Regenerative dentistry

Tooth fairies

It may soon be possible for adults to grow new teeth

PAUL SHARPE, a dental researcher at King's College, London, is not too worried about eating sweets. As any dentist would be happy to remind him, such sugary treats will rot his teeth. But Dr Sharpe believes that his researches should one day enable him—and everyone else—to grow a completely new set of gnashers.

Although human babies are born without visible teeth, they have "proto-teeth" hidden in their gums. These proto-teeth, known as primordia, derive from an interaction between two basic cell types, called epithelial and mesenchymal cells. By culturing these cells, and putting them together as they would come together naturally, Dr Sharpe has managed to form an artificial primordium.

To do so, he starts with human neural stem cells (these are undifferentiated cells similar to those found in embryos, and which are capable of developing into a variety of cell types). He aggregates his stem cells into small pieces of tissue, then overlays a piece of oral epithelium on them. The cells of oral epithelium already know they are supposed to become part of a tooth, and they "instruct" the stem cells to turn into oral mesenchymal cells. When the resulting primordium is transplanted into a mouse kidney (a good environment for this sort of thing, since it is well supplied with blood and oxygen) it turns into a tooth.

Dr Sharpe has dubbed this area of research "regenerative dentistry". His hope is that it will become possible to implant the primordium into a patient's gum, in the place of a removed or lost tooth. After implantation, it would grow, form roots that would attach themselves to the jaw, and eventually erupt into the mouth after only a few weeks.

For the process to work reliably, however, it will be necessary to persuade the primordium to develop into a full-fledged tooth. This would be done by activating appropriate genes. The trick remaining is to identify exactly which ones. Though thousands of genes are involved in the development of an organ such as a tooth, these genes are switched on in a cascade, with the activity of one triggering the activation of the next. So it is only necessary to identify, and kick-start, the first genes in the cascade, which are likely to be few in number. One such gene that has already been identified is called Barx1. This gene is expressed only in cells in primordia that are destined to become molars, so it is probably a gene that controls the shape of a tooth.

With populations in rich countries getting long in the tooth, as it were, it seems likely that there will be a huge demand for regenerative dentistry. To exploit that demand, Dr Sharpe has started a company called Odontis. If it succeeds in commercialising his stem-cell technology, its shareholders will, indeed, have plenty to smile about. ■

Ripe for growth

Small-scale physics

Atto boy!

The shortest time yet measured, and the most sensitive set of scales

PEOPLE who think "nano" is the epitome of smallness should think again. A nanosomething is but a billionth of that something. Two new pieces of research concern themselves with attosomethings—billionths of the nano.

Ferenc Krausz, of Vienna University of Technology, and his colleagues, are concerned with attoseconds. They have just published a paper in *Nature* which describes their measurement of the shortest time interval ever recorded, a mere 100 attoseconds. Meanwhile, across the Atlantic, at Cornell University, Harold Craighead and his colleagues have succeeded in building a set of scales that are sensitive to a fraction of an attogram. Their work is due to appear in a forthcoming paper in the *Journal of Applied Physics.*

Dr Krausz's achievement was a byproduct of his studies of the orbitals of electrons around atomic nuclei. Quantum theory makes precise predictions about the energy of those orbitals, and Dr Krausz was checking that those predictions are correct. (They are.)

To measure the energy in question, he used two successive pulses of laser light, each 250 attoseconds long. The first knocked electrons free from their orbitals. The second scattered them. The scattering changed the momentum of the electrons in a way that depends on their original orbital position. Momentum is mass times velocity, but all electrons weigh the same, so measuring their velocity was enough.

Enough. But tricky. Dr Krausz did it by recording the arrival times of different electrons using a piece of equipment called a multi-channel plate detector. And he needed to be able to tell them apart as precisely as possible, to avoid recording two arrivals as one.

In this case "as precisely as possible" meant within 100 attoseconds. That is the limit imposed by Heisenberg's famous uncertainty principle (which states that the precision of a time measurement is limited by the precision of a corresponding energy measurement). And by careful crafting of the scattering pulses he was able to go all the way to that limit.

This sort of work is pretty abstruse. Dr Craighead and his colleagues have a more concrete goal in mind: identifying viruses by weighing them. Different sorts of viruses have different weights, but all viruses of a particular type weigh the same amount.

Dr Craighead created his tiny scales from crystals of silicon. Using beams of electrons, he carved a cantilever out of the edge of each crystal (think of a knife held down on a table, with the blade sticking out). Put an object on the end of such a cantilever and the lever will bend. It will also tend to vibrate at a frequency determined by the weight of the object. It was this vibrational frequency that the team measured.

Instead of actual viruses, Dr Craighead weighed small amounts of gold. The smallest was 0.39 attograms—about 10,000 atoms. That level of sensitivity should be enough to identify viruses, but it is not enough for Dr Craighead. By refining the system further, he expects to be able to weigh a zeptogram—a thousandth of an attogram. Move over nanotech, it seems that zeptotechnology is just around the corner.