Lecture 17 – Applications for somatic cell nuclear transfer

Review of SCNT

As we have learned before, pluripotent stem cells can be produced via in vitro fertilization, reprogramming differentiated cells (iPSC), or doing somatic cell nuclear transfer

Both iPSCs and SCNT-derived cells do have some **epigenetic memory**, so the genes they express are not exactly the same as IVF-derived embryonic stem cells

We learned last time that this is partially a result of **histone modifications** that are resistant to reprogramming

Even though SCNT is inefficient, it is possible to do, and the efficiency can be improved with different activation protocols (like adding in chemicals that affect histone modifications).

What are the applications for reproductive and therapeutic cloning?

Cloning of livestock

Cows, pigs, sheep and goats are routinely cloned in the agriculture industry to support breeding for the best traits

For example, let's say a farmer has a particularly healthy dairy cow that produces a lot of milk. She will be mated a lot to hopefully produce many offspring with these same beneficial traits. This usually involves IVF and a surrogate to carry the embryos.

When she is too old to reproduce, the farmer can have her cloned and the cloned offspring will be used primarily for breeding.

Cloned livestock are generally not used for food (just for breeding), but the Food and Drug Administration in the U.S. has approved cloned livestock for food, so some clones probably do end up in the food supply.

De-extinction

SCNT can be used to create clones of endangered species to help increase their numbers

SCNT can also be used to bring back extinct animals, which is known as **de-extinction**

What is necessary for de-extinction using SCNT?

De-extinction has only been done once and the clone only lived for 10 minutes. Let's look at that example.

The extinct animal was the Pyrenean ibex, also known as the bucardo. This animal is similar to a goat.

It went extinct in 2000 and before the last individual died, researchers obtained a tissue sample, so they had somatic cells

They used enucleated oocytes from goats and a goat-ibex hybrid as the surrogate. The procedure was incredibly inefficient, but they did create a short-lived clone, demonstrating that it is theoretically possible to use SCNT for de-extinction.

Let's say that the bucardo had actually survived. *Do you see any problems they might encounter bringing back the entire species from clones of one animal?*

De-extinction can also be done by doing gradual genetic modifications on closely related species until you have recreated the genome of the extinct animal. De-extinction research is expensive and time-consuming work. *Is it worth it? Do you think we have a moral obligation to bring back extinct animals?*

Research into bucardo de-extinction has stalled due to lack of money for the research. Other research is working on bringing back extinct animals like passenger pigeons and the woolly mammoth. If you want to learn more about these efforts (only some involve SCNT), start with this website: http://reviverestore.org/

Mitochondrial replacement therapy

As mentioned earlier, human cloning could potentially be used to make new embryonic stem cell lines that match the patient who needs the stem cell treatment.

Although some researchers are still working on this, most people now are focused on iPSCs for autologous transplants.

There is a similar technique as SCNT called **mitochondrial replacement therapy** that has been used to help women produce a child without a mitochondrial disease

Mitochondria are cellular structures that are important for producing cellular energy (ATP). They contain their own DNA that is used to synthesize some of the mitochondrial proteins.

Interestingly, mitochondria come completely from the oocyte not the sperm, so all **mitochondrial DNA** in one person is the same as their mother's mitochondrial DNA.

Mutations in maternal mitochondrial DNA will also be passed on to all offspring. This is one case where embryo selection will not work, because all embryos will have the mutations.

If a potential mother has a mitochondrial disease caused by a mutation in her mitochondrial DNA and she does not want to pass on this disease to her child, then she can try mitochondrial replacement therapy.

In this procedure, a donor oocyte is used with healthy mitochondria. The nuclear DNA is removed and replaced with the nuclear DNA from the potential mother's oocyte.

This modified oocyte is then fertilized by sperm using normal IVF procedures.

Thus, the child will have nuclear DNA from the mother and father, but mitochondrial DNA from the oocyte donor – genes from 3 people!

The mitochondrial DNA, though, only makes up 0.1% of all the genes and doesn't have any genes for the way a person looks.

This therapy was recently approved in the U.K. It is not approved in the U.S. although doctors from the U.S. performed the procedure in 2016 in Mexico and the mother had a seemingly healthy baby.

What do you think about this? Any ethical issues beyond the usual anti-IVF arguments?