50 Years Ago

PROF. A. C. AITKEN, in a pamphlet entitled *The Case Against Decimalisation*, presents very skilfully the case against decimalization in general, starting with a lucid and cogent historical review ... He is less persuasive, however, in arguing for the duodecimal system, adoption of which in coinage, with a pound of twelve shillings, he suggests. He claims that this is a much more efficient system than the decimal system and that its adoption offers substantial advantages on practical as well as on arithmetical grounds.
From *Nature* 12 May 1962

100 Years Ago

One of the chief objections to the Daylight Saving Bill is the dislocation the scheme would effect in the zone system of time reckoning established by international conferences held successively in Rome and Washington thirty years ago. Mr. W. Ellis, F.R.S., refers particularly to this point in a short article in the March number of *The Horological Journal*. At present the prime meridian of Greenwich regulates the time of the civilized world. If the clocks of Great Britain are put forward one hour in summer, as proposed by the Bill, they will not show Greenwich time, but mid-European time; that is to say, our prime meridian, accepted by nations as regulating the time of the world, will be discarded by us for five months in every year ... An Act to enforce the alteration of clocks by putting them forward for one hour in the summer would introduce confusion in a scientific system and disturb accepted international standards. We cannot believe that such a proposal will ever be seriously entertained by Parliament.
From *Nature* 9 May 1912

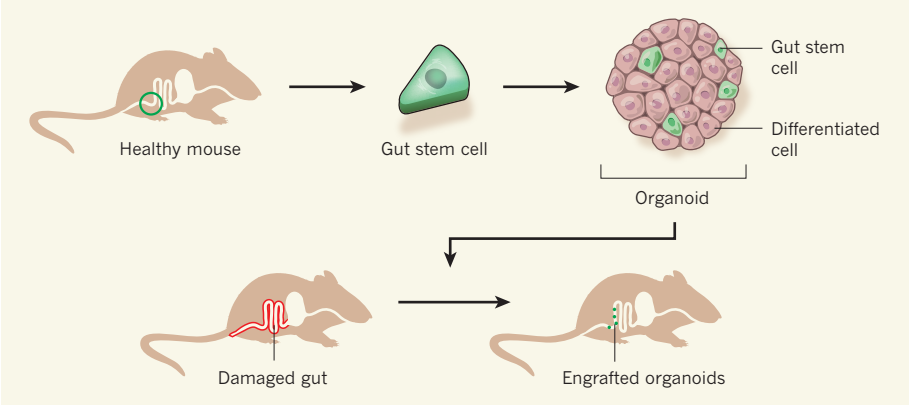

Figure 1 | Fixing a damaged intestine. Yui *et al.*[1] isolated individual stem cells from the gut of healthy mice and grew them *in vitro* using a medium that induced the cells to produce mini-organs (organoids) that contained stem cells and other types of differentiated cells commonly found in the colon. The authors expanded the organoids *in vitro* and then introduced them into mice whose intestines had been superficially damaged. Some of the organoids successfully attached to the damaged areas and survived for the six-month duration of the experiment.

in a way that resembles the effects of human ulcerative colitis — a form of inflammatory bowel disease. The authors introduced the organoids into the animals' intestine using an enema, which is a drug-delivery method often used in humans. Remarkably, the transplanted organoids were found to attach to the damaged areas and generated an epithelium that was reminiscent of that of normal colon and contained all the relevant cell types. Furthermore, because the donor Lgr5-expressing cells were fluorescent, the researchers were able to trace the engrafted tissue and determine that it was still self-renewing 25 weeks after treatment. The treated mice gained more weight than untreated animals during the experiment, suggesting possible disease amelioration.

The authors' findings[1] have exciting implications. It has been shown[5,6] that organoids isolated directly from normal intestine contain stem cells, can engraft onto damaged gut epithelium, and can support long-term epithelial regeneration. However, the current study goes one step further by showing that donor stem cells can be expanded *in vitro* to grow large numbers of organoids, which can then be transplanted and successfully engrafted into a host with a damaged gut. Therefore, using these techniques, stem cells from a patient's gut could be cultured in the laboratory to generate organoids that could then be used to provide functional intestinal tissue to the original donor. The stem cells could be isolated from samples taken during routine diagnostic procedures such as gastrointestinal endoscopy. What's more, the authors' study suggests that an enema-based system might be a viable mode of delivery.

However, much work remains to be done before a similar treatment in humans could be considered. In addition to weight gain, other parameters that are indicative of accelerated tissue healing should be monitored in future studies. Such parameters include the lack of diarrhoea, of blood in stools and of microscopic tissue damage. It will also be crucial to show that the transplanted epithelium not only is apparently intact but also functions normally. In Yui and colleagues' work, the organoids were engrafted only on areas of damaged tissue, which could be a limitation for the application of this approach in patients with short-bowel syndrome, a disorder in which areas of the small intestine are missing because of surgery or a birth defect. For these patients, engraftment onto the residual, normal intestine — in addition to generation of muscle, nerves and connective tissue — would be required.

Furthermore, the authors report a low rate of engraftment — this would need to be optimized to achieve reasonable therapeutic efficacy. Although it is encouraging that Yui *et al.* did not detect precancerous changes or polyps in the mice up to 25 weeks after transplantation, longer observation periods will be required to fully address the safety of the therapy. Despite these caveats, the study represents an important step towards realizing the promise of stem-cell-based therapies for gastrointestinal disorders. ■

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