Dormant stem cells can be awakened with interferon alpha

With a number of new papers published in renowned scientific journals, Prof. Dr. Andreas Trumpp has been able to further cement his outstanding reputation as one of the world leaders in stem cell research. Trumpp, who has been professor and head of the Department of Cell Biology at the German Cancer Research Centre (DKFZ) since summer 2008, also became head of the newly founded “Heidelberg Institute for Stem Cell Technology and Experimental Medicine” (HI-STEM gGmbH) which works closely with the DKFZ, Heidelberg University Hospital and Heidelberg University in the advancement of stem cell research towards use in therapies. The researchers are primarily interested in the identification and destruction of cancer stem cells.
Andreas Trumpp, born in 1964, studied biology at the University of Freiburg and did his doctorate on a developmental biology topic under Rolf Zeller and Thomas Graf at the EMBL in Heidelberg. In 1994, he went to the USA where he spent six years at the University of California in San Francisco in the laboratories of John Michael Bishop (Nobel Laureate - 1989) and Gail R. Martin. He developed mouse models in order to investigate the fibroblast growth factor 8 (Fgf8) gene and the c-Myc oncogene. In April 2000, he became head of the Genetics and Stem Cell Laboratory at the Swiss Institute for Experimental Cancer Research (ISREC) in the city of Epalinges close to Lausanne. In 2005, he was appointed Professor for Molecular Oncology and Stem Cell Biology at the École Polytechnique Fédérale de Lausanne (EPFL; Swiss Federal Institute of Technology) and in 2008 he accepted the offer from the DKFZ in Heidelberg.

Dormancy as an effective protection for stem cells

Trumpp and some colleagues from the Ludwig Institute for Cancer Research in Lausanne, including Dr. Anne Wilson, discovered a small population of well-hidden stem cells in the bone marrow niches of mice. These stem cells remain in a state of dormancy for virtually their entire lives and are only activated in cases of emergency. Haematopoietic mouse stem cells normally divide approximately once a month; the dormant stem cells, which account for about 15 percent of the entire mouse stem cell population, only divide five times during a mouse’s lifetime. Transferred to humans, this corresponds to a cell division rate of once every 18 years. If, however, these cells are awakened, for example if there is a bone marrow injury or messenger substances such as G-CSF are released, they reveal the highest self-renewal potential of all stem cells. Transplanted into irradiated mice, these cells are able to replace the destroyed bone marrow and restore the entire haematopoietic system. When the bone marrow has been repaired and restored to a healthy state,
these particular stem cells once again fall into a deep sleep while the large majority of stem cells is occupied in actively maintaining the physiological equilibrium of blood cells.

Dormancy is an important protection mechanism for stem cells because it helps them to avoid being attacked by chemotherapy drugs and many cytotoxins, which only act on dividing cells. It also protects the stem cells’ genetic material from genetic alterations, which also occur primarily during cell division.

Trumpp and his colleagues have made considerable contributions to characterising the haematopoietic stem cell niche and they have discovered that the c-Myc oncogene controls the niche entry and exit of these haematopoietic stem cells. In a recent paper published in Nature (Marieke Essers et al., Nature, February 11, 2009), the researchers showed that interferon alpha, an immune system messenger substance, activates the dormant haematopoietic stem cells in the bone marrow, thus making them vulnerable to the effect of many drugs, including 5-fluorouracil.

For Andreas Trumpp, these results are also key to the understanding of cancer stem cells whose role in the initiation and growth of tumours is a major issue in oncology research. Under the leadership of the DKFZ's chairman and chief scientific officer, Professor Dr. Otmar D. Wiestler, the DKFZ is focusing specifically on stem cell research and using the results to develop new cancer therapy strategies. Trumpp and Wiestler published the current state of knowledge and therapy concepts in a comprehensive review in Nature Clinical Practice Oncology, April 22, 2008.
The HI-STEM Institute

The “Heidelberg Institute for Stem Cell Technology and Experimental Medicine” (HI-STEM gGmbH), under the scientific leadership of Andreas Trumpp, brings together application-oriented research on cancer stem cells. The HI-STEM was established jointly by the Dietmar Hopp Foundation, a private foundation that is the institute’s major shareholder, and the DKFZ, where HI-STEM will be located. The institute is the core of the Stem Cell Network that was selected in the German Federal Ministry of Research and Education’s Top Cluster Competition as one of the priorities in the further development of the “Cell-based and molecular biology in the Rhine Neckar Metropolitan Region” BioRN cluster. Winning the Top Cluster Competition has brought additional BMBF funding to Trumpp and his new research groups at the HI-STEM. By combining basic research, translational medicine and economic potential of a cutting-edge research topic, the research projects at the HI-STEM are of central importance for the development of the BioRN cluster.

Cancer stem cells that induce metastases

Cancer stem cells (CSC), which were discovered in leukaemias, have revolutionised the theory of cancer development and metastasing. Not all cancer cells that disseminate from the primary tumour have the ability to form remote metastases. It is believed that this can only be achieved by a tiny subpopulation called “metastasis inducing cancer stem cells” or MICs. Normally, these cells, like all other stem cells, are in a dormant state and only rarely divide; they also have an unlimited potential for self-renewal as well as the capacity to produce different cell types. Of great importance is the fact that cancer stem cells are resistant to treatment with standard chemotherapeutic drugs. They hide in stem cell niches where they remain dormant and can only be destroyed with difficulty. This explains why chemotherapies initially lead to the disappearance of the cancer because the tumour cells, which represent the mass of the primary tumour, are barely or not at all resistant to treatment. But the tumour can and does recur many years after treatment due to chemotherapy-resistant MICs. Therapies that specifically target cancer stem cells might have a more favourable outcome. The researchers led by Trumpp have developed a special xenograft mouse model with which it is possible to identify MICs in human blood or bone marrow. The model enables the targeted search for substances that are specifically directed against the target molecules on the MICs. This would open up completely new treatment strategies for patients with metastatic tumours, which are the cause of the majority of cancer deaths.

Further information:

Press and Public Relations
German Cancer Research Centre (DKFZ)
Im Neuenheimer Feld 280
69120 Heidelberg
E-mail: presse(at)dkfz.de