Drug may give cells a fresh start

A chemical could switch adult cells from one type to another.
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Might we one day regenerate limbs like an salamander?
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Chemists in California have found a synthetic molecule that seems to reprogramme adult cells to make them more like youthful ones. If the discovery pans out, it could provide an easy source of cells to regenerate tissues damaged by disease or injury.

Sheng Ding and colleagues of the Scripps Research Institute in La Jolla discovered the molecule, which they named reversine. When they treated mouse muscle-forming cells with the drug, the cells apparently reverted to a 'blank' state capable of forming other kinds of tissues. The researchers were then able to guide the cells into becoming bone or fat cells instead[1].

"It is potentially interesting, but leaves some key questions

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unanswered", says Azim Surani of the Wellcome Trust/Cancer Research UK Gurdon Institute of Cancer and Developmental Biology in Cambridge, UK, who works on cell reprogramming. The team has not, for example, convincingly shown that the cells regressed to this primitive blank state. That will need to be checked, he says.

It is also unclear how efficient the process is, whether the technique would work in human or other types of cells, and whether some of the cells die in the treatment, warns Surani. Until such questions are answered, the clinical potential of the work remains to be seen.

Turning back the clock

The cells in our bodies have mostly become specialized or 'differentiated' into one type or another, such as red blood cells or kidney cells. But 'stem cells' haven't yet made their career decision, and so can potentially grow into more than one type of tissue.

Many researchers are working on ways to harvest stem cells from the body and turn them into cell types that could repair damaged tissues. One possible, but ethically controversial, source of stem cells is human embryos.

A handful of others are trying to 'dedifferentiate' adult cells instead — effectively turning back the clock on grown-up cells so they revert into stem cells. This research is inspired by organisms such as the salamander, whose cells can dedifferentiate when it regenerates a lost limb or tail.

This feat has been achieved in mammalian cells before — Mark Keating and his colleagues at Harvard Medical School in Boston, Massachusetts, have previously described[2] a way to induce the dedifferentiation of mouse muscle cells by switching on a gene called msx1.

One small molecule

Now the Scripps team has found a simple chemical compound that seems to cause the same effect. A small drug-like molecule could potentially be easier to use in the clinic than fiddling around with genes, Keating says. "I like their approach — it's neat and I'd like to try their drug," he says.

The team hit upon reversine by systematically treating mouse muscle cells with some 50,000 different candidate molecules that they hoped might stick to and switch on enzymes capable of producing dedifferentiation. The cells treated with reversine switched off muscle-related genes and no longer gave rise to muscle cells, suggesting that they had

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dedifferentiated. When plied with particular chemicals, these cells then appeared to form fat or muscle cells.

To make the result more convincing, the team now need to carefully document the muscle cells regressing into a stem-cell-like state, says Keating. They must also work out which enzymes reversine interferes with, and whether this might cause problems in the human body.

References

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