Back to the Future

Gabriel is 78 years old. The photos below show his hairline from 1945 through today.

The Status of Cloning in 2004

By Robert Bernstein, M.D.

Almost every day we are asked: “When will cloning be available to produce that unlimited supply of hair we dream of?” Too many people (and some doctors as well) are hyping the idea that cloning is just around the corner. So, for those still holding their breath, we have put together a brief summary of the various processes that can potentially lead to that unlimited supply of hair.

What is Cloning?

Cloning is the production of genetically identical organisms. As we all know, the first clone of an adult animal was Dolly, the famous Edinburgh sheep. Although technically not an exact replica of her mother (and therefore not a true clone), Dolly overturned the long-held view that non-sex cells (somatic cells) of an adult were differentiated to such a degree that they lost any potential to develop into a new adult organism. Scientists had believed that once a cell became specialized as a lung, liver, or any other type of adult cell, the change was irreversible. The other major challenge was to be able to initiate the multiplication of the genetically altered cell and provide the proper growth environment for the new organism.

With Dolly, scientists transferred genetic material from the nucleus of a donor adult sheep cell to an egg whose nucleus, and thus its genetic material, had been removed. Once the donor DNA was added, the egg had to be treated with chemicals or an electric current in order to stimulate cell division. When the cloned embryo reached a suitable stage, it was transferred to a very hospitable environment – the uterus of another sheep – where it continued to develop until birth.

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FOX™ Procedure: (Follicular Unit Extraction)

By William Rassman, M.D.

The FOX™ procedure, where individual follicular units are extracted from the donor area without a traditional linear incision, was described in our paper “Follicular Unit Extraction: Minimally Invasive Surgery for Hair Transplantation” published in Dermatologic Surgery in 2002. The technique has been attempted by many doctors and remains controversial because of the difficulty in performing the procedure and in obtaining consistently good results.

At the recent annual meeting of the International Society of Hair Restoration Surgery in New York, doctors discussed
Cloning vs. Genetic Engineering

In contrast to replicating whole organisms, in genetic engineering one alters the DNA of a particular cell so that it can manufacture proteins to correct genetic defects or produce other beneficial changes in an organism. The initial step in genetic engineering is to isolate the gene that is responsible for the problem. The next step is to clone (multiply) the gene. The last step is to insert the gene inside the cell so that it can work to alter bodily function.

Dr. Angela Christiano at Columbia University discovered the first gene causing hair loss in humans. Individuals with this gene are born with hair similar to infant hair that falls out, but, unlike infant hair, it never grows back. They mapped the disease to chromosome 8p21 in humans and cloned a related hair loss gene in mice. Although a huge step forward, this mouse gene is not the same as the one(s) causing common baldness. Fortunately, Dr. Christiano’s lab continues its work to isolate the genetic material responsible for androgenetic alopecia. We will keep you posted on their progress.

What is Hair Multiplication?

In hair multiplication, hairs are simply plucked from the donor area and then implanted into the bald part of the scalp. The idea is that some germinative cells at the base of the hair follicle will be pulled out along with the hair. Once the hair is re-implanted, these cells would be able to regenerate a new follicle. In theory, microscopic examination of the plucked hair could help the doctor determine which hairs have the most stem cells attached and thus which are most likely to regrow. The procedure is called “hair multiplication” since the plucked follicles would regrow a new hair, potentially giving an unlimited supply.

In a modification of this procedure, the bulbs of the hair are separated from the shafts and then cultivated in vitro (outside the body). After the cells are multiplied, they are injected into the pores of local, dormant hair follicles in the balding area. The problem with both techniques is threefold: the matrix keratinocytes (the plucked cells) are only transient amplifiers (limited in nature); the important stem cells around the bulge region of the follicle are currently not harvested in significant numbers; and the stem cells can’t be readily activated to produce a hair.

The Hair Cloning Model

When it comes to cloning, hair follicles are in a tough spot. They are too complex to be simply cultured (growing hair follicles in a test tube would be like trying to grow a set of teeth) and follicles are not whole organisms (like Dolly) and, therefore, cannot be cloned outright. Fortunately, a pair of clever scientists, Drs. Amanda Reynolds and Colin Jahoda (now working with Dr. Christiano), seem to have made great headway in solving this dilemma.

They have shown that dermal sheath cells, found in the lower part of the human follicle, can be isolated from one person and injected into the skin of another to promote the new hair formation. The implanted cells interact locally to stimulate the creation of full terminal (i.e. normal) hair follicles. Although this is not actually cloning, the dermal sheath cells can potentially be multiplied in a Petri dish and then injected to produce a full head of hair. We highlight the word potentially, as multiplication has not yet been accomplished. It seems, however, that the hair “induction” process is the model most likely to work.

Another interesting aspect of their experiment is that the male donor cells grew hair in a female recipient, showing that donor cells can be transferred from one person to another without being rejected. In this experiment, repeat implantations did not provoke typical rejection responses even though the donor was of the opposite sex with a significantly different genetic profile. This indicates that the dermal sheath cells have a special immune status. One of the body’s "immune privileged" sites is the lower two-thirds of the hair follicle.

In addition, there is evidence that recipient skin can influence hair appearance. Thus, the final look of the patient may more closely resemble the recipient’s original hair than that of the donor. A person-to-person transfer of cells is important in situations where there is a total absence of hair. Fortunately, in androgenetic alopecia (genetic hair loss) there is a supply of hair on the back and sides of the scalp to serve as a source of dermal sheath cells, so such person-to-person transfers would rarely be necessary.

Probably the most important aspect of this experiment is that the “inducer” dermal sheath cells are fibroblasts. Fibroblasts are among the easiest of all cells to culture, so, the donor area could potentially serve as an unlimited hair supply.

What Needs to be Done

At the 2003 meeting of the ISHRS, Dr.
Jerry Cooley succinctly pointed out the problems that still confront us in cloning hair (or what he more accurately terms ‘Follicle Cell Implantation’). First, there is the need to determine the most appropriate follicular components to use (dermal sheath cells, the ones used in the Collin/Jahoda experiment, are hard to isolate and may not actually produce the best hair). Next, these extracted cells must be successfully cultured outside the body. Third, an introduction of a cell matrix might be needed to keep the cells properly aligned while they are growing. Finally, the cells must be successfully injected into the recipient scalp and consistently induce hair growth.

Unlike Follicular Unit Transplantation (FUT), in which an intact follicular unit is planted into the scalp in the exact direction the surgeon wants the hair to grow, cell implantation provides no guarantee that induced hairs will grow in the right direction or have the color, hair thickness or texture to look natural. To circumvent this problem, one might use induced hair in the central part of the scalp for volume and then use traditional FUT to create a natural appearance. However, it is not certain that induced follicles will grow long enough to produce cosmetically significant hair. And once that hair is shed in the normal hair cycle, there are no assurances that it will grow and cycle again.

A major technical problem is that cells in culture begin to de-differentiate as they multiply and revert to acting like fibroblasts, rather than hair. Finding the proper environment to maintain a differentiated (hair-like) state appears to be the single greatest challenge preventing this form of therapy from becoming a reality. Similarly, the environment where embryonic cells grow is the key to proper differentiation and survival when cloning entire organisms.

Finally, although remote, there may be safety concerns that hair-inducing cells could also induce tumors, or exhibit malignant growth. Once these obstacles have been overcome, there are still FDA requirements ensuring further testing to measure effectiveness. This process involves three very formalized stages of clinical testing and generally takes years.

On the status of cloning – it is still a work in progress. Although there has been recent success and we finally have a working model, much still needs to be done. Hold onto your hats; the final product is still years away.

New Life at 50
I often receive letters from patients that make my day. J.T. was a patient, like many, who couldn’t wait to see his results. After reading his letter, a big smile ran across my face. I think his words say it best. - Dr. R.

Dr. Rassman,
I can’t believe the results of my hair transplant. I had completely told myself that I would never go out in public without a baseball cap. You might remember the day I came in for my consultation – you happened to be in the office that day. I told you I was tired of looking like a “dog with mange.” My hair loss was class 7 but receding irregularly, so I looked very odd.

It is just 6 months after about 1,900 grafts and your wonderful female assistants told me I was going to be very happy with my results. They couldn’t have been more precise. My hair is coming in excellent and I can’t wait to come back to your facility in 4 to 5 months to show you the results. I’ll make a decision then to see if I want another procedure. I’ve read it before in your brochures and was a little skeptical, but I look great. I even got rid of my hats. You’ve truly changed my life at 50 years old. Thank you!

- J.T.

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FOX™ Procedure: (Follicular Unit Extraction)

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their experience with the Follicular Unit Extraction (FUE) procedure and the challenges that it poses for the practitioner. The frustration in performing this technically difficult procedure was bantered about by many physicians in a series of ‘talks’ on the subject. Two of the doctors were scheduled to perform a live demonstration at a workshop during the symposium. One cancelled before the meeting and the other suddenly left town the morning of the scheduled surgery. Many of the attendees wondered if this was “telling” of an over-hyped procedure.

We have made improvements in the FOX™ procedure by designing instruments which facilitate the removal of hair follicles from the donor area through the very small incisions. Approximately 90% of patients are now candidates for a procedure which originally was much more restrictive. This procedure remains an exciting advance. The promise of an almost scar-less surgery is enticing to both the patient and the surgeon. However, the difficulty in performing the procedure makes it illusive to both.

The major limitation of the Follicular Unit Extraction (FUE) procedure is the inability to harvest as much donor hair as with Follicular Unit Transplantation (FUT); either in an individual session or in the long-term. With FUE, the surgeon only removes select follicles from the mid-portion of the permanent zone. In FUT, due to single strip harvesting and stereo-microscopic dissection, all the follicles can be used, making the total yield in the FUT procedure much greater.

Despite few physicians having any long-term experience with the technique, without adequately discussing the long-term limitations. For the surgeon, the learning period is lengthy and the risks of less-than-desirable fullness are distinct. Inexperienced surgeons will have to confront these realities, as patients may not receive their promised results.

Indications for the FOX™ procedure:

This procedure should be confined to special cases since there is a limit on graft harvesting in a single session (range 300-900).

- Low Demand / High Supply - people who require small sessions and those with little anticipated hair loss.
- Aesthetic Needs - no linear scarring for those who act, model or easily scar.
- Scar Treatment - the treatment of scars resulting from traditional strip excision. This includes those who have scars for any reason (i.e. head trauma).
- Other Transplants - Eyebrow, eyelash, beard or other similar transplants.

Recent claims that body hair will be an alternative source for head hair transplants have been appearing in various internet promotions. Without any published results in any medical forum, others are using the FOX™ procedure to remove body hair in some patients. Although I am enthusiastic to learn from the experience of others, I remain skeptical of the various incarnations of this procedure that have been put forth without a scientific foundation and without results appearing in formal publications. Time will tell much.

ANNOUNCEMENT: There is no longer a fee for performing the FOX™ test.