Stem Cell Research in Germany

Chapter 1 | LEBENDER KOLUMNENTITEL

Regenerative Therapies

Computational Stem Cell Biology

Disease Modeling

Pluripotency

Drug Development

Diseases

Stem Cells

Somatic Stem Cell Re-Programming

Cancer Stem Cells

Disease Modeling

Photo: HI-STEM / Martin Sprick
Stem cells in diseases (cancer stem cells)

Targeting the seeds of tumors

Increasingly, the concept of cancer stem cells is gaining acceptance within the medical community. Around the world, researchers regard these rare malignant stem cells as key to understanding the biology of many tumors and as the source of recurrence following an otherwise successful cancer treatment. Germany boasts a number of excellent research groups that have made seminal contributions to our understanding of cancer stem cell biology. One of the GSCN working groups is dedicated to bringing the expertise of these groups together under one umbrella in order to more effectively develop future therapies for cancer.

A number of tumor entities are not made up of a single type of transformed cell but instead are characterized as consisting of a heterogeneous range of malignant cells. In a structure that resembles a classic hierarchy of normal tissues and organs, some tumors contain abnormal cells that, unfortunately for the patient, also exhibit the characteristic of stem cells. Increasingly, the field of cancer research is turning its sights to focus on these rare kinds of cells. Because the so-called cancer stem cell (CSC) hypothesis can help to explain why cells begin to proliferate and disperse, and why cancer can flare up again even after an apparently successful treatment, many scientists see CSCs as key to understanding the insidious nature of tumors.

The cause of a range of tumors

"Following the demonstration of the stem cell concept for leukemia, it has become increasingly clear that this model also plays a role in many solid forms of cancer, such as carcinomas," says Andreas Trumpp, President of the German Stem Cell Network (GSCN) and initiator of GSCN working group 'Stem cells in diseases'. Trumpp heads the Division of Stem Cells and Cancer at the German Cancer Research Center (DKFZ) in Heidelberg. Here, several research groups are busy interrogating the fundamental biology of CSCs. Other DKFZ researchers also focus on developing novel therapies that target CSCs: Hanno Glimm is investigating their role in colon cancer and Ana Martin-Villalba is developing strategies for the destruction of CSCs in glioblastoma. The important questions being pursued by the researchers include: How do CSCs develop in different types of cancer? How do they promote tumor development? How can they be detected?

Terminating the survival tricks

For the field of cancer medicine, the central characteristic of CSCs is their ability to develop resistance to conventional radio- and chemotherapy through a range of survival tricks. These resistance mechanisms are regarded as a central explanation for the phenomenon of disease relapses after treatment.

Among other work, Trumpp and his team are now trying to decode the nature of these survival tricks. In work on a leukemia mouse model conducted together with Marike Essers, the scientist discovered so-called ‘dormant’ cancer stem cells. “Using specific cytokines, we can place these cells under stress and wake them up. They then begin to divide and thus become susceptible to chemotherapy," explains Trumpp. This serves as the basis for an effective combination therapy, which the Heidelberg-based scientists now want to transfer to clinical practice. Trumpp is also the managing director of the HI-STEM Heidelberg Institute for Stem Cell Technology and Experimental Medicine. Together with partners from hospital clinics, scientists at HI-STEM are concentrating on application-oriented research targeting tumor- and metastasis stem cells. In this way, they have succeeded in detecting and molecularly characterizing metastasis-inducing cancer stem cells (MICs) circulating in the blood of breast cancer patients. It has been demonstrated that patients with a large number of these cells in the blood have a particularly poor prognosis. This work could lead to the development of detection methods for such MICs in the blood and also provide new approaches for the development of medications for metastatic breast cancer.

Research network for cancer stem cells

The German Consortium for Translational Cancer Research (DKTK), one of the six German Centers for Health Research, is also based in Heidelberg. This makes the city an important hub for German cancer stem cell research. The DKTK is the headquarters for the translational...
research program, Stem Cells in Oncology. The program combines the work of specialists from seven leading centers including research groups from Berlin, Dresden, Frankfurt/Mainz, Freiburg, Munich, Tübingen, Essen/Düsseldorf and of course the DKFZ. Within this program, intensive effort is focused on illuminating the properties of cancer and metastasis stem cells, and to develop novel therapeutic strategies to target these cells. At the Freiburg University Medical Center, the team headed by Thomas Brabletz, co-initiator of this GSCN working group, is investigating the CSC concept in solid forms of cancer. He is interested in how tumors emerge in the gastrointestinal tract and the molecular changes that stimulate a cancer cell to migrate throughout the body. In pioneering work, the Freiburg-based researchers have demonstrated that specific embryonic development programs are reactivated in these kinds of cells, lending the cancer stem cells an abnormal mobility and enabling them to spread throughout the body. Jochen Maurer in Freiburg is also concentrating on the role of stem cells in breast cancer and on targeted treatment strategies, while Gabriele Niedermann and her team are occupied with non-invasive diagnostic methods that identify tumor stem cells in patients.

The hunt for a molecular fingerprint

Frankfurt am Main is home to several clinical research organizations that are working to deepen our understanding of CSCs. A key partner in this work is the LOEWE Center for Cell and Gene Therapy, which is funded by the State of Hessen. At Frankfurt University Hospital, the team led by Michael Rieger is studying the molecular regulation of developmental decisions in leukemia, breast and colon CSCs. Likewise, the team of scientists headed by Hubert Serve at the Department of Hematology and Oncology are studying leukemia stem cells, and Florian Greten (Georg-Speyer-Haus) is investigating so-called niches, namely the cellular microenvironment in the tissue in which colon cancer origi-
HI-STEM gGmbH is a non-profit public-private partnership between the German Cancer Research Center (DKFZ) in Heidelberg and the Dietmar Hopp Foundation (DHS).

HI-STEM performs cutting-edge research on stem cells with the aim of translating these results into novel clinical applications. This includes the development of novel diagnostic tools and innovative therapies to monitor and target leukemic and solid tumor stem cells as well as metastatic disease.

HI-STEM was founded in 2008 and is located in newly renovated laboratories and offices within the main building of the DKFZ. The managing director of HI-STEM, Professor Dr. Andreas Trumpp and five Junior Group Leaders direct an international team of more than fifty scientists, PhD/Masters students and technical staff. Together, this forms an excellent environment to perform cutting edge translational research and to train the next generation of outstanding young scientists.

The HI-STEM Research Groups:
- Hematopoietic and Leukemic Stem Cells (A. Trumpp)
- Experimental Hematology (M. Milsom)
- Stress induced activation of HSCs (M. Essers)
- Cancer Stem Cells and Metastasis (A. Trumpp & M. Spick)
- Metastatic Niches (T. Oskarsson)
- Biomarker Discovery (C. Rösli)

Researchers at HI-STEM are working in close collaboration with colleagues of the University Clinical Centers in Heidelberg, Mannheim and other cities as well as with the National Center for Tumor Diseases (NCT) in Heidelberg. In addition, HI-STEM collaborates with various biotechnology and pharmaceutical companies to investigate and develop novel strategies to push forward the development of new drugs and effective treatments for different types of cancer and to promote their clinical application.

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