IMBA Press Release

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Stem cells go on a diet

In the up-to-the-minute field of stem cell research, researchers at the IMBA – Institute of Molecular Biotechnology at the Austrian Academy of Sciences – are causing a stir with two discoveries: when stem cells are no longer needed, they starve themselves to death. It is the stem cells' metabolism that seals their fate.

In every animal embryo, stem cells ensure the build-up of tissues and organs, growth, and regeneration. But at some point the stem cells have served their purpose and need to disappear. In the fly they disappear completely; in mammals and humans a few remain. But if unneeded stem cells remain, they might develop into malignant tumors.

Stem cell tumors in infants and small children

Such stem cell tumors have been observed in infants and small children. They appear in the brain, among other places, and are nearly impossible to cure despite aggressive therapies. Fortunately, these so-called rhabdoid tumors are uncommon, but that also means that not much research has been conducted into them. 80 percent of small children with such a brain tumor die within two years of diagnosis.

The stem cells take leave

Jürgen Knoblich, stem cell researcher and vice-director of the IMBA, has now worked with his team to discover the mechanism that ensures that stem cells grow into normal cells after organs and tissues have developed.

For this it is important to understand that a stem cell divides asymmetrically during embryo development. It divides into a larger cell that remains a stem cell, and a smaller cell that becomes specialized, for example as a nerve cell. Nerve cells are what make up the brain. During this division, the stem cell loses some of its mass and then grows again to its original size before the next division takes place.

Once enough nerve cells have been formed and the stem cell is no longer needed, it must disappear. In the renowned scientific journal Cell, post-doctoral researcher Catarina Homem has now published the mechanism she discovered in the fruit fly: "After the division the stem cells simply don't grow again. That means they become smaller with each division until asymmetrical division is no longer possible. The final step is then a symmetrical division into two nerve cells, and the stem cell has disappeared."

Metabolism is the main control element

The second new insight is that the metabolism of the cell evidently determines in which direction the cell develops. Steroid hormones control whether the cell completely burns its sugar with the help of oxygen, or whether it remains without oxygen and thus retains certain fragments. These later will be used to build up new fats or amino acids needed for growth. If the sugar is completely burned, as in the first option, the cell at some point no longer has any building blocks and cannot grow.

So if the stem cell needs to disappear, this metabolism option is essential. The cell then puts itself on a diet and burns its sugar so completely that it can no longer regenerate to its original size after division. It thus becomes smaller and smaller until eventually only one last symmetrical division is possible.

The second metabolism option, in which sugar ferments to lactate for lack of oxygen, is the same process tumor cells need to develop.
“What is surprising about this work is how strongly metabolism can influence the destiny of a cell,” said Knoblich about the insights gained during this study. “In general it is believed that cells go through a certain development program and thereby regulate their metabolism. But our work shows that it‘s the other way around: metabolism controls the destiny of the cell. This casts an entirely new light on the role of nutrition for our bodies, including tumor development.”

Now that it appears likely that the mechanism discovered in the fruit fly also occurs in mammals and humans, it may be possible to determine in the near future how stem cells in the brains of infants and small children are able to develop into aggressive rhabdoid tumors. Further studies will deliver more precise insights.

The following publication appeared on this topic in the renowned professional journal Cell on 14 August 2014:
Homem, C. et. al. (2014). Ecdysone and Mediator change energy metabolism to terminate proliferation in Drosophila neural stem cells. Cell.