Good Golly, Miss Dolly!

Les Hearn looks at the realities of cloning

THE recently announced cloning of the sheep "Dolly", using DNA from a cell from the body of another sheep, is an important breakthrough. It suggests that the specialisation of cells as an animal develops may not be irreversible, as previously thought.

All the cells in an organism, be it animal, plant or fungus, carry the complete instructions in the form of DNA for making that organism. Nevertheless, after quite a short time in the life of an embryo, each cell develops in a special way, with its own function. This process is called differentiation.

In some organisms this process can be reversed; one of these cells can be induced to develop into a new individual. This will be genetically identical to the old one, in other words, a clone. In many plants a single cell or group of cells from one part may grow into a complete new plant which is a clone of the original. This may occur naturally or artificially. However, in animals, this can usually only occur in the very young embryo, with very few cells. This is how identical twins arise. Later, the cells seem to become fixed in their destiny to become part of a tissue or organ. They still contain all the DNA but it seems to have been partially deactivated. Only the genes needed for that organ or tissue are "switched on".

The problem of how differentiation occurs has been one of the major themes of developmental biology. Cloning from mature body cells represents a reversal of that process and the knowledge gained could be invaluable in understanding such problems of development as cancer or regeneration of damaged spinal cords. In agriculture, valuable animals or plants, perhaps developed by genetic engineering, could be cloned.

Over 20 years ago, frog cells from gut and skin were successfully cloned. This did not represent such a great breakthrough, though, as differentiation in amphibians was known to be less permanent. Even whole limbs can regenerate if lost by accident. Unfortunately, mammals cannot regenerate even a lost toe, while the inability of severed spinal nerves to regenerate is the cause of much paralysis among human accident victims. This makes the cloning of Dolly all the more impressive.

The process involved the following steps:

- An udder cell was removed and kept in a salt solution with minimal nourishment. This put the cell in a state of hibernation, with its genes shut down.
- An egg cell from another sheep had its DNA removed.
- The two cells were placed together and induced to fuse with a small electric current.
- The egg cell somehow reprogrammed the DNA from the udder cell and allowed it to direct the development of a complete individual. (The mechanism of this will be the subject of intensive research for years to come.)

Dolly the sheep is genetically the identical twin of the owner of the udder. Her genetic parents are the parents of the "udder" sheep; her birth parent is the sheep that carried her foetus to term. This situation parallels that of human identical twins born to different women at different times, through the mediation of In Vitro Fertilisation techniques.

The presentation of Dolly to the world has unleashed a torrent of ill-informed and alarmist speculation. The prospect of human cloning was immediately raised and Ian Wilmut, a member of the cloning team, gave his view that this could be possible within two years. This is undoubtedly true since the most technically difficult part has already been done. However, he also pointed out that human cloning would be illegal in Britain and in his opinion unethical.

Some of the speculation has been truly bizarre. *Die Welt* thought that cloning humans would fit into a Nazi world view and asked how long it would be before "a new Einstein, Lollobrigida or even Hitler populates the brave new world". This ignores the fact that identical twins are not the same people. Even in the womb, they do not experience exactly the same environment; nor do the same genes work in exactly the same way all the time.

The director of a fertility clinic in Britain thought that it might be possible to clone embryonic stem cells, that give rise to blood-forming tissues, immune cells, skin or gut cells. These could be used to replace tissues in people who had perhaps lost their own through cancer treatment. But he then speculated on the production of a matching human body with its brain removed from which spare parts could be taken. This would and surely should be illegal in every society. A cloned human is a human with the rights of a human. It is no more the property of the donor of the DNA than a child is the property of its parents.

The moral arguments over cloning humans will be debated for some time. Whatever the outcome, I believe there is a very good practical argument against. There is good reason to believe that a clone would live less long than the DNA donor. The explanation for this lies with things call telomores.

When a chromosome is duplicated during cell division, an enzyme called DNA polymerase has to attach to the end and then copy the chromosome. But the bit it attaches to is not copied. If this was part of a gene the cell would soon develop faults and die. Instead, there are several repeated segments called telomores. These are lost over time as the cell divides. Finally, there are none left and the cell stops dividing and eventually dies. The fertilised egg has the normal number of telomores but a cell from an adult has less. The egg of a clone would therefore start off with less than normal and should die younger, on average at the same time as the donor.

At the moment, cloning is a very hit and miss affair. Dolly was the only success out of 277 attempts. Given the telomore problem, it is difficult to see why anyone would want to go to all the trouble when they could get half their genes into a child in the normal way (and have more fun). In the meantime, natural human clones will continue to be born in their thousands, in the form of twins.