

Stem cells

What do we mean by stem cells?

If a differentiated cell divides by mitosis, all its descendants will be identical to it and to one another. A stem cell can do more, producing stem cells or differentiating into specialised cells. They're also self-renewing, which means that they can go on and on dividing to create more stem cells, maintaining the stem cell pool.

Stem cells vary in their potency (how much they can differentiate). A newly fertilised egg, or zygote, and the products of its first few divisions are made of totipotent cells. These cells can give rise to any cell type in the body, and the placenta, and so can produce a whole organism. Embryonic stem cells, a few steps beyond the egg in development, are pluripotent – they can become many types of specialised cell, but not placental cells.

Multipotent cells, which can give rise to just a few types of cell, include those in bone marrow that can generate red or white blood cells. Most adult stem cells (those found in differentiated tissues and organs) are multipotent. Unipotent cells, such as those in the skin, make just one fully differentiated cell type, usually where lots of new cells are needed regularly.

A lot of research focuses on the transitions between these states. One basic question is whether pluripotent cells maintain pluripotency 'by default' or need a continuing signal to keep them differentiating.

Recent research suggests that pluripotency, in embryonic stem cells, is mediated by a network of epigenetics (proteins that influence whether or not a gene is read) by activating genes involved in sustaining pluripotency and repressing genes that are involved in differentiation and development. Furthermore, it has been suggested that epigenetic multipotent regulation (factors that affect how easily DNA can be read) works alongside transcription factors to maintain pluripotency by preventing development-related genes being read. It has also been suggested that this allows these genes to be inactive but still ready to be used if the cell needs to undergo rapid differentiation.

If we can learn how to control the differentiation of stem cells, we might be able to remedy many kinds of cell damage in the body. Embryonic stem cells are pluripotent, and so the most versatile, but their use is not without controversy.

Using advances in our understanding of how embryonic stem cells maintain pluripotency, scientists have been able to 'reprogramme' adult cells into a pluripotent state – so-called induced pluripotent stem (iPS) cells. The simplest reprogramming method enforces the expression of a set of core transcription factors, known to be essential in maintaining pluripotency in embryonic stem cells, in the adult somatic cell. This gives rise to cell colonies that appear to be morphologically and molecularly similar to embryonic stem cells.

How are cells specialised for their roles?

Each cell type is specialised for its role; specific characteristics range from making key proteins to general properties like shape. Red blood cells, for example, are small biconcave discs. This shape gives a large surface area, helping the cells to transport oxygen from the lungs to the tissues, and a little carbon dioxide the other way.

The shape also gives flexibility, helping the cells squeeze through the smallest capillaries. Developing red blood cells begin with a nucleus and organelles but lose them before they start work, which in effect reduces the cells to bags full of haemoglobin (the protein that carries oxygen and carbon dioxide). If their shape is distorted, disease can result. For example, in the inherited disease sickle-cell anaemia, some red blood cells become sickle shaped owing to abnormal haemoglobin molecules clumping together.

Organs often contain subpopulations of cells. The pancreas, for instance, makes a range of hormones and digestive enzymes. Small regions of the pancreas known as the islets of Langerhans contain four different

cell types, which each make different hormones. The most common cells are beta cells, which make insulin.

How do cells specialise? A stem cell will receive signals from its surroundings that trigger a change in the pattern of genes that are turned on and off, directing the cell towards a more specialised state through the synthesis of specific proteins.

Direction is important in cells' development and function

A cell's development – including its direction – is constantly influenced by the cells surrounding it. An epithelial sheet, for example, is asymmetric. One face (the apical surface) is exposed to the watery contents of the gut or to the air in the lungs. The opposite face (the basal surface) sits on supporting layers of collagen and connective tissue. Cells that secrete molecules into the gut need different membrane proteins at the top and bottom, and so do those specialised for absorption. The cell keeps track of which end is which, so molecules go the right way.

A more complex example is found in the ear, where a type of epithelial cell in the inner ear turns vibrational signals into electrical impulses so we can hear. These hair cells, which have a bundle of fine cilia, have a top and bottom but have to be arranged in the right direction along another axis as well. If they lose this orientation, or planar polarity, the sense of hearing may be impaired.