3rd Annual Conference of the German Stem Cell Network 2015 from 9 - 11 September 2015

Stem cells, mini organs and translation

In September it was that time again: 400 scientists from all over Germany met for an intensive three-day meeting in Frankfurt am Main. 2015 was the third edition of the GSCN conference, which already has a strong tradition. But tradition is no barrier to progress in this young field of research and young network. A new development in the conference format, the central presidential symposium with presentations by the GSCN prize winners, was very well received by participants. Another positive development is the growing number of exhibiting companies – 25 firms showcased themselves with booths and lectures. The network is growing not only in numbers but also in significance.

For three days, more than 400 German and international researchers discussed all aspects of stem cells in poster sessions, after presentations or while networking during the breaks and evening events. The GSCN conference took place in a very attractive environment: the newly built Otto-Stern- Center has large auditoriums, a foyer for exhibitors and catering filled with natural daylight, and a sunny terrace.


Paul Riley

The conference got off to a vigorous start on Wednesday with opening addresses from Enrico Schleiff, Vice Chancellor of Goethe University Frankfurt, and GSCN President Thomas Braun as the patron. Paul Riley (University of Oxford, U.K.) opened the scientific program with a keynote lecture in which he presented new findings from his lab on epicardium activation using Thymosin ß4. Riley's team has found that Thymosin ß4 interacts with a chromatin remodeling complex to express the Wilms' tumor gene (Wt1), which also plays an important role in epithelial-mesenchymal transition of the epicardium. Moreover, a long antisense oriented non-coding RNA produced by the Wt1 locus appears to play an important role in maintaining Wt1 expression. These processes are central to the epigenetic reprogramming of epicardium-derived cells and could lead to new approaches to treating heart disease. Hans-Willem Snoeck, from Columbia University in New York, reported in the second keynote presentation about his recent progress in modeling the developing human lung in a Petri dish using iPS cells. He presented highly convincing data on the specific differentiation of human pluripotent stem cells into foregut endoderm cells and especially into distal lung cells. Snoek showed that the sequential application of defined cytokines and low molecular weight compounds that activate or inhibit signaling pathways results in robust differentiation protocols. His work is a good example of the translation of knowledge from the basic principles of developmental biology in mice to the selective differentiation of human pluripotent stem cells. It shows that complex multi-stage organ development can be imitated in a Petri dish.


Hans Willem Snoek

The scientific sessions

One characteristic feature of the GCSN conferences is their function as a platform for young up-and-coming scientists, in particular, to present their latest findings. The best papers were selected for ten parallel sessions. The conference program therefore reflects current issues in stem-cell research, including nuclease-based techniques such as TALENs and CRISPR/Cas, which are precise new genome

Photos: GSCN

editing tools that can effect highly accurate changes in the genome. The development of stem cells as disease models in cell culture – including organoids (three-dimensional mini-organs in a culture) – also played an important role. Reprogramming and transdifferentiation of body cells, particularly neural cells, were also themes of the third annual conference. The whole conference program included 42 presentations selected from 180 submitted abstracts, including seven papers in the strategic working group sessions and nine presentations by partner companies. "The program is incredibly exciting and packed," GSCN President Braun enthused. "The quality and scientific level are very high. I get the impression that year on year we go deeper into the subject."

"An exciting and packed program"

These were some of the key highlights from the presentations: In the "Stem cells in disease modeling and drug development" session, Sina Bartfeld (Hubrecht Institute, Utrecht, now at the Research Center for Infectious Diseases [ZINF] in Würzburg) gave a paper on organoids from adult stomach stem cells and their use in infection biology. Stem cells can be obtained from patient tissue samples, and can grow in vitro into small three-dimensional structures, or organoids, which can be (apparently unlimitedly) expanded in culture. Human stomach organoids infected with the stomach pathogen Helicobacter pylori showed a strong inflammatory response. The strength of this response depends on the cellular composition of the organoids. Organoids from tumor tissue can also be used in drug testing. In the session on hematopoietic stem cells, Nicole Mende of TU Dresden showed that the fitness of human blood stem cells (HSCs) depends on the length of the G1 phase of the cell cycle. She demonstrated that specifically shortening the early G1 phase transit in human HSCs made it possible for the blood stem cells to produce a greater number of mature blood cells over a prolonged period, after transplantation into a suitable mouse model. It is conceivable that in future, stem cell function can be improved in the human body by accelerating the cell cycle transit. Lina Jankauskaite (UGMLC, Gießen) reported in the session "Stem cell in regenerative therapies: Mesenchymal stem/stroma cells" on the use of MSCs as a putative therapy for influenza-virus induced pneumonia. In a murine model of influenca virus infection intratracheal therapy with bone marrow-derived stromal cells (BMSC) was shown to reduce virus-induced injury of alveolar epithelial cells (AECs) and to increase virus clearance. Mechanistically, BMSCs reduced AEC apoptosis by secretion of stanniocalcin-1 in vitro corresponding to improved regeneration of damaged AECs in vivo.

One novelty and highlight of the GSCN conference was the presidential symposium, at which the GSCN awards, inaugurated just last year, were presented and the winners gave lectures. To kick off the symposium, GSCN Founding President Oliver Brüstle gave a lecture entitled "Evolving stem cell-based strategies for targeting neurological disorders." He introduced new strategies for using patient-specific stem cells in researching and treating neurological diseases. His team used neurogenic and gliogenic stem cells, which are derived from induced pluripotent stem cells (iPS cells) or obtained by direct conversion from blood cells. Such stable intermediates allow highly standardized modeling of earlier pathogenic processes, such as protein aggregation in polyglutamine diseases and the preparation of patient-specific donor cells, including cell-based enzyme substitution in lysosomal storage diseases. Julia Ladewig of the Institute of Reconstructive Neurobiology in Bonn, and winner of the GSCN Young Investigator Award 2015, presented her latest data on the human in vitro development of neural stem cells in comparison to neural stem cells in vivo. The study describes a matrix for examining the relationships between cell types derived from pluripotent stem cells and comparable native cell types. Ladewig also presented recent data on the production and standardization of self-organizing cortical organoids. This latest technology is particularly relevant when the complex cellular interactions that occur in human tissue are examined in the cell culture.

"I am delighted to accept the GSCN Award, because it is important for us junior research group leaders to receive public recognition for our scientific achievements early on in our careers. For me, the GSCN Young Investigator Award is a great signal that encourages me to increase my scientific efforts and shows me that I am on the right track," Ladewig enthused.

Magdalena Götz was also visibly delighted with her GSCN Female Scientist Award: "I feel very honored and am truly thrilled with the GSCN Award." In the lecture she gave after accepting the award, Götz presented new, groundbreaking data, showing that the efficiency of directly reprogramming fibroblasts and glial cells in vitro into neurons by neurogenic transcription factors depends largely on a successful transition from predominantly glycolytic to oxidative metabolism. Glial cells and fi-

Photos: GSCN

broblasts which fail to make this transition during a critical phase in the reprogramming process undergo cell death mediated by reactive oxygen species (ROS), which is referred to as ferroptosis. In contrast, reducing the formation of ROS and overexpression of Bcl2 promotes reprogramming. The enormous significance of these findings is emphasized by the fact that, as Götz showed, overexpression of Bcl2 also significantly promotes neuronal reprogramming of glial cells in the injured neocortex.

The GSCN Publication of the Year 2015 Award went to Jijang Wang, a doctoral candidate in the Mobile DNA research group and his group leader Zsuzsanna Izsvák of the Max Delbrück Center for Molecular Medicine (MDC) in Berlin-Buch, with their publication "Primate-specific endogenous retrovirus driven transcription defines naïve-like stem cells" (Wang, J. et al, 2014, Nature, doi:10.1038/nature13804). They were able to demonstrate new ways of identifying naïve, and thus original human embryonic, stem cells. "I am deeply honored and touched to receive this award. I am very grateful that the German stem cell community has selected our publication as the best of the year," Wang said on receiving the award. Group leader Izsvák was equally delighted. "My lab is working with repetitive, genetically identifiable but replaceable elements. This means that we are naturally asking different questions from the ones a 'typical' stem researcher poses. As newcomers, we are particularly proud that we could contribute something fundamentally new to the field of stem cell research. It was a wonderful journey with great colleagues. In a nutshell, we have determined how remnants of an ancient retrovirus family, which on first sight look like typical junk DNA, have taken on a new cellular function to regulate real pluripotency in human cells."

Daniel Besser, Managing Director of the GSCN, was very pleased with the success of the redesigned conference program. "The presentations were exciting and it is great that the presidential symposium is now a key element of the program for all participants," he said. The majority of the conference participants agreed, and in an online survey gave very positive assessments of the program and the structure and quality of the presentations.

The two poster sessions generated a great deal of interest and were particularly well attended. Intense discussions took place around many of the posters. The poster prizes, provided by GSCN member company Peprotech, were awarded to the following:

- Chiara Cencioni (Goethe University Frankfurt): "Nitric oxide synthesis and Zeb1 transcription factor inactivation characterize very early mesendoderm precursors in mouse embryonic stem cells"
- Nico Lachmann (Hannover Medical School): "Pulmonary macrophage transplantation employing HSC- or iPSC-derived cells as an innovative gene therapy approach in pulmonary alveolar proteinosis"

Photos : GSCN

Leibniz Institute on Aging - Fritz Lipmann Institute (FLI)

Research for better aging

The Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) has dedicated to biomedical aging research since 2004. More than 330 members from over 30 nations explore the molecular mechanisms underlying aging processes and age-associated diseases. It is one of only two national research institutes on basic mechanisms of aging in Germany.
The main aim of research at FLI is to delineate how aging leads to the development of tissue dysfunction and diseases in the elderly. If the understanding of the aging process contributes to the extension of healthy lifespan, the strains on society can be minimized and the society's future development will be enriched by the wealth of knowledge and experience older people possess.
As one of 89 institutes of the Leibniz Association, the FLI is publically funded by the German Federal Ministry of Education and Research (BMBF) and the State of Thuringia.

Leibniz Institute on Aging – Fritz Lipmann Institute (FLI)
Beutenbergstraße 11, 07745 Jena
www.leibniz-fli.de

- Krishna Moorthy Sreenivasan (Max Planck Institute, Bad Nauheim): "A high-throughput RNAi screen identifies chromatin modifiers regulation muscle stem cell self-renewal and differentiation"
- Ting Zhang (Max Planck Institute, Bad Nauheim): "Epigenetic control of muscle progenitor and adult stem cell homeostasis"

The scientific program of the conference concluded with a joint session with the LOEWE Center for Cell and Gene Therapy Frankfurt (CGT) and two more keynote lectures. Andras Nagy of the Lunenfeld-Tanenbaum Research Institute in Canada presented his latest results in the presentation on "Pluripotency in the artificial cell space." He presented an inducible reprogramming system that has been successfully used to define intermediate molecular genetic stages during the somatic cell reprogramming process. This made it possible to characterize a new (F-iPS) subtype of iPS cells that are fundamentally different from the fully reprogrammed iPS cell in terms of genetics, epigenetics and phenotype. Unlike the fully reprogrammed iPS cells, F-iPS cells can be produced on an industrial scale because of their great potential for self-renewal. They can then be differentiated according to the respective end cells required for use in regenerative medicine. Since Lorenz Studer was unfortunately unwell, Andreas Trumpp of the German Cancer Research Center in Heidelberg stepped in at short notice as the fourth keynote speaker. He opened his presentation on "Stem cell dormancy and MYC" with an overview of the molecular and cellular basis of self-renewal and differentiation in hematopoietic stem cells (HSCs) and their interaction with stem cell niches. He then presented the new data supporting the concept of reversible dormancy (inactive sleep-like state) in HSCs during homeostasis and under stress, based on whole genome transcriptome analysis on the single cell level. These investigations and detailed functional analysis revealed that the oncogene MYC plays a key role in controlling the initiation and cessation of dormancy in HSCs and embryonic stem cells. Finally, he presented exciting data indicating that deactivating the MYC oncogene in pluripotent epiblast cells in the embryo before implantation in the uterus initiates what is known as the diapause state. Diapause is a temporary resting state that is the embryo's response to signals from the immediate environment (e.g. during breastfeeding). This restricts all metabolic activity and protein production in the embryo, while the network for maintaining pluripotency remains highly active. It may also be possible to evoke this situation in inactive metastatic cells. Trumpp pointed out that the MYC reactivation in such cells (for example, in cases of inflammation) could lead to the onset of metastatic growth, often years after apparently successful chemotherapy.

„It was a wonderful journey with great colleagues"

The CGT organized excellent presentations in the final session:

- Gergana Dobreva, Max Planck Institute for Heart and Lung Research, Bad Nauheim: "Regulation of second heart field progenitor cells: discovering key molecular players"
- Johnny Kim, Max Planck Institute for Heart and Lung Research, Bad Nauheim: "Functional systems analysis of the adult muscle stem cell identifies crucial regulators of muscle regeneration"
- Michael Rieger, Goethe University and LOEWE CGT Frankfurt: "Hematopoietic stem cell fate decision control at single cell resolution"
- Zoltán Ivics, Paul Ehrlich Institute, Langen: "The Sleeping Beauty transposon system for genetic engineering in stem cells"

Spontaneous meet-the-expert tables

Always on the lookout for improvements and innovations, at this year's conference some professors on the GSCN Extended Board spontaneously decided to offer a number of meet-the-expert tables, where participants could talk directly to principal investigators. A lively lunchtime discussion culture developed, and some conference participants used the opportunity to discuss their research and scientific issues directly and informally with Andreas Trumpp, Claudia Waskow, Hartmut Geiger and Hans Schöler. "This was a very interesting and lively encounter," Claudia Waskow said. Meet-the-expert tables with Sebastian Diecke and Ralf Kühn had been planned in advance by the technologies working group. They joined the wider debate and discussed burning questions relating to the genome editing techniques CRISPR/Cas9 and TALENs. "That was an exciting workshop, and I was pleased to see how many questions were thrown at us," said Diecke (Max Delbrück Center for Molecular Medicine).

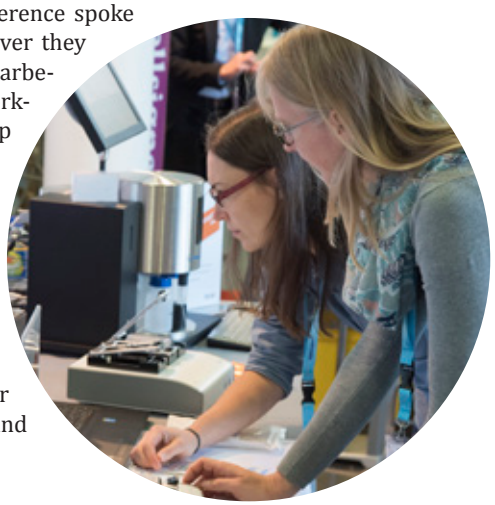
Poster awardees

Photos : GSCN

The drop-in booth was another format in the conference program that generated absorbing direct Q&A sessions. Egbert Flory (Paul Ehrlich Institute) and Natalie Mount (Cell Therapy Catapult, U.K.) briefed participants on regulation, translation and clinical trials. The theme of translation pervaded many discussions and presentations. Last but not least, the workshop of the strategic working group on public outreach, with Ira Herrmann and Tobias Cantz, confronted the conference participants with citations from websites offering unverified stem cell therapies. The participants were asked to deal with the citations and to evaluate the content. This was not an easy task, but the workshop reached its goal: on the terrace there were lively discussions about clinical trials, translation, dealing with patients' expectations, and the gap between hopes and promises.

New stem cell genome editing techniques, clinical trials, translation, regulatory issues and career development in science and science-related professions were other topics at the strategic working group sessions. The GSCN conference in Frankfurt, like its predecessors, was evaluated very positively in the online surveys of participants and exhibiting companies. It was suggested, however, that the GSCN should do even more to increase collaboration between basic researchers and the clinicians who ultimately use the applications on their patients.

"Good networks need good parties – and we know how to celebrate," said new GSCN President Ulrich Martin (Hannover Medical School). On the networking evening, the scientific community rode in open-top buses through downtown Frankfurt to the Westend campus. A stroll past the colorfully lit lake and old university buildings took the scientists into the grand wood-paneled banqueting hall where they enjoyed an evening of food, chats and dancing in a relaxed atmosphere. The evening celebrations and gatherings at the conference spoke for themselves. Wherever they were, at the summery barbecue or the GSCN Networking Evening, dressed up in the photo booth, at the sumptuous buffet, or bopping away on the dance floor, the stem cell researchers showed that they know how to party, thereby laying excellent foundations for personal exchange and collaboration.



Podium discussion for the Frankfurt public

The conference concluded with a public event entitled "Modern cell therapies – stem cells in the fight against heart attacks and blood cancer." New German Stem Cell Network films were shown on the Westend campus, and the interested public had the opportunity to take part in a discussion with Andreas Zeiher and Hubert Serve (both of Frankfurt University Hospital and LOEWE CGT), and Thomas Braun. To a full house, Stefanie Seltmann (German Cancer Research Center, Heidelberg) moderated a lively podium discussion about the heart's capacity for regeneration and the potential clinical use of cell therapies. The GSCN films about the potential application of cell therapies present Andreas Zeiher's and Hubert Serve's cardiology and leukemia research, and are available in German and English on the GSCN website.

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GermanStemCellNetwork

4th Annual GSCN Conference

12 – 14 September 2016

Hannover Medical School (MHH)

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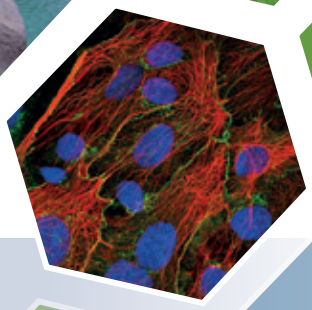


International keynote speakers

Peter Coffey (London) · Alexander Meissner (Cambridge) · Sean Morrison (Dallas) · Hiroshi Nagashima (Tokyo) · Peter Zandstra (Toronto)

Presidential Symposium

Thomas Eschenhagen (Hamburg), GSCN Awardees: Young Investigator, Female Scientist, Publication of the Year

Abstract submission deadline for oral presentations: 31 May 2016
Oral presentations chosen from the best abstracts

Scientific sessions

- Pluripotency and reprograming
- Somatic stem cells and development
- Tissue engineering and organoids
- Hematopoietic stem cells
- Stem cells in development
- Stem cells in diseases: cancer stem cells
- Stem cells in regenerative therapies
- Stem cells in disease modeling and drug development
- Computational stem cell biology and systems biology
- Stems cells and ageing, genome stability and epigenetics
- Genome engineering and gene therapy

Program committee
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