PROMOTION OF YOUNG SCIENTISTS

In collaboration with the Graduate School for Infection Research at the HZI (GS-FIRE) and the Graduate School of Life Sciences (GSLs) at JMU, HIRI has developed the new graduate program “RNA & Infection”. Integral parts of the program are initial laboratory rotations, structured supervision, and multi-year funding.

The three six-week laboratory assignments offer PhD students the opportunity to get an overview of the research at HIRI at the beginning of their doctorate. They can then make an informed decision on which topic they wish to work on for their PhD. In the first call for applications in autumn, about 160 candidates applied for a spot in the new program. From all applications, two excellent candidates were selected in a multi-stage selection process and will begin their doctoral studies in spring 2019. For excellent doctoral candidates, the Dr Eckernkamp Fellowship of the Vogel Foundation was established in summer. The first fellowship recipient is Falk Ponath, who is researching *Fusobacterium nucleatum*, a bacterium associated with colon cancer.

As of this year, HIRI is also involved in teaching at the JMU via elective courses. The three-day intensive course “RNA Biology” started in September. In the future, this course will alternate with the “Infection Biology” course planned for May 2019. Both courses are mandatory for all PhD students and postdocs at HIRI and are intended to provide young scientists with a solid foundation in the fields of RNA and infection biology.

INFRASTRUCTURE



Dr Eckernkamp Fellow Falk Ponath at work under oxygen-deficient conditions. Image: Mario Schmitt, © HIRI / HZI

With the LabCyte Echo, HIRI has acquired a state-of-the-art liquid handling robot. Utilizing high-frequency sound, the robot makes it possible to accurately transfer mere nanolitres into microtitre plates - a quantum leap.

In addition, from June we were able to obtain a second anaerobic workstation. This was urgently needed for work on bacteria that can only survive under low oxygen conditions. Examples include *Fusobacterium nucleatum* and *Bacteroides* bacteria, which are very common in the human intestine.



ANNUAL REVIEW 2018

RESEARCH FUNDING

In its first calendar year, HIRI has already acquired third-party funding of around 180,000 euros. These were mainly provided by the Helmholtz Association, the DFG, DARPA, and Agilent.

Mathias Munschauer successfully applied for a Helmholtz Young Investigators Group and began planning his move from the Broad Institute in the USA to Würzburg. Thus, HIRI was successful in the highly competitive Helmholtz Young Investigator Program for two consecutive years.

Jörg Vogel and Emmanuel Saliba participated in the application for the EU-FET flagship project "LifeTime" of the Helmholtz Association with the Institute Curie. LifeTime aims to map and analyze tissue on the single-cell level in order to reliably predict the onset and development of a disease. Following the success of the preproposal, the initiative will receive one million euros for one year starting in 2019. It will then be decided in Brussels whether and which of the six initially funded research initiatives the EU will continue to support on a large scale, meaning up to a billion euros.



Dr Mathias Munschauer to become head of a new Helmholtz Young Investigator Group at the HIRI. Image: Mario Schmitt, ©HIRI / HZI

AWARDS AND POSITIONS



HIRI junior professor Neva Caliskan.
Image: Mario Schmitt, ©HIRI / HZI

Chase Beisel was appointed as member of the Scientific Advisory Board of Benson Hill Inc. (USA). The biotech start-up, based in Raleigh, North Carolina (USA), develops biotechnological approaches to increase crop yields.

Neva Caliskan received a "Young Leader in Science Training Program Award" of the Schering Foundation. The associated program provides effective management skills and tools for leaders in science.

CONFERENCES

Starting in December, the RNA Society sponsored the HIRI RNA Seminar as part of its "RNA Salon" program. In addition to monetary funding, this adds HIRI to a growing international network of renowned RNA research institutes.

Throughout the year, HIRI group leaders were present at 32 scientific events worldwide, 23 times as invited speakers.

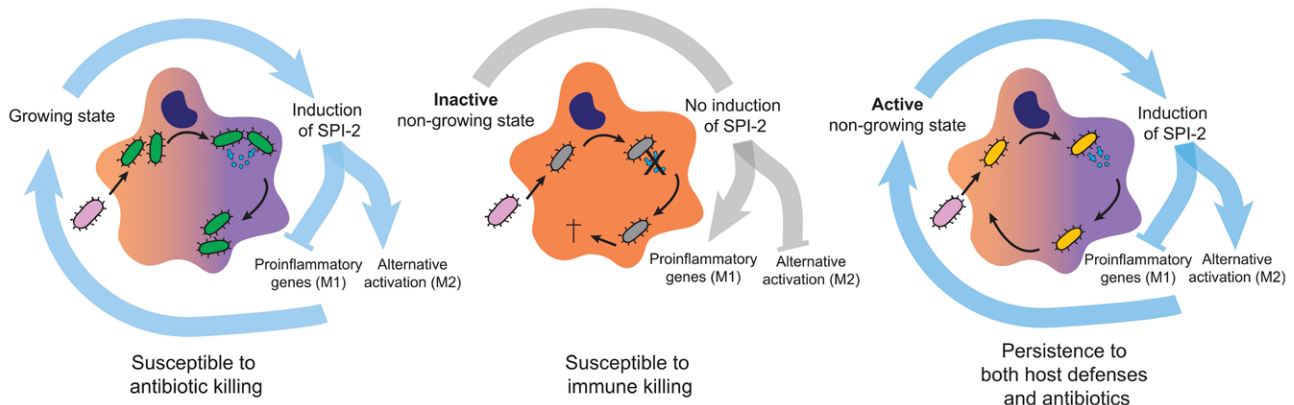


PUBLICATIONS

In 2018, HIRI scientists published 37 papers; a full 18 of them appeared in high-profile international journals. These included a research article in *Nature*, in which the heterogeneity in the antigen variation of trypanosomes was characterized with high resolution using state-of-the-art single-cell RNA sequencing approaches (co-authors: E. Saliba, J. Vogel). In a joint research article in *Science*, HIRI co-authors Saliba, Vogel and Westermann, together with the research group of Sophie Helaine of the Imperial College London, described how *Salmonella* persister stages can infiltrate the immune system despite antibiotic treatment (see image on next page).



ANNUAL REVIEW 2018



From Stapels et al., Science; 362: 1156-1160 (2018). Reprinted with permission from AAAS.

The Seed Grant projects, launched in 2017 to promote the swift publication of joint research results from HIRI, HZI, JMU, and the University Hospital of Würzburg, have already produced nine publications by the end of the one-year project period, and 12 further manuscripts are in preparation. Emmanuel Saliba published the results of his successful collaboration with Jochen Hühn (HZI) within the framework of a HIRI Seed Grant, which provides new insights into the immune system of newborns, in *Nature Communications*.

Three papers were published in the renowned journal *Molecular Cell*. The first project was also the result of a Seed Grant, this time between HIRI group leader Chase Beisel and Cynthia Sharma from JMU, who together described a new RNA-dependent CRISPR system in the pathogen *Campylobacter jejuni*. HIRI scientists Jörg Vogel and Lars Barquist identified target structures of the RNA-binding protein ProQ in *Salmonella* and *E. coli* and reported on a new mechanism of post-transcriptional regulation in enterobacteria. In the third publication, Chase Beisel showed how cell-free transcription-translation systems can be used to effectively characterize CRISPR technologies.

OUTREACH & EVENTS

HIRI has established social media presences on Twitter and LinkedIn, and has been building its community of followers. We are always keen to explain RNA and infection research to the general public. In this context, our booth at the Campus Festival of the JMU made a great contribution. Through games and small experiments, science became tangible for interested citizens.

To strengthen the team spirit, we organized the first institute outing, which took us to the Würzburg Hubland. During a guided tour, we learned about the eventful history of this district and current urban redevelopment. Afterwards we rounded off the day with pizza and conversation.



Nina Panitz & HIRI colleagues at the JMU Campus festival. © HIRI / HZI



ANNUAL REVIEW 2018



The HIRI group leaders taking a short break during the first retreat.
© Nina Panitz

During our first retreat in the Allgäu Alps, the group leaders put their heads together professionally and personally for three days. To relax, the HIRI team enjoyed hiking in front of the breathtaking natural backdrop.

On June 4th, a beautiful summer day, we celebrated our 1st birthday. We looked back on an eventful first year and introduced ourselves. We officially launched the Dr Eckernkamp Fellowship and awarded the first HIRI trophy for “Fostering the HIRI Spirit” to Nina Panitz. Among the guests at the birthday party were Dirk Heinz, Scientific Director of the HZI, Alfred Forchel, President of the JMU, and Matthias Frosch, Dean of the Medical Faculty of the JMU.



A lot has happened in 2018 and we enjoyed our first successes – to be continued in 2019!



ANNUAL REVIEW 2019

In 2019, the HIRI continued to gain momentum. With a newly recruited Helmholtz Young Investigator, we now have eight research groups making the cutting-edge science at HIRI internationally visible. Five PhD students were recruited through our graduate program “RNA & Infection”, making a total of 60 staff members from 17 nations. Renowned figures from science and culture visited the institute, and the new HIRI building embarked upon project planning and detailed design.

PERSONNEL

Mathias Munschauer (previously at the Broad Institute of MIT and Harvard, Cambridge, MA) started his new Helmholtz Young Investigators Group “LncRNA in Infections” (LRIB) on July 1st. With the affiliation of Lorenz Meinel (Chair of Pharmaceutical Technology and Biopharmacy) and Utz Fischer (Chair of Biochemistry), a total of four chair holders of the Julius-Maximilians-University of Würzburg (JMU) are now associated with the HIRI. Peter Fineran (Otago, NZ) secured a Humboldt Fellowship with the support of HIRI group leader Chase Beisel and began his visits to HIRI as guest scientist in October. At the end of the year, HIRI has eight working groups with over 60 staff from 17 nations.



HIRI's new Helmholtz Young Investigator Group “LncRNA in Infections”. From left to right: Jens Ade, Mathias Munschauer, Sabina Ganskih, Simone Werner. Image: Hilde Merkert, © HIRI / HZI

NEW BUILDING



Winner's model new HIRI building. © doranth postarchitekten GmbH

At the beginning of the year, the contract for the construction of the new HIRI building was signed with the architectural office **doranth post architekten** (Munich). This was followed by the planning of demolition and site clearance by the Staatliches Bauamt Würzburg. After the kick-off meeting in March, the planning team “new HIRI building” began its regular meetings. In July, the ground lease and permission contracts were signed. This gave the HIRI the go-ahead for the construction of the new building on the grounds of the University Hospital.

SEMINARS

Renowned international scientists enriched this year's RNA seminar as speakers. In the winter semester, Ciarán Condon (CNRS, Université de Paris, France), Peter Nielsen (University of Copenhagen, Denmark), Thorsten Stafforst (University of Tübingen, Germany), and Noam Stern-Ginossar (Weizmann Institute of Science, Israel) gave insights into their work. In the summer semester, Chris Ponting (University of Edinburgh, Scotland), and Daniel Wilson (University of Hamburg, Germany) presented their research. The following winter semester opened with a double bill of Anna Pyle (Yale University, USA; currently President of the RNA Society) and Gisela Storz (NIH, Bethesda, USA). Closing off the year, HIRI heard talks from the new CIIM director Yang Li (Hannover, Germany), Markus Landthaler (Max Delbrück Center Berlin, Germany), and Samuel Sternberg (Columbia University, New York, USA).



Full house at the opening of the RNA seminar in WS2019/2020 with Anna Pyle and Gisela Storz. Image: Tim Schnyder, © HIRI/HZI



ANNUAL REVIEW 2019

PROMOTION OF YOUNG SCIENTISTS



Excerpt from the poster announcing the HIRI Graduate Training Program.
© HIRI/HZI

As part of the first call for the HIRI “RNA & Infection” graduate program, HIRI selected two doctoral students from a large pool of applicants. These high calibre students, Sandra Gawlitt and Christophe Toussaint, completed their three internships in the research groups of their choice before choosing their supervisor and project for their doctoral thesis. In the second call in late summer 2019, HIRI recruited three successful applicants, Elise Bornet, Marco Olguin, and Sebastian Zielinski, with their lab rotations set to begin in early 2020.

HIRI is becoming increasingly involved in teaching at JMU. In May, the three-day intensive course “Infection Biology” took place for the first time. This course complements the “RNA Biology” intensive course offered in autumn. Both courses are part of the HIRI “RNA & Infection” program, and are intended to provide future scientists with a solid knowledge base in the fields of RNA and infection biology.

In the winter term 2018/19 Emmanuel Saliba started his lecture series “Single Cell Biology” at the JMU Würzburg with 24 students.

INFRASTRUCTURE

The HIRI acquired several new pieces of laboratory equipment. At the beginning of the year, the MST Nanotemper was installed to measure the interactions between molecules using fluorescence. This was followed by the Illumina Miniseq allowing HIRI research groups access to fast and efficient sequencing. Finally, a device for “medium pressure liquid chromatography” (MPLC), the chemical separation and enrichment of certain components from a mixture of substances, complemented the HIRI’s laboratory equipment.

The institute’s transportation fleet was opened with the brand new HIRI scooter, allowing HIRI staff to leave the long distances on the first floor behind them in a matter of seconds. At the end of the year, the HIRI scooter was joined by the e-bike “Matthias”. From now on, HIRI employees can reach the Hubland campus in a time and environmentally friendly way, while still doing something for their own fitness.



HIRI e-bike “Matthias” and HIRI employees getting their e-bike driving licence. © HIRI / HZI

RESEARCH FUNDING



HIRI group leader Chase Beisel obtains the first ERC grant for the institute.
Image: Mario Schmitt, ©HIRI / HZI

Within the framework of the so-called “Program-oriented Funding (POF)”, the Helmholtz Association regularly evaluates the research performance and future research plan of all its research fields and institutions. As part of the Helmholtz Centre for Infection Research (HZI), the submitted concept of the HIRI Research Field (Topic 1) was rated “outstanding”.

With his project “CRISPR Combo”, Chase Beisel received a 2 million euro ‘Consolidator Grant’ – the first ERC Grant at HIRI. This award will be used to study CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats). CRISPR are sections of repeating DNA that occur in the genomes of many bacteria and archaeae and are the basis of CRISPR



ANNUAL REVIEW 2019

technologies that have revolutionized how genetic modifications are made in different organisms. In “CRISPR Combo”, Beisel will study the natural properties of CRISPR and how these DNA elements can be exploited to better interrogate pathogens and how they affect their host.

Beisel acquired further funding of 1.8 million euros from the transnational ERA-Net (JPI-AMR) leading a group of five principal investigators from three different countries to develop CRISPR-Cas approaches against the respiratory pathogen *Klebsiella pneumoniae*, and another half a million euros from the US Agency for Defense Research Projects Development (DARPA) for new tools for monitoring and controlling technologies that can alter genetic information.

AWARDS AND POSITIONS

Jörg Vogel received one of two Feldberg Prizes 2019 in the amount of 12,500 euros for his contribution to German-British exchange in the life sciences; he gave the Feldberg-lecture at the Laboratory of Molecular Biology in Cambridge. Vogel was also elected as a member to the “Board of Directors” of the RNA Society. He was also re-elected for a further two years as Chairman of the DFG Committee on Scientific Instrumentation and Information Technology.



HIRI director Jörg Vogel. Image by Mario Schmitt, ©HIRI / HZI

Chase Beisel became a member of the Technology Development Committee of the HZI.

CONFERENCES



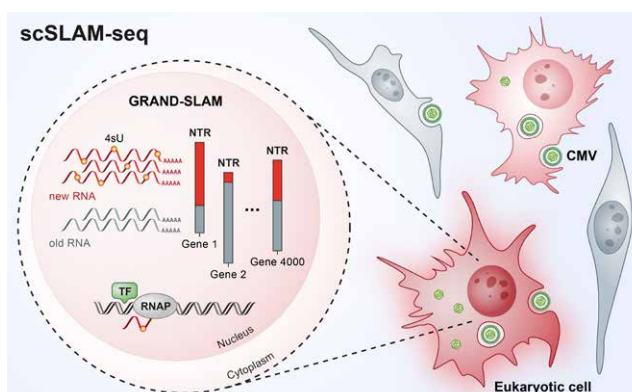
HIRI group leader Neva Caliskan during a presentation. © HIRI / HZI

HIRI group leaders presented at 58 scientific events worldwide, including 45 times as invited speakers. The HIRI organized and hosted the “International Conference on CRISPR Technologies - CRISPR 2019” and the workshop “Single-cell Biology of Infection” in Würzburg, Germany, and was involved in the organization of two other international events, the EMBO Symposium “The Non-Coding Genome” (EMBL, Heidelberg, Germany) and the conference “Cold Spring Harbor Asia Bacterial Infection and Host Defense” (Suzhou, China).

PUBLICATIONS

20 articles are published by HIRI scientist, six of which appear in particularly high-profile international journals. In *Nature*, Emmanuel Saliba and HIRI-affiliated virologist Lars Dölken (JMU) described scSLAM-seq, which for the first time enables researchers to temporally observe the synthesis of new cellular RNA in individual cells.

In *Nature Communications*, Chase Beisel and his postdoc Chunyu Liao described their newly developed technique that makes it much easier to edit multiple genes at one time with CRISPR technologies, facilitating their broad use in basic research and human therapeutics. The technique also allowed them to learn more about the bacterial defense that gave rise to these technologies.



Graphical abstract of the scSLAM-seq publication by Emmanuel Saliba and Lars Dölken in *Nature*. Figure: Sandy Pernitzsch, © HIRI / HZI



ANNUAL REVIEW 2019

EVENTS

At the HIRI New Year's reception, the challenge cup "Fostering the HIRI Spirit" was awarded to Hilde Merkert. In May, HIRI had the honour of hosting the biannual meetings of the HZI's supervisory board and scientific committee in Würzburg. Shortly after, our group leaders packed their bags and retreated for two days into the Palatinate forest.

In early July, the HIRI staff went on a culturally oriented excursion to see the German-English performance of "Black Rider" at the Mainfranken Theater in Würzburg. The annual joint summer party of IMIB, RVZ and HIRI followed on July 4th, with Otmar Wiestler, the President of the Helmholtz Association, among the guests.

Shortly before the end of the year, on November 25th, we held the first HIRI Science Slam, sponsored by the company Lexogen. The participants were coached by the winner of the science slam series "Fame Lab", Veli Uslu. From an exciting line up, the winner of the Science Slam was PhD student Anuja Kibe from Neva Caliskan's research group. Congratulations!

As always, the successful end of the year was marked by the joint Christmas party organized by HIRI and the Institute for Molecular Infection Biology (IMIB) in building D15 on December 12th.



The HIRI at the performance of "Black Rider" at the Mainfranken Theater in Würzburg. © HIRI / HZI

OUTREACH

In February, the official HIRI website www.helmholtz-hiri.de went online, replacing the preliminary website www.hiri-on-air.de. In April, Jörg Vogel spoke at the ARD Campus Talks about "How we can use the bacteria in our intestines to fight disease". At the beginning of the year, HIRI received a high-ranking visitor, State Secretary Roland Weigert (Bavarian State Ministry of Economic Affairs, Regional Development and Energy). In July, we welcomed Helmholtz President Otmar Wiestler for a personal impression of "his" institute and a bratwurst at the institute's summer party. Later in July, we had the pleasure of welcoming newly elected MdL Patrick Friedl at HIRI. Finally, in October, we were visited by the President of the District Government of Lower Franconia, Dr Eugen Ehmann, and presented our institute and our research at the "Nature Careers" fair in London.



Otmar Wiestler and Jörg Vogel at the summer party 2019. © HIRI / HZI



ANNUAL REVIEW 2019

Many thanks to everyone who helped to make 2019 a successful year for HIRI.
We are already looking forward to 2020!





ANNUAL REVIEW 2020

The corona pandemic did not spare the HIRI; it affected all areas of the institute's daily life and suddenly presented us with innumerable new challenges. However, thanks to the rapid action of our scientists, we have been able to contribute to a better understanding of the infection process of SARS-CoV-2 within a very short time span. At the HIRI, we all pulled together to counter the pandemic and to establish new routines: A number of "RNA & Infection" PhD students joined us this year, the new HIRI building is underway and scientific operations were digitized as much as possible.

DEALING WITH THE PANDEMIC

No area at the HIRI was spared from the novel corona virus. During the first wave of infections in spring, it was unclear which areas of everyday life posed risk, especially since good nose and mouth covering masks were in short supply. Many employees worked from home for weeks, whilst scientists worked in the laboratories in shifts. The relaxation of restrictions in the summer months created an illusion of normality; however, the second wave of infections has been hard-hitting and has demanded an even greater commitment from all employees.

As the year winds to an end, the world has learnt the good news that several vaccines will soon be approved, including two based on mRNA. This new hope underlines the HIRI's mission to use RNA to combat infectious diseases.



PERSONNEL



Sushila Pisano joined the science administration team in autumn 2020. © HIRI / HZI

This year the HIRI has recruited a number of scientific, technical and administrative staff. Since September, Sushila Pisano (University of Aberdeen, UK) joined the scientific coordinators working in public relations.

By the end of the year, the Institute has grown to 80 employees from 18 different countries.

NEW BUILDING

The new HIRI building became official: In March 2020, the building site was entered into the land register of the city of Würzburg. In September, the new building was included in Bavaria's high-tech agenda, considerably increasing funds as a result. The demolition of the existing building and the groundbreaking ceremony will take place in 2021.



ANNUAL REVIEW 2020

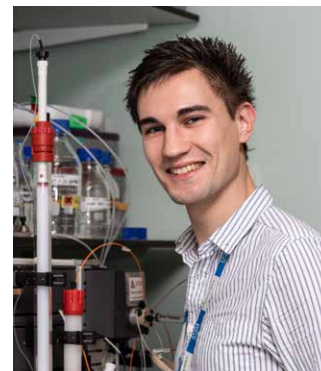
SEMINARS

Shortly before the pandemic hit in spring, Gunter Meister (University of Regensburg, Germany) and David Corey (University of Texas Southwestern Medical Center, USA) visited the HIRI to talk about their research in the RNA Seminar series. In September, Chris Hill (University of Cambridge, UK) visited the institute to share an insight into his work on the structural biology of viruses.

In order to promote scientific exchange even during the pandemic, the HIRI also participated in the RNA Collaborative Seminar Series: a joint project initiated by the RNA Society that organizes and broadcasts regular online seminars from international scientists in the field of RNA research.



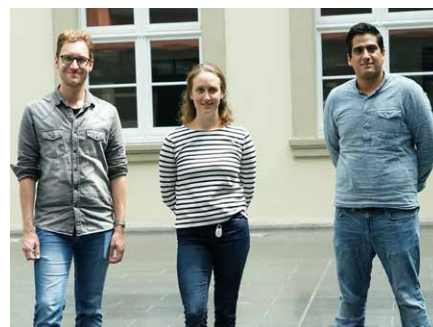
Meanwhile, the HIRI's RNA Salon entered its second phase as Neva Caliskan received confirmation from the RNA Society that the institute's RNA Seminar funding will be extended. Congratulations!



Chris Hill (Queen's College Cambridge, UK) visited the institute and presented the latest results of his work in September. © Brian Callingham, Queen's College Cambridge

PROMOTION OF YOUNG SCIENTISTS

During the spring of 2020, the HIRI graduate program welcomed three newcomers, selected last autumn, in Würzburg: Elise Bornet (École Supérieure de Biotechnologie de Strasbourg, France), Marco Olguín (Universidad Nacional Autónoma de México) and Sebastian Zielinski (Technische Universität München, Germany) began their doctoral projects in the research group of their choice after completing three laboratory rotations. The call for applications in spring 2020 resulted in the addition of two more international candidates: Adini Arifa (Wageningen University, Netherlands) and Xiangyi Wang (Imperial College London, UK) who joined the HIRI at the end of the year. In the autumn call, Taís Franco de Carvalho (Universidade Federal do Paraná, Brazil) and Hoda Kooshapur (Ludwig-Maximilians-Universität Munich, Germany) were selected for the HIRI graduate program. They will start next February.



The three new HIRI graduate students in early summer 2020. Image: Hilde Merkert, © HIRI / HZI

In parallel, the HIRI Research Career Development Fellowships were created to support exceptional postdoctoral candidates in the structured development of their individual research identity. This new funding scheme is particularly aimed at supporting young female scientists in a transitional phase such as starting a family, thus enabling them to pursue a career as research group leaders.

INFRASTRUCTURE



HIRI can call the Leica Thunder 3D microscope its own. Image: Hilde Merkert, © HIRI / HZI

In 2020, the HIRI added new state-of-the-art equipment to its inventory. At the beginning of the year, for example, the Leica Thunder microscope was purchased. This imaging system enables the acquisition of sharp images of three-dimensional specimens – in real time. In order to get started with SARS-CoV-2 research, the S3 laboratory was substantially upgraded in April. The HIRI also acquired a NovoCyte Quanteon (Agilent Technologies), a highly advanced and precise flow cytometer. A new anaerobic workbench increased the capacity for working with organisms under oxygen-deficient or oxygen-free conditions.



ANNUAL REVIEW 2020

In November, the cell dispenser b.sight from Cytena also arrived at the HIRI labs. It is capable of separating individual bacterial cells and is therefore unique on the market. A further special feature, high-resolution photo documentation, can be used to subsequently verify whether the cells have indeed been separated. The I-DOT combined with the b.sight dispenser doses liquids contact-free in the nanoliter range. It is used to further process the cells separated by the b.sight. Thus, the HIRI further optimized its workflow in the field of single-cell analysis.

At the end of the year, the 10x Chromium Controller complemented the equipment in the S3 laboratory. With its help, single-cell analysis has made its way to biosafety level 3 at the HIRI.

RESEARCH FUNDING

Neva Caliskan received a Starting Grant from the European Research Council (ERC) in September. The ERC Starting Grants are specifically designed to enable young scientists to advance their careers as top independent researchers. The prestigious grant is endowed with 1.5 million euros over a period of five years. With her project “T-FRAME”, she is investigating the question of how so-called frame shifting is regulated in eukaryotic cells during viral infections.



HIRI Junior Professor Neva Caliskan received an ERC Starting Grant. Image: Hilde Merkert, © HIRI / HZI

HIRI group leader Chase Beisel was doubly successful this year: His idea to use the CRISPR/Cas genetic scissors for a groundbreaking diagnostic platform has earned him initial funding from the BMBF's GO-Bio program as well as the Bavarian Medical Valley Award. The funding is enabling him to perform proof of concept work in the laboratory. In addition, market and patent analyses were commissioned to actively promote the first HIRI spin-off.

Furthermore, the joint project Rbiotics of Lars Barquist and Jörg Vogel, together with Franziska Faber (Institute for Molecular Infection Biology, JMU), to develop new strategies against multi-resistant pathogens using digital networking is underway. This project is being funded with a total of 1.4 million euros within the Bavarian research network bayresq.net, of the Bavarian State Ministry of Science and the Arts (STMWK).

AWARDS AND POSITIONS



EMBO Young Investigator and HIRI group leader Antoine-Emmanuel Saliba. Image: Mario Schmitt, ©HIRI / HZI

Emmanuel Saliba was selected as EMBO Young Investigator in December, making him one of 30 to be included in the Excellence Program this year. EMBO Young Investigators receive financial support of 45,000 euros over four years. In addition, as a member of the program, he has access to a wide range of mentoring and networking schemes to support him in this phase of his career.



ANNUAL REVIEW 2020

CONFERENCES

Emmanuel Saliba organized the virtual workshop “Temporal Single Cell Analysis” on September 15th as part of the Single Cell Omics Germany (SCOG) initiative.

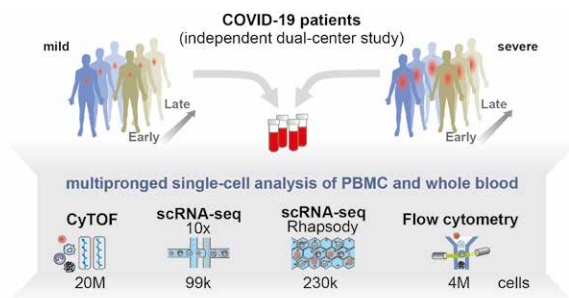


The joint conference of the French, German, Swedish and British academies of science “Microbiology 2020”, initially planned for 2020, was postponed until next year due to the pandemic, as are all other events planned for this year at the HIRI. Most symposia were cancelled or converted into digital formats. Nevertheless, HIRI group leaders presented their work and the institute at a total of 13 events, 11 of them as invited speakers.

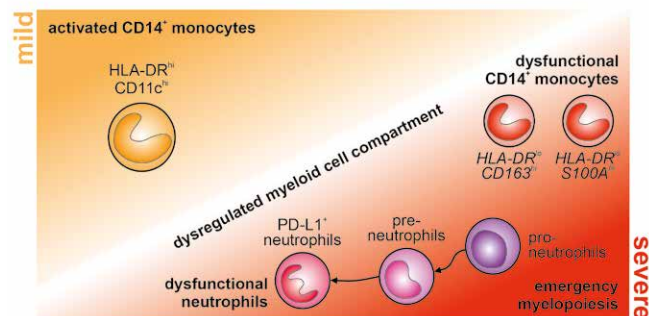
PUBLICATIONS

The HIRI published 42 publications in 2020, 17 in high-impact journals.

In a joint publication in *Nature Microbiology*, Jörg Vogel and Emmanuel Saliba provided novel insights into the RNA world of individual bacteria. The newly developed method of bacterial single cell RNA-seq can measure gene activity in individual bacterial cells and thus contribute to our understanding of the development of antibiotic resistance.



The Saliba lab also played a major role in a nationwide study on the course of disease in COVID-19 patients, which was published in *Cell* in September. With the help of single-cell RNA-seq and other techniques, it was discovered that neutrophils can contribute to a severe course of COVID-19.



Graphical abstract of the publication in *Cell*. Reprinted from: *Cell* 182 (6): 1419–1440, Schulte-Schrepping J, ..., Saliba AE, Sander LE, Severe COVID-19 is marked by a dysregulated myeloid cell compartment, © 2020 Elsevier Inc., with permission from Elsevier.

In the July issue of *Nature Communications*, Lars Barquist, Alexander Westermann and Jörg Vogel delivered new insights into the biology and host-pathogen interactions of *Orientia tsutsugamushi*, the causative agent of Japanese river fever. They achieved this by combining dual RNA-seq, comparative genomics and proteomics with machine learning. This approach offers the possibility to characterize comprehensively those pathogens that had remained largely unstudied in the past.

Furthermore, Chase Beisel and his team published their work in *Science Advances*, which describes the detection of new PAM sequences that can be used to improve the precision of CRISPR genome editing technologies.



ANNUAL REVIEW 2020

OUTREACH & EVENTS



Lively crowd at the opening of HIRI meets Alkymi Materialbar. Image: Hilde Merkert, © HIRI / HZI

On February 18th, we organized the HIRI meets Alkymi Materialbar exhibition. The HIRI supported the information design students Anastasia Meid and Magdalena Skala (Alkymi Materialbar) of the University of Applied Sciences Würzburg Schweinfurt in the realization of their biodesign project. For this project, the designers aimed to combine environmentally friendly textile dyeing with a possible medical application.

This year we were delighted to welcome a series of guests from the world of politics, despite the pandemic. In February, Dr Robert Geiger and Dr Sabine Jarothé from the Bavarian State Ministry of Economic Affairs visited us. On April 29th, we hosted Bernd Sibler, the Bavarian State Minister of Science and Art (STMWK), to discuss the effects of the corona pandemic and how to best mitigate the impact of infectious diseases in the future. In summer, Dorothee

Bär, Minister of State for Digital Affairs at the Federal Chancellery, made a short visit to inquire about the progress of the new HIRI building. With Christian Schuchardt, Lord Mayor of Würzburg, and Barbara Stamm, former President of the Bavarian Parliament, we hosted two important HIRI sponsors in September. Last but not least, in November we had a rendezvous with the newly elected President of the Julius-Maximilians-Universität of Würzburg, Prof. Paul Pauli.



High visit at HIRI. Christian Schuchardt (OB Würzburg), Alice Hohn (HIRI head of administration), Barbara Stamm (former president of the Bavarian parliament) and Jörg Vogel (HIRI director). Image: Tim Schnyder, © HIRI / HZI



Dorothee Bär (center), Minister of State for Digital Affairs in the Federal Chancellery, also makes a short visit to the HIRI. Pictured here together with Jörg Vogel (left) and Alice Hohn (right). Image: Tim Schnyder, © HIRI / HZI

With the groundbreaking for the new HIRI building and the RNA-based SARS-CoV-2 vaccine approaching, we are looking forward to a promising 2021!

Institution of

HZI **HELMHOLTZ**
Centre for Infection Research

In cooperation with

