A Tale about Regeneration and Stem Cells

„Off with their heads!“ In humans this command given by the queen of hearts inevitably leads to death. In fact cutting off any limbs without medical treatment has the same effect, and a missing arm or leg will be gone forever. Humans and other mammals cannot regrow lost body parts, but there are animals that have that amazing ability. Some amphibians like newts or salamanders are able to regrow fully functional limbs after amputation in just 30 to 40 days. Growing a new limb is not as easy as it sounds. The leg of a newt is not just a lump of flesh. Instead it is, like the arm of a human, tremendously complex. It consists of many different structures, like bones, muscles, vessels and many more. The newt has to build more cells in order to replace the lost mass, these cells have to differentiate to make the variate tissues and these structures have to be organized. First of all, the bone should be inside and the skin on the outside. The toes should be farthest away from the shoulder and not end up at the elbow. Also regulation of this growth should be taken into consideration, so that the leg does not get bigger than the rest of the newt.

Growing a new limb is an extraordinary achievement, but it gets even more fantastic. Planarians are small, free living flatworms, their bodies consisting of a head, body and tail. These creatures have astonishing regenerating capabilities. They can be divided into several pieces, each of them capable of rebuilding a new organism. A head piece will rebuild a missing tail and vice versa. Body pieces as small as 10 000 cells were shown to reform an entire organism. Taking into consideration that the size of a planaria varies between 1 and 20 millimeters and therefor each animal is build up of several millions of cells, this is an impressive capability. Several planarian species even choose this form of division as an asexual reproduction strategy. Would it not be nice to just conjure up an arm or leg after amputation? But that only works for Harry Potter, like when he has to painfully regrow his arm bones after a Quiddich match. Real-life regenerative medicine lags far behind fiction.

The keyword in all this is regeneration. In a biological sense regeneration describes the process of renewal, rebuilding and the growth of cells, tissues, body parts or even whole organisms. The newt is able to regenerate a whole functional limb, including cells, tissues and their organization and for the planaria it is even possible to rebuild a whole organism out of a couple of cells.

The mediators of this fascinating ability are cells called the stem cells. These cells are distributed throughout the body and look small and totally unremarkable. It is easy to guess the function of a muscle cell, with all its movable fibers, but those small cells gave researchers a hard time for many years. Yet, they are the basis of every multicellular organism. Stem cells have the capability to divide, to differentiate into diverse specialized cell

types and to self-renew to produce more stem cells. These remarkable cells come in different varieties: omnipotent , totipotent, or unipotent. Omnipotent cells can differentiate into any kind of cell in the body for example a human zygote, which is the fertilized egg that will later form the embryo. Totipotent cells can only become different types of a certain cell linage. The haematopoetic stem cells for example can become any type of blood cell but not anything else. Unipotent stem cells now are only able to produce one specific cell type, like the stem cells in the skin, which regenerate epidermal cells. Stem cells and the specialized cells they created, called the somatic cells, work together to form a living and growing organisms. In an embryo, stem cells divide and form all the organs and tissues. They are responsible for the growth of a child and the healing of wounds. In an adult these cells replace dying cells. Without that, we humans would soon shrink and probably die of organ failure, because all our cells have to be replaced from time to time. This balance of replacement has to be highly controlled. Shrinking as well as overdone growth is not desirable. In cancer for example this balance is disrupted in favor of uncontrolled growth. Cancer influences the body in many ways. It disrupts the metabolism, by using up most of the available nutrients. It destroys organ functions and whole tissues by its enormous local growth. That way cancer is responsible for millions of deaths worldwide each year.

Stem cell research is one of the major foci of modern science. Understanding the underlying principles of stem cell biology could help to grow the field of human regenerative medicine. The big question here is, which principles apply for humans, newts or planarians. Where are the differences and similarities and how can this knowledge be used in the future. Scientists are already able to grow small pieces of tissue, originating from a patients body, to rebuild damaged tissue after severe injuries. Stem cell therapy is already successfully applied in tendon injuries, too. Future potential treatments include rebuilding many different tissues, for example neuronal tissue after a stroke or degenerative diseases like Alzheimer´s disease. Stimulating cells to grow after injuries and reducing the formation of scar tissue would be of great importance in plastic medicine. Furthermore cancer therapy has improved much in recent years, but its advancement is still of great importance. Therefore understanding the principles of regeneration is one of the most important tasks of modern science. It will not be possible for many years to regrow full limbs, but maybe regrowing Harry Potter´s bones is not so far away any more.

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