Høring om terapeutisk kloning og forskning i menneskelige befrugtede æg og fosteranlæg

Christiansborg 1-133 onsdag 30. november 2005 kl 13-15

Professor dr. med. Thomas G. Jensen

Kennedy Instituttet

Nature 1996 Mar 7;380(6569):64-6

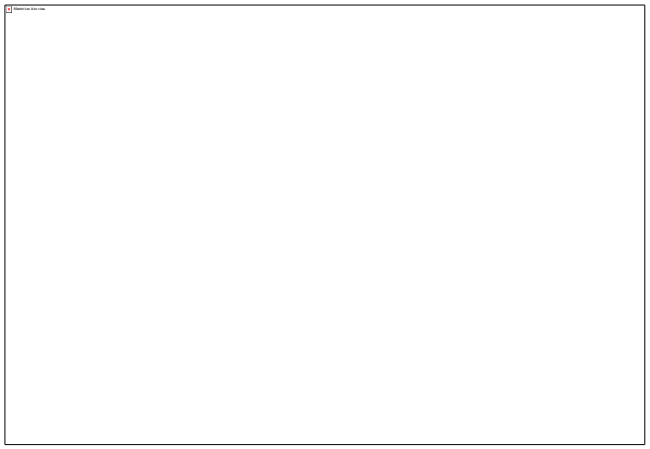
Sheep cloned by nuclear transfer from a cultured cell line.

Campbell KH, McWhir J, Ritchie WA, Wilmut I.
Roslin Institute (Edinburgh), UK.

Nuclear transfer has been used in mammals as both a valuable tool in embryological studies and as a method for the multiplication of 'elite' embryos. Offspring have only been reported when early embryos, or embryo-derived cells during primary culture, were used as nuclear donors. Here we provide the first report, to our knowledge, of live mammalian offspring following nuclear transfer from an established cell line. Lambs were born after cells derived from sheep embryos, which had been cultured for 6 to 13 passages, were induced to quiesce by serum starvation before transfer of their nuclei into enucleated oocytes. Induction of quiescence in the donor cells may modify the donor chromatin structure to help nuclear reprogramming and allow development. This approach will provide the same powerful opportunities for analysis and modification of gene function in livestock species that are available in the mouse through the use of embryonic stem cells.

A cat cloned by nuclear transplantation.
Shin T, Kraemer D, Pryor J, Liu L, Rugila J, Howe L, Buck S, Murphy K, Lyons L, Westhusin M.
Nature 2002 Feb 21;415(6874):859

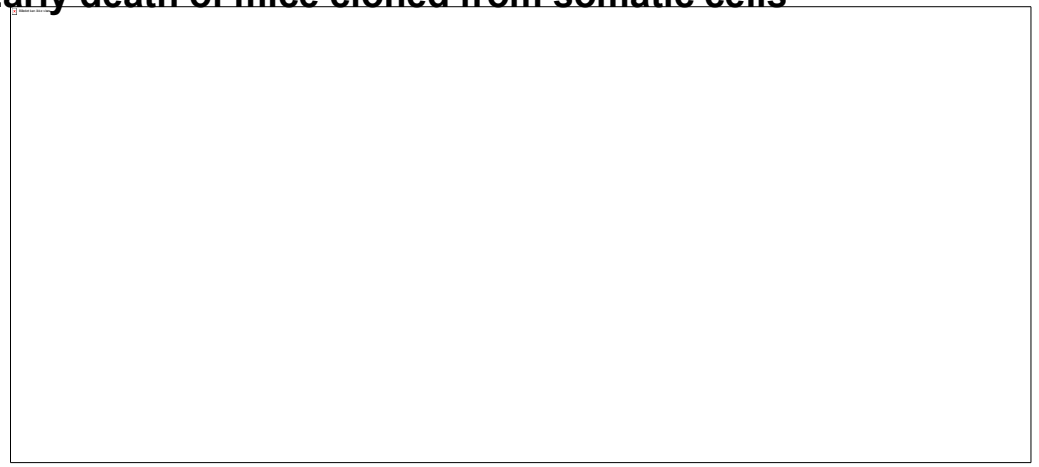
Cloning of male mice from adult tail-tip cells.
Wakayama T, Yanagimachi R.
Nat Genet 1999 Jun;22(2):127-8



Plus: Cattle, goats, pigs...

11 February 2002, DOI:10.1038/ng841
Nature Genetics
volume 30 no. 3 pp 253 - 254

Early death of mice cloned from somatic cells



DOI:10.1038/nm0302-262
March 2002 Volume 8 Number 3 pp 262 - 267

Cloned mice have an obese phenotype not transmitted to their offspring

DOI:10.1038/nm0302-215
March 2002 Volume 8 Number 3 pp 215 - 216

Are there any normal cloned mammals?

Ian Wilmut

Patient-specifikke embryonale stamceller:

Evidence of a pluripotent human embryonic stem cell line derived from a cloned blastocyst.
Hwang et al
Science. 2004 Mar 12

Patient-specific embryonic stem cells derived from human SCNT blastocysts.
Hwang et al
Science. 2005 Jun 17

- Medfødt hypogammaglobulinæmi
- Rygmarvslæsion
- Type-1 diabetes

Patient-specific, immune-matched human embryonic stem cells (hESCs) are anticipated to be of great biomedical importance for studies of disease and development and to advance clinical deliberations regarding stem cell transplantation. Eleven hESC lines were established by somatic cell nuclear transfer (SCNT) of skin cells from patients with disease or injury into donated oocytes. These lines, nuclear transfer (NT)-hESCs, grown on human feeders from the same NT donor or from genetically unrelated individuals, were established at high rates, regardless of NT donor sex or age. NT-hESCs were pluripotent, chromosomally normal, and matched the NT patient's DNA. The major histocompatibility complex identity of each NT-hESC when compared to the patient's own showed immunological compatibility, which is important for eventual transplantation. With the generation of these NT-hESCs, evaluations of genetic and epigenetic stability can be made. Additional work remains to be done regarding the development of reliable directed differentiation and the elimination of remaining animal components. Before clinical use of these cells can occur, preclinical evidence is required to prove that transplantation of differentiated NT-hESCs can be safe, effective, and tolerated.

Kombineret gen- og embryonal stamcelleterapi:

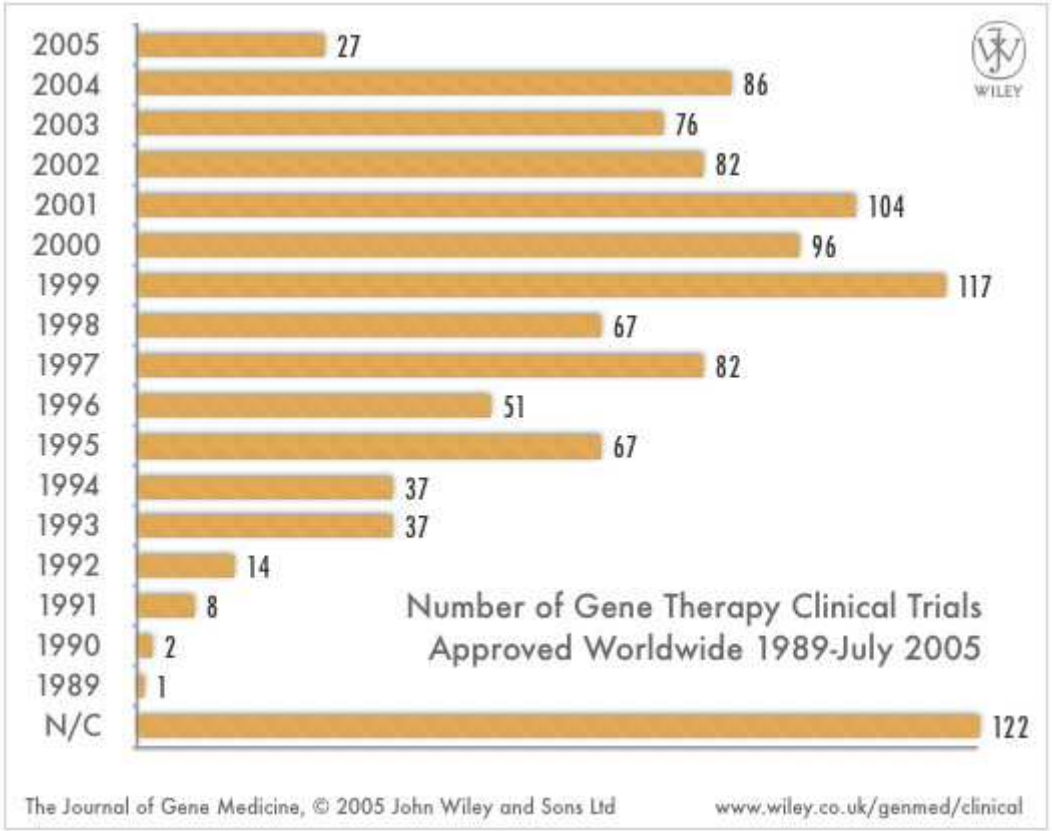
Correction of a genetic defect by nuclear transplantation and combined cell and gene therapy

Immune-deficient Rag2(-/-) mice were used as nuclear donors for transfer into enucleated oocytes, and the resulting blastocysts were cultured to isolate an isogenic embryonic stem cell line. One of the mutated alleles in the Rag2(-/-) ES cells was repaired by homologous recombination, thereby restoring normal Rag2 gene structure. Mutant mice were treated with the repaired ES cells in two ways. (1) Immune-competent mice were generated from the repaired ES cells by tetraploid embryo complementation and were used as bone marrow donors for transplantation. (2) Hematopoietic precursors were derived by in vitro differentiation from the repaired ES cells and engrafted into mutant mice. Mature myeloid and lymphoid cells as well as immunoglobulins became detectable 3-4 weeks after transplantation. Our results establish a paradigm for the treatment of a genetic disorder by combining therapeutic cloning with gene therapy.

Jaenisch et al, Cell 2002

Kliniske genterapi-projekter der har vist effekt

- Arvelige immundefekter - tre forskellige former (24/27 kureret. 26/27 i live)
- Nedsat blodforsyning - i benene og i hjertet
- Hoved-hals cancer
- Hjernesvulster
- Blødersygdomme
- Graft versus host disease
- Prostata cancer (fase 3 forsøg)
- Genterapi registreret som lægemiddel mod cancer i Kina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Number of Gene Therapy Clinical Trials
Approved Worldwide 1989-July 2005
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