46th Annual Scientific Meeting (ISEH) – travel grant report

The annual meeting of the International Society for Experimental Hematology (ISEH) gathers every year high-quality scientists from top universities worldwide. It covers a wide range of hematopoietic research topics from healthy to malignant hematopoiesis and blood-cell reprogramming to clinically oriented stem-cell maintenance and ex vivo expansion. In addition to the latest scientific breakthroughs, major advances in cutting-edge technologies are presented in respective sessions. To compliment this year's scientific program, a career-oriented session provided useful advice to scientists wishing to transition between different stages in academia (doctoral students, postdocs, group leaders).

My attendance to the ISEH meeting held at the Goethe University in Frankfurt, Germany from August 24th to 27th allowed me to gain insights on the latest research in my field: the role of the local bone marrow microenvironment in normal and malignant hematopoiesis. In particular, recent data from the Adams group (Max Planck Institute, Muenster) provided mechanistic insights in how endothelium regulates hematopoietic stem cell numbers through notch signaling under homeostasis in adult and aged mice. Data from the Lo Celso group (Imperial College London) revealed major remodeling of bone marrow osteoblasts during T-cell acute lymphoid leukemia (TALL), whereas in the case of acute myeloid leukemias (AML) the vasculature was mainly re-structured. In early stages of AML, cancer cells were able to grow in the expense of normal blood (stem) cells by eliminating individual niche sub-populations essential for the steady-state hematopoiesis. My presence to this conference enable me to interact with those principal investigators, discuss critical experimental details and establish new contacts extremely valuable for my future academic research and career.

Obtaining the German Stem Cell Network travel grant further allowed me to present my recent data on dissecting the bone marrow hematopoietic niche using a novel approach for deep-tissue, full bone, quantitative imaging. My poster was warmly received and triggered stimulating scientific discussions. Importantly, several groups expressed a strong interest to use my data and BM imaging technique, thus paving the way for establishing international collaborations.

In summary, I am very grateful to the German Stem Cell Network for financially supporting my attendance to the ISEH meeting. It was a unique experience to meet and discuss with world's leading experts in the field of hematology, make valuable connections and drastically increase my scientific network.

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Dirk Löffler – ISEH 2017 personal experience report for GSCN

The annual International Society for Experimental Hematology (ISEH) meets once per year. This year´s meeting was held in Frankfurt/Main Germany at the Westend Campus of the Goethe-University Frankfurt and organized among others by Prof. Michael Rieger and the by now former ETH president Prof. Timm Schroeder.

With just over 500 participants this year, the meeting created an informal atmosphere where international phD students and postDocs from all over the world were able to get to know each other while also having plenty of opportunities to approach established leaders of hematologic stem cell field. One of the most known and senior participants, Irving Weissman from Stanford, received the Donald Metcalf award for his decade long contributions to the hematology field. He was presenting his recent work on how cancer cells can be efficiently targeted by macrophages when the "Don´t eat me" signal expressed on many cancer cells is blocked using anti-CD47 antibodies. Further did he show that the principle of blocking antibodies can also be utilized to eradicate the entire hematopoietic system. This approach holds the potential to improve the quality of life of many cancer patients while also making bone marrow transplantation therapy applicable to patients that are currently too weak to receive standard chemotherapy and therefore couldn't be treated using bone marrow transplant so far.

A central topic of this year´s conference was about the influence of mitochondria activation and metabolism in general on hematopoietic stem cell self-renewal and differentiation. Although some controversies remain, overall the evidence is accumulating that mitochondria and their activity play and important role in stem cell maintenance and differentiation. In this context an exciting talk given by Hans-Willem Snoek highlighted a previous unappreciated role of calcium signaling and its role in self-renewal. Unexpectedly, the bone marrow seems to be a calcium sink and low levels of calcium are crucial to maintain hematopoietic stem cells in vivo as well as in vitro.

Beyond that many other interesting talks were presented and the field seems to move further towards quantitative and also continuous analytic approaches as highlighted by Cristina Lo Celso presentation "Intra-vital microscopy reveals dynamic and selective microenvironment remodeling by diverse types of acute leukemia" and Elaine Dzierzak´s presentation about in vivo imaging of a fluorescence Gata2

reporter mouse. Work from the Schroeder lab presented by Martin Etzrodt also demonstrated a novel approach in which microfluidics are utilized to stimulate hematopoietic cells with varying time intervals during continuous quantitative time-lapse imaging. This approach has the potential to shed light on the underlying principles of signaling processes and their integration and regulation during the execution of lineage decisions.

I was presenting my work as a poster titled “Asymmetric cell division of hematopoietic stem cells: Asymmetric inheritance of cell fate determinants and its role in cell fate decisions” twice at this year’s meeting. The first presentation was held in the Pre-Meeting Workshop before the actual start of the meeting. The second time in the main poster session during the meeting. Overall a lot of participants ranging from the phD to the PI level were interested in my poster. I was trying to raise awareness that asymmetric cell division of hematopoietic stem cells as a mechanism has so far not been demonstrated in hematopoietic stem cells and that the few studies that so far were trying to address this question suffer from multiple drawbacks leading to controversial observations. My line of argumentation was well received and people seemed to agree with the points I was communicating.

Besides that plenty of opportunities were provided by the organizers to network in sessions like the “New Investigators Meet the Expert Mixer”, the Social Event or more informal dinners at the City Garden in down town Frankfurt. During these events I was able to catch up with former collaborators while also getting to know phD students and postDocs conducting exciting research across the globe. I am looking already forward to next year´s ISEH and recommend this meeting to young phD and postDocs excited about hematopoietic stem cell research.

Dirk Löffler

The 46th International Society for Experimental Hematology (ISEH) Annual Scientific Meeting (Frankfurt, Germany, Aug24-27, 2017) Report

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Scientific highlights

Dr. Hans-Willem Snoek (Columbia University, USA) presented a strategy to grow hematopoietic stem cells (HSC) in culture in the presence of low level of Ca^{2+}, which is a long sought-after task in the field as *ex vivo* expansion of HSCs has a wide range of applications for therapeutic use. He then linked the underlying mechanism to the metabolic state of HSCs associated with mitochondria. Previously, he and colleagues showed that lymphoid-biased HSCs express high level of mitofusin 2 (Mfn2), which is involved in tethering of mitochondria to the endoplasmic reticulum, resulting in buffering of intracellular Ca^{2+}. Here, he presented additional evidence that lower Ca^{2+} level is present in the bone marrow interstitial fluid compared to serum and that HSCs express higher levels of PMCA pumps that mediate the efflux of Ca^{2+}.

Dr. Claudia Waskow (Technical University of Dresden, Germany) presented interesting data on how cell cycle progression acts to regulate stem cell fate. She asked the question of whether shortening the G1 phase favors HSC self-renewal over differentiation. She showed that the overexpression of CDK4 and cyclin D increased the leukocyte engraftment potential in mice long-term while the overexpression of CDK2 and cyclin E decreased the engraftment potential. As CDK4/cyclinD and CDK2/cyclinE regulate different stages of G1 progression, her data indicated an intricate cell cycle phase regulation mechanism of HSC fate.

Dr. Wilson Wong (Boston University, USA) presented synthetic biology approaches to develop genetic tools to improve the efficacy and safety of tumor-targeting T cells for cancer immunotherapy. He presented advanced chimeric antigen receptor (CAR) design for improved specificity and control. For instance, combinations of different CAR modules can improve the specificity; split CARs can enable inducible control and flexibility in changes of targets. CARs with logic control can also be implemented to confer an ON/OFF switch or control the downstream signalling pathways.

Personal interactions

At my poster session, I had interesting discussion and exchange of ideas with a number of researchers as well as gained knowledge on the topology and new markers that identify human HSC subsets (from unpublished data). During the new investigator career session, I have learned from newly established principle investigators about the hiring process and funding opportunities for transitioning from a post-doc to independent group leader. At the "meet the expert" dinner event, I had the opportunities to talk to three leading scientists in the field and learned from their personal experience how to manage the group dynamics to foster a positive, synergistic, high-quality research environment. In addition, I have gained knowledge on current breakthroughs in scientific findings and

state-of-the-art technologies and methods such as gene editing using CRISPR-Cas9 from talks, posters and discussions throughout the meeting.

I would like to thank the German Stem Cell Network for granting me the travel award to attend this highly interactive and unique conference. The knowledge, experience and network that I have obtained and established will be of great value for my current and future research career.