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Trans-Gender Induction of Hair Follicles

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Human follicle cells can be induced to grow in an incompatible host of the other sex.

Adult hair growth and the cyclic regeneration of hair follicles are driven by finely regulated interactions between dermal and epidermal tissue at the base of the follicle 1,2. In rodents, isolated hair-follicle dermal cells that are reintroduced in vivo can induce new follicles 3,4 , but this has never been achieved in humans. Despite the great advances in human tissue and organ transplantation, rejection processes severely restrict the transfer of cells between immunologically incompatible individuals, although the hair follicle is considered to be one a group of organs that display 'immune privilege' 5.

Here we show that transplantation of human follicle dermal sheath tissue between incompatible individuals of different sex can induce the formation of new hair follicles.

To test the inductive and immunoreactive properties of human hair follicle dermis, we micro-dissected dermal sheath tissue from the base of scalp skin follicles of one of us (C.A.B.J.), a male. We implanted this tissue into shallow skin wounds on the inner forearm of another one of us (A.J.R.), a genetically unrelated and immunologically incompatible female recipient (Fig. 1a-f).

Five months later, the same female received grafts of follicle dermal sheath and dermal papilla from the same male donor and, in a third experiment, dermal sheath from a second unrelated male donor.

All the wound sites healed rapidly and lacked any overt inflammatory reaction. Remarkably, each of the sites of dermal-sheath implantation produced new follicles and fibres 3 to 5 weeks after the graft (Fig. 1g). Unlike the tiny, unpigmented vellus hairs of the arm, the newly induced hairs were larger and thicker, mostly pigmented, and grew in variable directions. None of the new follicles showed evidence of rejection when biopsied between 41 and 77 days after the graft. Histology confirmed that the new follicles were morphologically normal, with oval dermal papillae overlaid by a pigmented epidermal matrix at their base. We observed a light inflammatory infiltrate around the upper regions of one specimen.

To demonstrate that the follicles were induced by the implanted dermal tissue, we analyzed DNA from our histological specimens. We used laser capture microdissection 6 to isolate dermal papilla cells from one of the follicles (Fig. 1h) and performed polymerase chain reaction (PCR)-based gender determination and restriction analysis of

simultaneously amplified ZFX and ZFY sequences 7. This confirmed that the DNA extracted from the papilla cells had an X and Y complement (and was therefore male), whereas cells taken from other regions of the same follicle and epidermis in the immediate vicinity had only X chromosomes and so were female (Fig. 1i).

We have shown that just a few hundred cells of follicle dermal-sheath tissue from the scalp of an adult human male was sufficient to form new dermal papillae and induce new hair follicles in the skin of a genetically unrelated female. Moreover, these follicles survived prolonged periods without being rejected. However, the failure of the dermal papillae to induce follicles is surprising because the papilla has previously been shown to be highly inductive 4.

The formation of follicles requires inter-action between the host epidermal and donor dermal cells, which can occur only if the male tissue is tolerated. Our donor and host were different with regard to blood group and major histocompatibility complex (MHC), but there was no strong evidence of graft rejection, even after repeated grafting, when a rapid second-set rejection might have been expected.

Grafts are more likely to be tolerated if there is no coincidental transfer of passenger leukocytes, which express the donor's class II MHC molecules, Langerhans cells or blood-vessel endothelial cells, all of which can stimulate the host's alloreactive response 8,9

We washed the tissue repeatedly to remove adherent cells and it was unlikely to have included blood vessels. Small-scale tissue damage, which can also trigger the host's immune response 10, was also negligible in our minimally invasive procedure.

But, the main reason why the graft was not rejected probably lies with the tissue itself. Immuno-histochemical investigations have previously indicated that the lower-most tissues of rat and human hair follicles have special immune status 11.

Our findings support this idea and further indicate that the follicle-end bulb dermal sheath is
among a restricted group of immuno-privileged tissues that can be transplanted to foreign
sites without being rejected 5.

Our results show that follicle dermal cells from a human adult can initiate epithelial-mesenchymal interactions and create new follicles without being rejected. This mini-organ morphogenesis shows how adult cells with inductive properties might be used in tissue and organ engineering and, more immediately, might be used in new treatments for hair loss.

This work was approved by the Newcastle Health Authority Joint Ethics Committee, the University of Newcastle upon Tyne.