Adult stem cells – hope for regenerative therapies

Stem cells are the source for the formation of all body cells. In addition to the much-discussed embryonic stem cells, stem cells with the ability to form new specialised cells are also found in the human body after the embryonic state and even in adulthood. These adult stem cells secure the continuous replenishment of cells, therefore enabling the constant replacement of dying cells by new ones. Progress in the characterisation, isolation and specific differentiation of adult stem cells over recent years raises hopes for the future use of the cells in the therapy of degenerative diseases. Knowledge about adult stem cells also has the potential to lead to new therapies for the treatment of cancer.

Our body undergoes constant reorganisation and renewal processes. The controlled death of cells is crucial for controlling the number of cells in the body, for removing old and malignant cells as well as for the selection of immune cells. The human body possesses a reservoir of adult stem cells for the production of new specialised cells that can replace old and malignant cells and regenerate injured tissue in the form of wound healing. In contrast to embryonic stem cells, these adult stem cells only have a limited self-renewal and differentiation potential and bring forth specific tissues and cell types. For example, skin stem cells only replenish skin cells and neural stem cells only give rise to nervous system cells. This is why such stem cell reservoirs are found in most tissues and organs.

Even though adult stem cells are not as versatile and able to divide as often as their embryonic relatives, they still do an amazing job. For example, skin stem cells continuously replenish the desquamating skin cells of the epidermis and renew the skin once every four weeks or so. This extraordinary renewal potential makes them highly interesting for application in regenerative medicine.

Adult stem cells isolated from adipose tissue and cultivated in the laboratory.

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Adult stem cells are ethically acceptable and can even be obtained directly from the patient undergoing stem cell treatment. Therefore, researchers have the vision of being able to use autologous adult stem cells for the therapy of degenerative diseases, as these cells do not trigger rejection reactions in the patient's body. However, allogeneic adult stem cells, i.e. cells removed from a suitable donor, are also a promising source of cell renewal.

Bone marrow stem cells as model

The therapeutic application of adult stem cells is already standard in the treatment of bone marrow diseases. For many years, the Multiple Myeloma Section at Heidelberg University Hospital has used autologous stem cell transplantations for the treatment of multiple myeloma, a cancer of the haematopoietic bone marrow. This application raises hope for the treatment of many other diseases, in particular degenerative diseases, and research is increasingly focussed on the use of adult stem cells for such purposes.

With the "Adult Stem Cells 2009" programme, the Baden-Württemberg Stiftung funds basic research with the goal of developing cell-based regenerative therapies. The follow-up funding programme also funds projects focussed on targeted therapeutic approaches. Intensive research efforts have in the meantime led to numerous animal models and clinical trials involving humans for assessing the use of neural stem cells for diseases such as Parkinson's and Alzheimer's, to name but two examples.

However, such therapies have not yet been approved for human application and stem cell transplantation is currently only used for the treatment of severe diseases of the haematopoietic system.

Stem cells isolated from adipose tissue are differentiated into cartilage cells in the laboratory, and hence lead to cartilage tissue.
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Haematopoietic, i.e. blood-forming stem cells are arguably the best understood stem cell system. They are found in the bone marrow of the large bones, i.e. mainly in the iliac crest, thigh and upper arm. They continuously generate new blood cells by dividing asymmetrically, resulting in a new stem cell that remains in the tissue and a new progenitor cell that divides rapidly and leads to new blood cells. There is a clear hierarchy from progenitor cells towards differentiated blood cells, something that is also assumed to exist in other stem cell systems.

Due to their frequency and the ability to withdraw them relatively easily from patients, even though the procedure is quite painful, bone marrow stem cells now carry the weight of expectations for many stem cell therapy options. Moreover, they seem to possess a far greater differentiation potential than other stem cells, as it is not only possible to differentiate them into blood cells, but also into nerve-like cells in the laboratory.

This is known as transdifferentiation, a process that has been subject to intensive research for quite a few years and is aimed at characterising the conditions under which this can be done as well as the potential of the cells. The transdifferentiation of bone marrow stem cells into nerve cells is associated with the advantage that they are much more common than neural stem cells and can also be isolated more easily. The isolation of a sufficiently large number of tissue-specific adult stem cells is still a huge problem. The appearance, structure, characteristics and exact location of the cells is often unknown.

In addition to haematopoietic stem cells, progress made by intensive basic research now also enables the isolation of stem cells from other types of tissues and their cultivation in the laboratory. For example, researchers from Med Cell Europe AG have succeeded in isolating stem cells from adipose tissue and differentiating them in vitro into insulin-producing cells or cartilage cells (see article entitled “Med Cell Europe AG: medicine from a patient’s own adipose tissue”).

New evidence of tumour stem cells

A relatively new area of stem cell research deals with the concept of cancer stem cells, which is still a matter of controversy amongst experts. Cancer stem cells are cancer cells found within tumours that possess characteristics associated with normal stem cells, in particular the ability to renew and differentiate. Although they only constitute a small proportion of cancer cells, they are assumed to be responsible for the growth of tumours, the formation of metastases and the resistance to therapies.

Some researchers have since provided evidence for the existence of such stem cells, and have thereby further substantiated the concept. A team of researchers led by Dr. Hanno Glimm from the National Center for Tumour Diseases (NCT) and the German Cancer Research Center (DKFZ) in Heidelberg have succeeded in identifying intestinal cancer stem cells in animals. These stem cells trigger the formation of metastases (see article entitled “Colon cancer: some tumour cells are more dangerous than others”). The researchers are aiming to better characterise the cells in order to enable the development of new cancer therapies that specifically target and destroy cancer stem cells.

Autologous all-rounders by reprogramming

The reprogramming of somatic cells into stem cells, for which John B. Gurdon and Shinya Yamanaka were awarded the Nobel Prize in Physiology or Medicine in 2012, was certainly a breakthrough in stem cell research (see article entitled “Nobel Prize for the reprogramming of cells”). The integration of four specific genes enabled the researchers to turn connective tissue cells back into undifferentiated stem cells. These so-called induced pluripotent stem (iPS) cells are then able to differentiate into specialised cells in a similar way to embryonic stem cells. They therefore represent a separate group of stem cells as they are produced from adult somatic cells, but are not adult stem cells in the natural sense.

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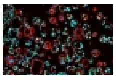

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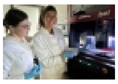

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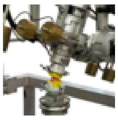

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