I bet you didn't know...

How to grow a new skin

Dr. Alison Trew, South West PSTT Area Mentor, links **cutting edge research** with the **principles of primary science**

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"SCIENTISTS GROW REPLACEMENT SKIN FOR BOY!"

But how much skin did they need and how did they stick it on?

It wasn't until I began work as a research scientist, in the Department of Dermatology at the University of Newcastle, that I heard the skin described as an organ.

I always thought of organs as internal structures (heart, lungs, liver and so on), each having its own special function. Well, we all do indeed have an external organ – the skin, and it, too, has important functions (see Figure 1). **This is something we can ask primary school children: what do you think the skin is for? What would happen if your skin came off?**

Children will probably suggest that skin is necessary to keep everything inside and stop their insides falling out. This is true, but what else? With a little prompting to look closely at the similarities and differences between skin from different areas of their bodies (get out the magnifying glasses), between different humans, or between different animals (a few photos will stimulate a discussion), children can develop their scientific literacy and by learning to justify their ideas, recognise that there may not be a single correct answer.

What colours are skins? Does the colour ever change? Does colour matter? Why does skin sometimes feel wet? Where does this wetness come from? Do you have hair everywhere? What is it for? What makes it grow? Can you stop hair growing? Why does it change colour? If scientists knew how to make hair grow, would we see any bald people? There are certainly scientists working on this, but also claims that have little scientific support! A discussion like this helps children appreciate that science cannot always give all the answers.

So, skin is amazing and does more than you first thought, but sometimes it doesn't work properly. Very recently, a nine-year-old Syrian boy was in the news because scientists were able to grow a replacement skin for him (see Figure 2) [1,2]. The boy was suffering from a rare illness called junctional epidermolysis bullosa (JEB) which caused the loss of 80% of his skin, leaving him covered in untreatable, infected, life-threatening wounds. JEB is caused by a mutation in a gene (LAMB3) that produces a protein (laminin 332) which anchors the epidermis (the top layer of cells) to the deeper layers of skin cells beneath. Without this protein, the skin blisters and the surface layer can be lost. You could share a short film clip with your class which introduces the boy and explains what happened to him [3].

Every child has experienced losing a part of their skin, often through falling over in the playground. They will be able to talk about how this felt and imagine what it might be like to have a wound over almost all of their body. So, why did the boy's skin fall off? Let's start by thinking about why our skin doesn't skin peel off if there is a hole in it. It is because the skin is made up of layers of cells. Normally the layers are 'glued' together by special proteins. We can model this in the classroom: layers of coloured paper or card can be glued together and compared with layers that are not glued – the top layer will slide off. Children may come up with other models using Lego, bricks, plasticine, etc. The main point to emphasise is that the top layer of skin slides off easily if the anchor protein is missing.

How does our skin repair itself? Normally, the top layer of skin cells is constantly renewed by stem cells contained in the deeper layers of skin. The turn-over of cells is about a month (see Figure 3).

Next, consider what the scientists have achieved. How did they grow the new skin in a laboratory? I know that this is difficult because I spent almost two years growing epidermal cells in culture flasks. It can take days, working in sterile conditions, to cover a 250 ml flask with cells, and then discover a fungal infection has rendered the flask useless! The team of Italian Scientists used a 4 cm^2 sample of boy's healthy skin (about the size of a postage stamp) and used a virus to insert the healthy LAMB3 gene into the stem cells' nuclei. This meant that the missing anchor protein could now be made. These genetically modified stem cells were grown into sheets of skin of 50 - 150 cm^2. In two surgeries, another team covered the boy's arms, legs, back, and some of his chest in the new skin. Two years later, the boy has no blisters and is living a normal life.

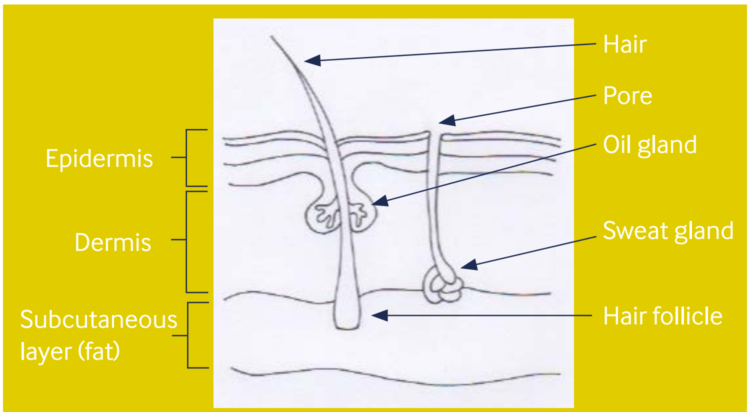

Figure 1: Cross-section of human skin. As well as hair follicles, sweat glands and oil glands, the dermis contains nerve endings and blood vessels.

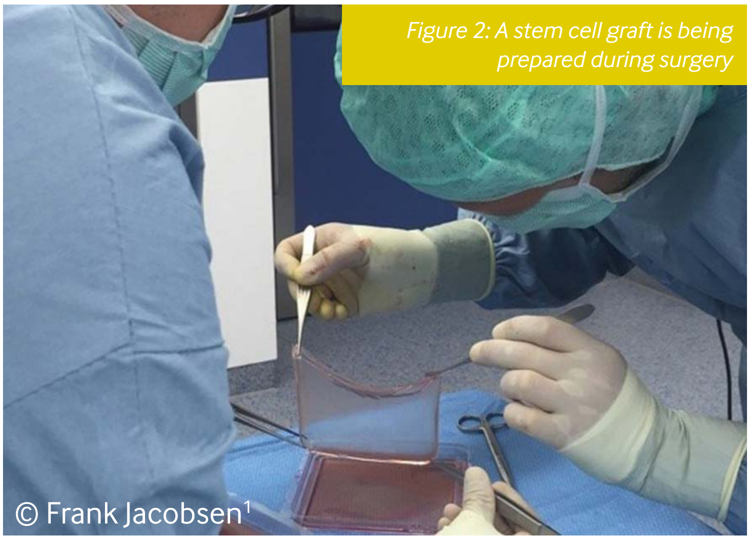

Figure 2: A stem cell graft is being prepared during surgery

To give children an appreciation of the size of cells, it would be worth looking at some cells[2] down a microscope (borrowed from a local secondary school or the Royal Microscopical Society has a lending scheme if you don't have your own). Then consider what size of skin is needed. Younger children could explore this by simply wrapping large pieces of sugar paper or fabric around their trunk and limbs and laying it out on the floor to see what their surface area looks like. Older children could measure the circumference and length of each limb and central body to calculate an approximation to the actual surface area of their body.

Whilst genetically modified epidermal cells have been successfully transplanted onto a patient's legs before, this is the first regeneration of an entire human skin from transgenic stem cells. It is possible, that in the future, other genetic skin diseases may be treated by targeting stem cells.

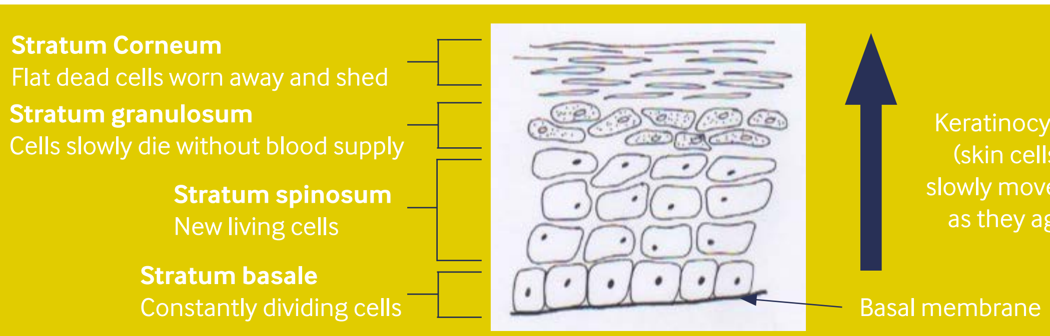

Figure 3: Cross-section of human epidermis. Stem cells in the basal layer (stratum basale) are responsible for the constant regeneration of the different layers of the epidermis.

References

[1]. T. Hirsch, et al. Nature 551, 327–332 http://dx.doi.org/10.1038/nature24487

[2]. https://www.newscientist.com/article/mg23631514-400-boy-with-a-genetic-disease-has-had-almost-all-his-skin-replaced/

[3]. https://www.youtube.com/watch?v=ZIjWJcz86PI

[1] Use of this image only permitted in connection with reporting of this activity. http://news.rub.de/english/press-releases/2017-11-08-worldwide-unique-boy-given-new-skin-thanks-gene-therapy

[2] CLEAPSS have a recommended procedure for looking at cheek cells http://science.cleapss.org.uk/Resource/PP033-Staining-and-observing-cheek-epithelial-cells.pdf

However, this is not permitted in Northern Ireland.