Rewinding the Clock

Stem cells have two special properties:

- They can divide indefinitely
- They can turn into any other cell type by a process called 'differentiation'.

This makes stem cells very exciting to use in research! It gives researchers the ability to understand how our cells develop, and what happens when this goes wrong. Stem cells also provide a model to test drug safety and due to their properties, they may be frozen for storage or distributed to other researchers.

Stem cells are usually derived from embryos, but scientists can also develop stem cells themselves in the laboratory. These are induced pluripotent stem cells, often abbreviated to iPSCs. iPSCs can be made from almost any adult cell in the body, though often they are made from skin cells as they are easier to obtain than other cell types. The process of converting a cell into an iPSC is called 'reprogramming'. Researchers study reprogramming because it tells us about how cells can change from one cell type to another. iPSCs are also useful models as they can be studied to understand how tissues develop during differentiation.

The process of cell reprogramming incorporates three steps; initiation, maturation and stabilisation.

RACE AGAINST THE AGEING CLOCK

STAGE 1: INITIATION

The adult cells lose specialised cell features

There are many ways to start the process of reprogramming, such as adding the specific proteins Oct4, Sox2, Klf4 and Myc (OSKM) to the cell, by exposing the cell to a specific combination of chemicals, or by changing the epigenetics inside the cell. Although we have identified many ways to start reprogramming, the process is very inefficient and only about 1 in 1000 starting cells will successfully become an iPSC.

Q1

Which of the following cells can an iPSC turn into?

- O Any cell in the body
- S Just heart cells
- K Just brain cells
- M Just liver cells

Q2

What percentage of cells become iPSCs during reprogramming?

- O 0%
- S 0.1%
- K 50%
- M 100%

Q3

How can you start reprogramming?

- O adding OSKM to the cell
- S adding specific chemicals to the cells
- K altering the epigenetics of the cell
- M all of the above

Q4

How many times can an iPSC divide?

- O Once
- S Twice
- K Indefinitely
- M Cannot divide

STAGE 2: MATURATION

Some stem cell genes are switched on

Every cell in the body contains the same set of genes, a gene is a section of the DNA, but only a subset of the genes are switched on in a particular cell type. The activity of genes is tightly controlled by a process called 'epigenetics'. During an epigenetic process a chemical group is added onto DNA so that the correct genes are switched on and off at the right time and in the right cell. An example is adding a methyl group, known as DNA methylation, to the DNA, which usually leads to switching a gene off. During reprogramming, epigenetic marks switch off genes that instruct the starting cell type (e.g. skin cell genes) and switch on genes that are needed in iPSCs.

Q5

Which of the following is an epigenetic mark?

- X DNA methylation
- Y Gene

STAGE 3: STABILISATION

The remaining stem cell genes are stably switched on

As we age, the pattern of epigenetic marks slowly changes. Researchers can calculate the biological age, the 'wear and tear' of the body, by examining the pattern changes of DNA methylation. The Epigenetic Clock, identified at the Babraham Institute, is a computer model used to calculate the biological age in mice. Normally, the biological age only moves forward. However, when cells are reprogrammed into iPSCs, their biological clock is rewound due to the changes happening to the epigenetic marks. As such, iPSCs always have their biological age stabilised at 0 years old, regardless of the age of the initial adult cells. At the Babraham Institute, we are researching this exciting characteristic of ageing to understand how the biological age of a cell can be reset and when this happens in the reprogramming process.

Q6

What happens to the biological age of cells after they are reprogrammed?

- X Goes up
- Y Goes down

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