

Conference Report 2017

5th GSCN Annual Conference

11 – 13 September 2017

Friedrich-Schiller-University Jena

Right in the middle of stem cell research

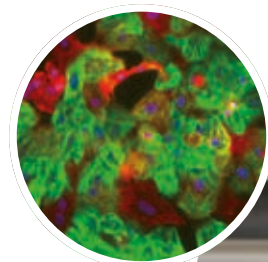
For a few days in September, everything in the city of Jena, which is located in the middle of Germany, revolved around stem cells: scientists from all corners of Germany and from some far-flown parts of the world travelled to the 5th GSCN Annual Conference in Jena to gather and exchange information about the very latest findings in the field of stem cell research. In its fifth year, the annual meeting of German stem cell researchers focused on the topics of stem cells and ageing and single cell technology. Over 350 scientists came together for three days to present their new data in lectures and poster sessions, establish new collaborative ventures, and decide on the submission of joint applications. The main focus of the conference is networking – and this is what happens before and after the sessions, during meals, and at the various parties. Networks exist not only between the scientists but also with various other partners, for example industry, which, with 26 stands, assumed an important place in the fabric of the conference.

» Stem cell research grows as the life's circles in Rilke's famous poem.«

SOURCE: WOLFGANG TIEFENSEE

Political presence

Walter Rosenthal, President of the Friedrich Schiller University Jena and an old friend of the GSCN (he gave the opening address at the founding conference in 2013 in Berlin, where he was based at the Max Delbrück Center for Molecular Medicine (MDC), and was closely involved in the establishment of the GSCN), presented the opening address at the 5th annual GSCN conference in Jena. In his welcoming address, Thuringia's Minister of Science, Wolfgang Tiefensee expressed his pleasure at the number of researchers who had travelled to Jena for the conference and demonstrated his familiarity with stem cell research – and, moreover, with poetry by quoting Rainer Maria Rilke's poem "I live my life in ever widening circles". Daniele Barthel from the Leibniz Institute on Aging – Fritz-Lipmann Institute (FLI) also extended a warm welcome to the participants and focused on the main theme of the conference – aging processes in stem cells.



Industry exhibitors
26

International Key Note Lectures
4

National Highlight Talks
4

Sessions
13

Meet-the-Expert-Tables
6

Poster
142

300
Germany

18
International

25
Europe

Extras

- Network Evening at the Volksbad Jena
- GSCN-Get Together
- Member Meeting
- PluriCore Meeting
- Non PI Workshop
- Boardmeetings

343
CONFERENCE PARTICIPANTS

32 % Students

68 % Regular

JENA
Friedrich-Schiller-University Jena

GSCN Awards
3

» Excellent Key Note Speaker«

SOURCE: GSCN ONLINE UMFRAGE

Results of the Conference Online Survey 2017

How do you rate...

Scale: 5 (excellent) to 1 (unsatisfactory)

the industry exhibition
4,02

the Meet-the-Expert-Tables
4,00

the Presidential Symposium
4,38

the network evening
4,60

the scientific program
3,65

the organisation of the conference
4,13

the industry session
3,78

the GSCN Get-together
4,13

» It is very positive, that there is an active stem cell community and that networking is made possible in a relaxed atmosphere with a adequate number of conference participants.«

SOURCE: GSCN ONLINE UMFRAGE

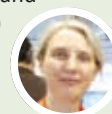
Public Event

Panel discussion with scientists and videos about

"Modern cell therapies – Stem cells at ageing, cancer and organoids"



with Florian Heidel (Jena), Jürgen Knoblich (Vienna), Andreas Trumpp (Heidelberg) and Claudia Waskow (Dresden)



Conference Report 2017

The keynotes: Set the stage for the discussions

The international keynotes at the GSCN conference were once again scientific highlights at the GSCN conference. The conference was kicked-off by a presentation from **Elaine Fuchs**, one of the pioneers in the biology of tissue stem cells, from Rockefeller University, New York, where she studies the stem cells of the skin and how they generate epidermis and hair follicles. She often has used the murine hair follicle, as it is an excellent model system to understand how stem cells remain quiescent during times of minimal wear and tear, how these cells become mobilized during the cyclical bouts of hair growth and wound-repair, and how the normal process of stem cell activation goes awry in cancer. The abundance of skin stem cells has also made it possible for her team to landscape the in vivo chromatin, transcriptional and translational dynamics that these stem cells undergo. In her keynote lecture, she presented her latest research on these dynamics. Of particular interest are the group's recent discovery that during wound repair, stem cells enter a transient state of plasticity, which they refer to as "lineage infidelity," where they acquire dual characteristics of hair follicle and epidermal stem cells. In malignancy, this state also appears, but becomes permanent, due to the high levels of activated RAS/MAPK, which superactivates a key transcription factor involved. Of additional intrigue was the group's study on inflammation, where they uncovered an epigenetic memory within inflammation-experienced skin stem cells that can persist for months after the inflammation has resolved. Previously thought to be exclusive to immune cells, the memory, detectable at the chromatin level within the epidermal stem cells, endowed a faster epidermal response upon the next inflammatory assault. This new work sheds light as to why, in a number of human disorders inflammation tends to recur in the same spots as previously.



Jena Somatic stem cells and development

Keynotes

Juniors

Industry
sessionPatient information
(stem cell therapies)

Henri Jasper reported in his lecture on the opening day of the conference on novel studies in his group focused on stem cell maintenance in aging. Working in the intestine of the fly *Drosophila melanogaster* and in the tracheal epithelium of the mouse, they show that the nutrient-sensing TSC/Tor signaling pathway plays critical roles during stem cell activation, but that repeated activation of Tor can lead to stem cell differentiation and thus exhaustion of the regenerative potential of the tissue. Previous work of the group had shown that in fly intestinal stem cells (ISCs) Tor activity is suppressed by the TSC1/2 complex in homeostatic conditions to ensure ISC maintenance. The new study shows that Tor becomes transiently activated during ISC activation to allow rapid entry into the mitotic cell cycle. That activation, however, increases the potential for stem cells to differentiate, and repeated rounds of damage thus lead to the loss of ISCs. The group observes a similar mechanism in the tracheal epithelium of mice, and find, consistently, that age-related stem cell loss in the mouse trachea can be prevented by pharmacologic inhibition of mammalian target of rapamycin complex 1 (mTORC1) signaling. These findings highlight an evolutionarily conserved role of Tor signaling in stem cell function and identify repeated rounds of mTORC1 activation as a driver of age-related stem cell decline.



» The international key notes
at the GSCN conference
are very inspiring
scientific highlights.«

SOURCE: ONLINE UMFRAGE

Basic, translational, applied hematopoiesis

Stem cells in disease modeling and drug development

Career development
Computational
stem cell biologyFunding
programs
and policies

Clinical trials and regulatory affairs

Ethical, legal and social aspects

Network

Stem cell
technologies

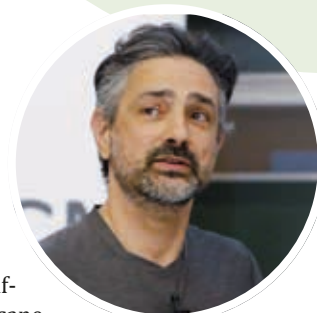
Pluripotency and re-programing

Stem cells
in regenerative
therapiesPublic engagement and
outreach activitiesStem cells in diseases
(cancer stem cells)

On the final conference day (Wednesday, 11 Sept. 2017) **Maike Sander** from the University of California in San Diego described recent findings in which her laboratory utilized a stepwise differentiation platform of human embryonic stem cells into pancreatic beta cells to identify mechanisms of beta cell differentiation and disease risk for type 2 diabetes. Her group generated comprehensive maps of chromatin state and transcription factor binding throughout the differentiation time course. Analysis of these maps revealed chromatin states and chromatin regulators that define signal responsiveness of developmental intermediates. They identified the histone demethylase LSD1 as a critical epigenetic regulator of receptiveness to retinoic acid signaling. The work helps explain why cells interpret signaling factors in a context-dependent manner. Dr. Sander further described how intersection of these chromatin maps with risk variants for type 2 diabetes led to the identification of a set of variants that regulate transcription of developmental genes, suggesting that misregulation of developmental processes contribute to type 2 diabetes risk.



In Jena one keynote speaker regrettably had to cancel – **Peggy Goodall** was occupied with supporting her lab in Houston, Texas after the big flooding following Hurricane Harvey (end of August 2017). This gave two upcoming young scientists in Germany the possibility to present their data. In the closing session **Yechiel Elkabetz** (MPI for Molecular Genetics, Berlin, picture) talked about "Meaningful modeling of cortical development and microcephaly in rosettes and organoids derived by combined pathway inhibition" and **Boris Greber** (MPI for molecular Biomedicine, Münster) presented his talk entitled: "EOMES is a context-dependent master regulator of cardiac induction in human ES cells". It was already the second time after Hannover 2016 that Boris saved the day by presenting novel data from his research replacing a keynote session. The session was completed with presentations from two Jena based scientists **Florian Heidel** (FLI Jena/University Jena) with his talk titled: "Maintenance of Jak-inhibitor treated MPN depends on cold shock protein Ybx1" and **Julia v. Maltzahn** (FLI, Jena) on "Functional relevance of Klotho for maintenance and regeneration of skeletal muscle".



Conference Report 2017

The Presidential Symposium: GSCN presidents invite and the annual GSCN Awards

Since the GSCN Annual Conference in Frankfurt 2015 the presidential symposium is a fixture of the GSCN conferences. The presidential symposium with the president invite and the award winners of the 2017 GSCN awards took place on the second conference day. In the lecture of the presidents invite **Jürgen Knoblich** presented novel finding in his laboratory on cerebral organoids. Human brain development involves complex interactions between different regions, including long-distance neuronal migration or formation of major axonal tracts. Different brain regions can be cultured in vitro within 3D cerebral organoids, but the random arrangement of regional identities limits the reliable analysis of complex phenotypes. In his lecture, he described a coculture method combining brain regions of choice within one organoid tissue. By fusing organoids of dorsal and ventral forebrain identities, his lab generates a dorsal-ventral axis. Using fluorescent reporters, they demonstrate CXCR4-dependent GABAergic interneuron migration from ventral to dorsal forebrain and describe methodology for time-lapse imaging of human interneuron migration. The results demonstrate that cerebral organoid fusion cultures can model complex interactions between different brain regions. Combined with reprogramming technology, fusions should offer researchers the possibility to analyze complex neurodevelopmental defects using cells from neurological disease patients and to test potential therapeutic compounds.



The Female Scientist of the Year Award in 2017 went to **Elly Tanaka** who had recently in 2016 moved from the CRTD in Dresden to the IMP in Vienna. In her award lecture, Elly Tanaka talked about her studies of the molecular program driving limb regeneration in the axolotl. Through expression cloning, biochemical, and other screening approaches, she has identified several extracellular factors that are necessary and sufficient for induction of cell migration, and the initiation of cell proliferation after limb amputation. In the second part of her talk, she described their recent success in assembling the 32 Gbp axolotl genome in collaboration with Gene Myers at the MPI-CBG in Dresden. The expanded genome features many retroviral repeat sequences in introns and intergenic sequences. The genome information has allowed her group to develop CRISPR-mediated knock-in approaches to follow stem cell populations during limb regeneration.

Francesco Neri from the Fritz Lipmann Institute (FLI) in Jena was the recipient of the 2017 GSCN Young Investigator Award 2017. His research interest lies in the epigenetic regulation of development and stemness. In mouse embryonic stem cells (ESCs), developmental gene promoters are hypomethylated, but maintained repressed by Polycomb Repressive Complex 2 (PRC2). Francesco Neri and his research team demonstrated that PRC2 recruits DNMT3L

(passive way) and TET1 (active way) to maintain the developmental associated gene promoters in a hypomethylated state to permit their further activation during differentiation and to maintain ESC plasticity. Dnmt3L interacts with the Polycomb PRC2 complex in competition with the DNA methyltransferases Dnmt3a and Dnmt3b, whereas Tet1 mediated an active DNA demethylation. By developing a new genome-wide method, named methylation-assisted bisulfite sequencing (MAB-seq), they identified all the DNA demethylation events in stem cells and demonstrated that actual promoter DNA methylation/demethylation occur also on highly-expressed genes. DNA methylation is a heritable epigenetic modification required for embryonic development and it causes transcriptional repression, when established on gene promoters. The molecular and biological functions of intragenic DNA methylation was unknown for long time, although deregulation of this epigenetic feature



GSCN Junior Award went to Francesco Neri (middle), here with Daniel Besser (left) and GSCN president Ulrich Martin.

had been associated with several diseases. Their results show that the Dnmt3b-dependent intragenic DNA methylation protects the gene body from RNA Polymerase II (RNA Pol II) spurious entry and cryptic transcription initiations to ensure gene transcription initiation fidelity.

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 91 institutes of the Leibniz Association, the FLI is publicly 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
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Award ceremony for the best publication with awardee Gray Camps (middle), Daniel Besser (left) and GSCN president Ulrich Martin.

The Publication of the Year 2017 Award went to **Gray Camp** and **Barbara Treutlein** at Max Planck Institute for Evolutionary Anthropology, Leipzig and Keisuke Sekine and Takanori Takebe from Cincinnati Children's Hospital Medical Center for their joined publication "Multilineage communication regulates human liver bud development from pluripotency" in the journal Nature (Camp, JG et al., 2017, Nature 546, 533-538, doi: 10.1038/nature22796). Recently, vascularized human liver tissue has been generated by mixing stem cell-derived human hepatic endoderm with endothelial and mesenchymal cells in vitro and transplanting these self-organized 3D liver buds into a mouse model. In the publication the authors describe the analysis of this system using

single-cell transcriptomics with the goal to understand how different cell types interact within a 3D microenvironment and signal during the formation of a 3D organ bud. This work revealed multilineage crosstalk and a dual role for stromal cells to both stimulate hepatic maturation and also regulate hypoxia and stress response in 3D microenvironments.



Gray Camp (GSCN Award 2017)

Scientific Sessions

Ralf Jauch (Guangzhou Institutes of Biomedicine and Health and GIBH- Max Planck Center for Regenerative Biomedicine) presented data demonstrating that endogenous reprogramming factors can be improved by both rational protein design and directed evolution. Using members from the POU and SOX families and pluripotent reprogramming to benchmark the method, his team identified artificially evolved transcription factors (eTFs) that outperform their wild-type counterparts in reprogramming speed, efficiency and yield. The researches are now applying their directed reprogramming factor evolution approach in lineage reprogramming with the goal to generate functional cells for biomedicine.

In the session "Stem cells in regenerative therapies" **Nico Lachmann** (Hannover Medical School, Cluster of Excellence Rebirth) gave insights into the current efforts to generate multiple mature hematopoietic cell types from human iPSC in large-scale quantities using stirred tank bioreactors. The researchers have used their immune cells to establish a new cell based and antibiotic independent treatment approach targeting acute pulmonary infections and are currently expanding this new form of treatment also to other disease entities.

Intensive discussions
in the scientific sessions



Baris Tursun presents insights from his research on *C.elegans*.



In the session "Pluripotency and Reprogramming" **Baris Tursun** presented a study illustrating that the nematode *Caenorhabditis elegans* is a powerful model organism for identifying barriers that limit the efficiency of cellular reprogramming. They identified the histone chaperone FACT as an impediment for transdifferentiation in *C. elegans* and provide evidence that FACT is an evolutionarily conserved reprogramming barrier also in human cells. Currently researchers in Dr. Tursun's group are investigating the molecular mechanism by which FACT counteracts cellular reprogramming in *C. elegans* and in human.

Strategic working groups

The GSCN strategic working groups presented three sessions at the conference on clinical trials and regulatory affairs, technologies in stem cell research, and career development. Given that not all scientists pursue careers in academia, it is important to support them in their career decisions by providing information about other professional options: for example, at the career development session, **Tobias Maier** from the Nationales Institut für Wissenschaftskommunikation (NaWiK) presented an account of his start in science communication and recommended that all scientists who enjoy writing and have strong opinions make a name for themselves as

Tobias Maier was first a blogger before he became a science communicator.



Fraunhofer Institute for Cell Therapy and Immunology IZI

The Fraunhofer Institute for Cell Therapy and Immunology IZI investigates and develops solutions to specific problems at the interfaces of medicine, life sciences and engineering. One of the institute's main tasks is to conduct contract research for companies, hospitals, diagnostic laboratories and research institutes operating in the field of biotechnology, pharmaceuticals and medical engineering.

The Fraunhofer IZI develops, optimizes and validates methods, materials and products for the business units Drugs, Cell Therapy, Diagnostics

and Biobanks. Its areas of competence lie in cell biology, immunology, drug biochemistry, bioanalytics and bioproduction as well as process development and automation. In these areas, research specifically focusses on the indications oncology, ischaemia, autoimmune and inflammatory diseases as well as infectious diseases and regenerative medicine. The institute works in close cooperation with hospital institutions and performs quality tests besides carrying out the GMP-compliant manufacture of clinical test samples. Furthermore, it helps partners obtain manufacturing licenses and permits.



Fraunhofer Institute for Cell Therapy and Immunology IZI
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STEM CELLS AND CANCER

10 th International Heinrich F.C. Behr Symposium

September 16-19, 2018

German Cancer Research Center (DKFZ) Heidelberg

www.scc2018.de

Pre-Conference
Clinical Workshop:
**Innovative
Strategies
to Target AML**

September 16, 2018
10:00 - 15:00



GermanStemCellNetwork

6th Annual GSCN Conference

19 – 21 September 2018

German Cancer Research Center (DKFZ)
Heidelberg
www.gscn.org

bloggers. This is the best way to become established in the field of writing and communication. **Stefanie Seltmann** described her career path as a communications manager in the public sector. As head of press and public relations at the German Cancer Research Centers (DKFZ), her work varies from tasks relating to the awarding of Nobel Prizes to crisis communication. Compared to this, the tasks of science communicators in the private sector are different: they must be more business-oriented in their thinking and activities. Both sectors are very promising and offer versatile options for scientists with an interest in communication.

*Scientists enjoy
the networking.*


No conference without parties

What would a GSCN conference be without its parties? Networking is simply unimaginable without a convivial setting involving food and drink, music, and a relaxed atmosphere. The conference participants had many opportunities to meet outside the conference sessions in Jena: the evenings of the non-PI and PluriCore meetings, the informal GSCN get-together with a buffet in the canteen, and the relaxed network evening in the Volksbad Jena culture center.

Public event

Following the conference, the GSCN invited interested members of the general public in Jena to a panel discussion on "Modern Cell Therapies – Stem Cells and Aging, Cancer & Organoids" at the Volksbad culture center. Stefanie Seltmann chaired the discussion with researchers Claudia Waskow (Dresden), Florian Heidel (Jena), Jürgen Knoblich (Vienna), and Andreas Trumpp (Heidelberg). Following the presentation of a short film about the scientists in their laboratories, Seltmann interviewed them about leukemia, mouse models, brain organoids, and cancer sleeper cells. This was followed by a lively discussion focusing on issues relating to health and ethics.

*Party atmosphere at the
Volksbad Jena*

The Collaborative Research Center SFB 873

Maintenance and differentiation of stem cells

The Collaborative Research Center SFB 873 "Maintenance and Differentiation of Stem Cells in Development and Disease" at Heidelberg University works towards defining the regulatory principles underlying the balance between maintenance, expansion and differentiation of stem cells in diverse systems on a mechanistic level. To this end the SFB873 studies a wide spectrum of experimental models ranging from plants to human to elucidate the inherent properties of specific stem cell systems, but also to uncover common and divergent principles behind regulatory regimes and molecular signals.

Our consortium brings together internationally recognized researchers, with unique scientific strengths in cell biology, biophysics, developmental biology, molecular medicine or modeling. With our research we hope to advance our understanding of principles underlying stem cell function and lay the foundation for translational approaches.

Centre for Organismal Studies (COS)
Im Neuenheimer Feld 230 · 69120 Heidelberg
www.sfb873.de

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