Cloning technology

a researcher ‘s view of animal cloning

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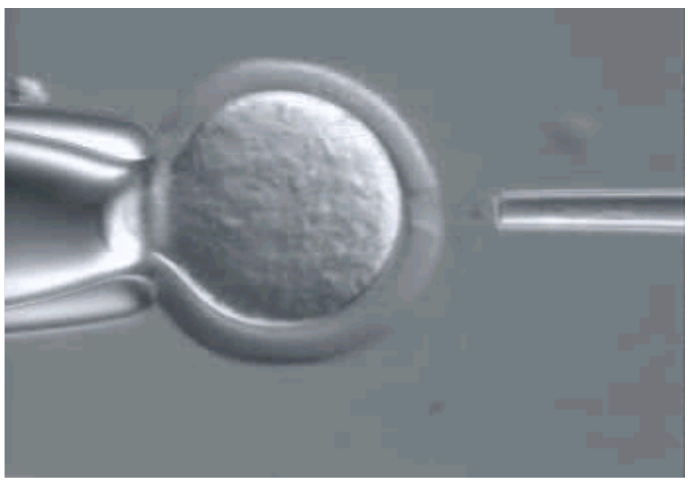
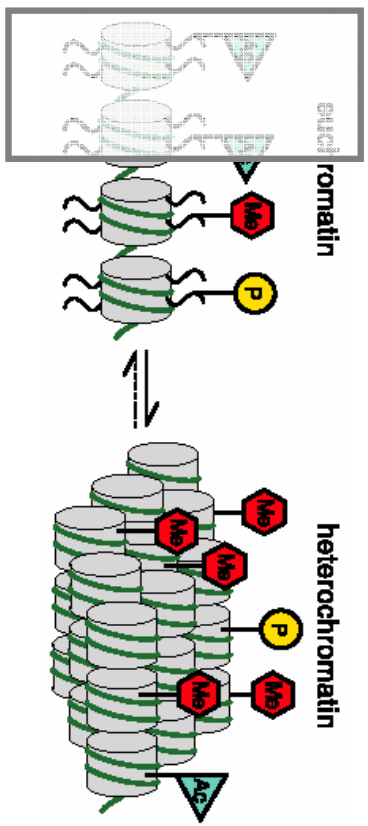
A Cloning requires the reprogramming of nuclear activities

- Cloning is the technique of somatic cell nucleus transfer SCNT

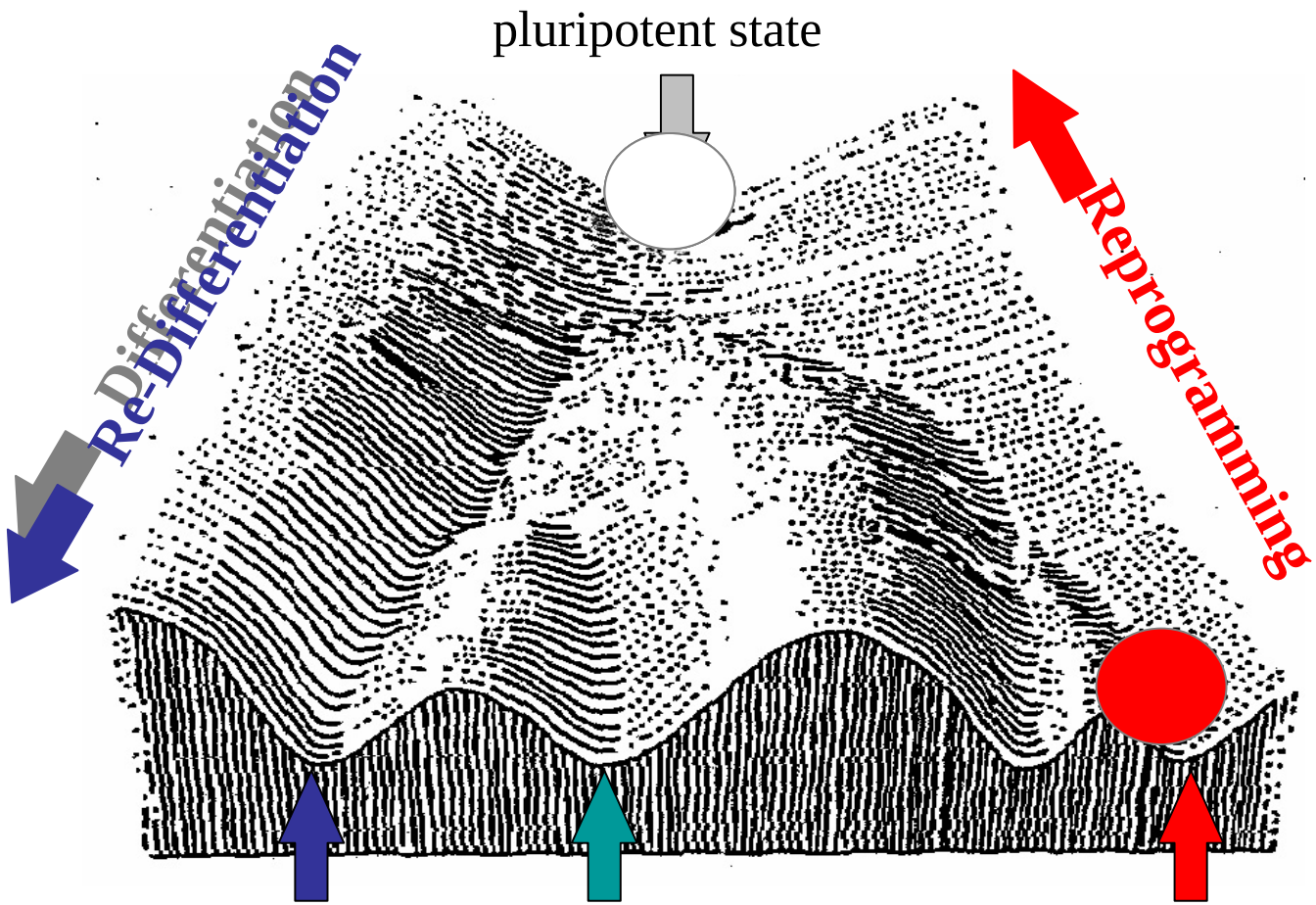


Reprogramming is an epigenetic-mediated process

Conrad Waddington: Epigenetic landscape and „canalization“



DNA methylation
Histone acetylation..



Sources: C. Waddington, Nature 1959; T. Jenuwein, Science 2002 modified: Timo C. Dinger & Albrecht Müller

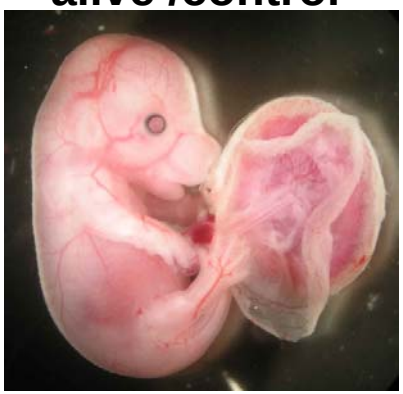
B

The low efficiency of cloning is the consequence of placental defects

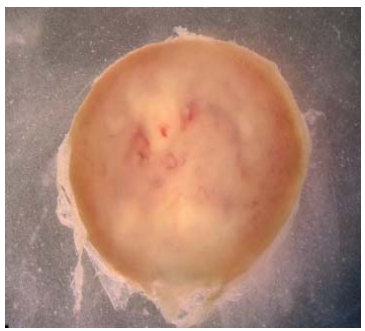
- Most of the clones that survive the perinatal period are healthy and of normal appearance. 10 to 20% of stillbirth
- The mortality rate of adult clones tends to be higher than for animals derived from sexual reproduction
- Long lasting consequences of reprogramming.

In the mouse placentomegaly of clones leads to oversised foetuses only from E15 onwards

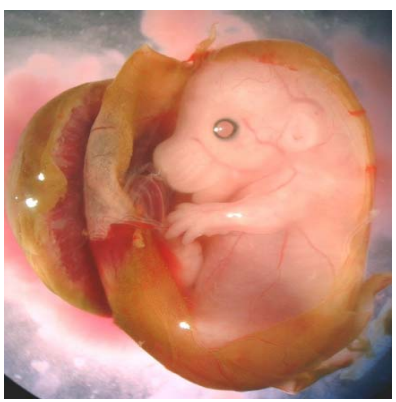
alive /control



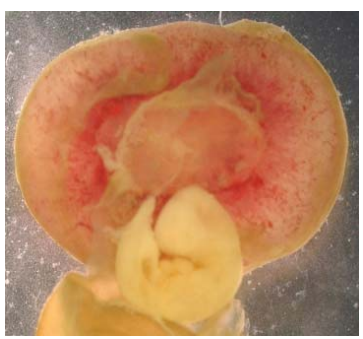
dead/cloned

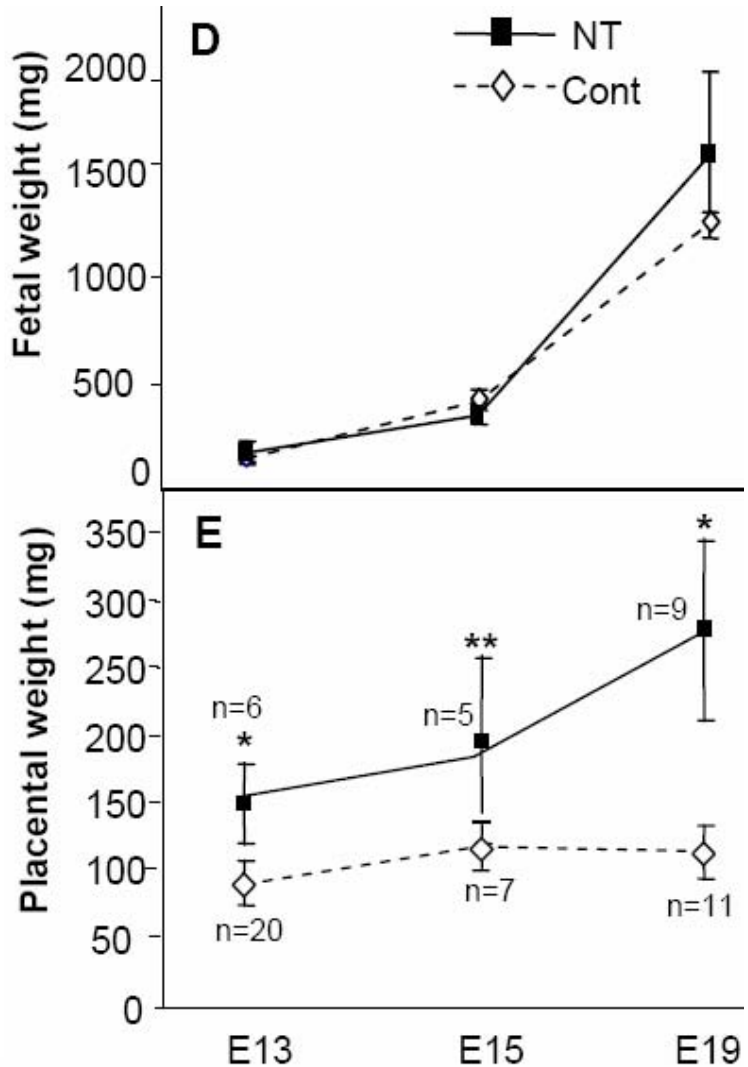


alive /cloned



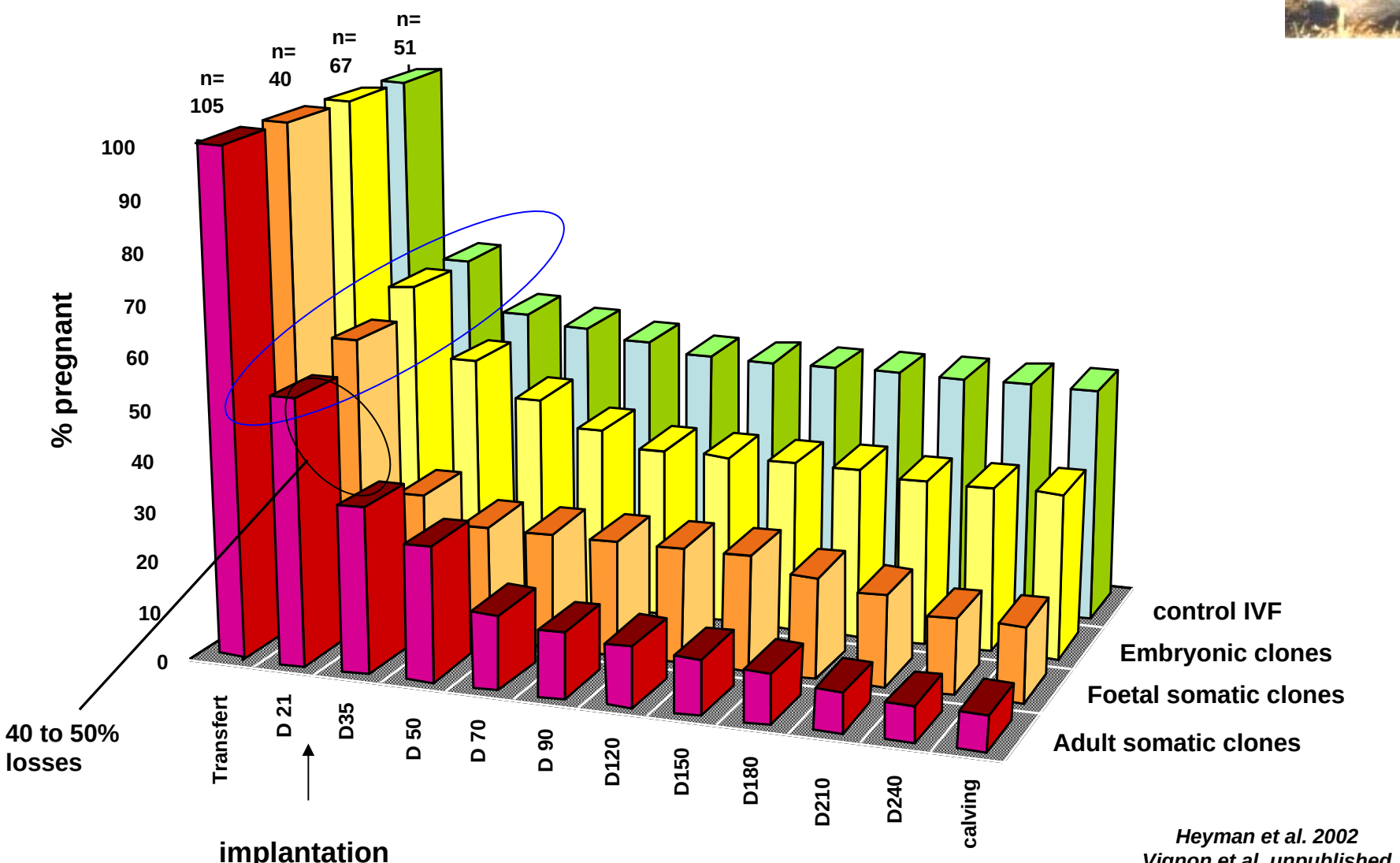
empty placenta





Jouneau et al., 2005

gestation profile of clones in cattle



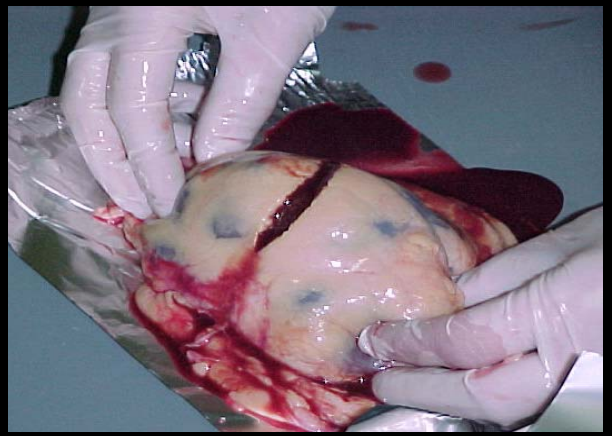
Heyman et al. 2002
Vignon et al, unpublished

typical features of compromised calves:

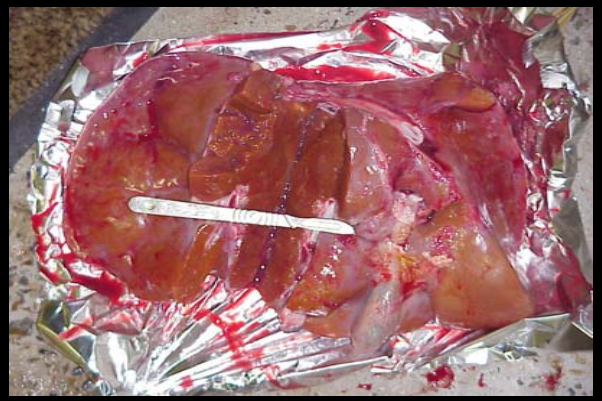
LOS
Large Offspring Syndrom

hydrops

Renal adnormalities, adypocyte infiltration



enlarged liver

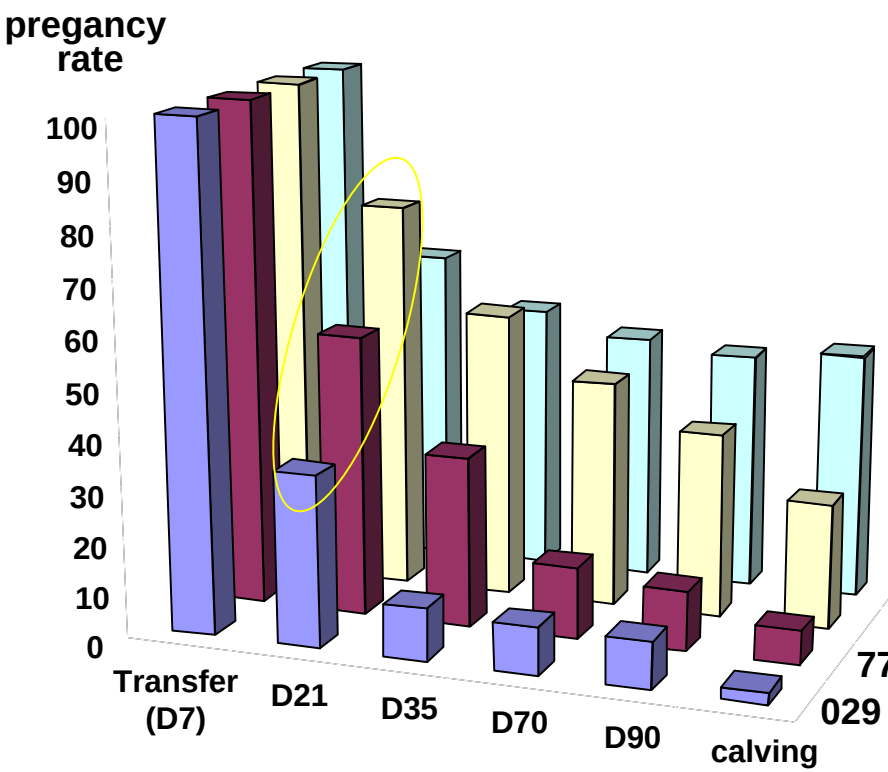


Hill et al. 1999, Chavatte-Palmer et al. 2002, Ogonuki et al. 2002, Lai et al. 2002, Rhind et al., 2003…

The efficiency of cloning can be surprisingly high

- In cattle 10% of the donor cell lines can lead to more than 20% of live calves from transferred clone embryos whereas 40% of the donor cell lines will provide no success.

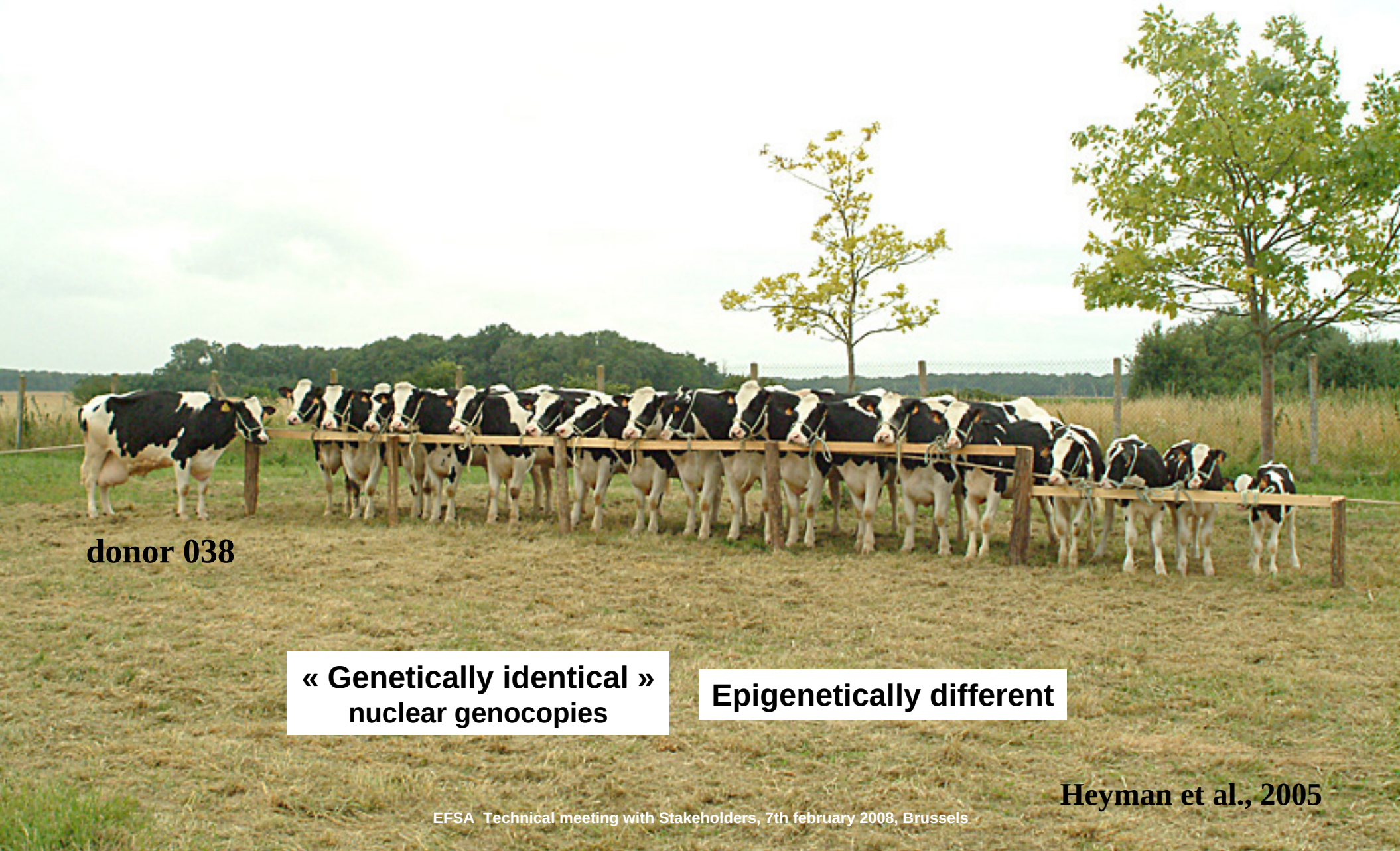
- This reflects both the potential of the technology and our present lack of understanding of the underlying biological processes



blast(%)	nb transf	D21	D35	calving
41.5% (n=201)	110	71% (G=78)	55% (G=50)	28.1% (n=31)
36,4% (n= 386)	203	53% (G= 108)	30.1% (G= 62)	6.4% (n=13)
38% (n=127)	123	57% (G=70)	32.5% (G=40)	2.3% (n=3)

Vignon et al. 2007; Smith et al submitted

Cattle clones can be physiologically normal and fertile



donor 038

« Genetically identical »
nuclear genocopies

Epigenetically different

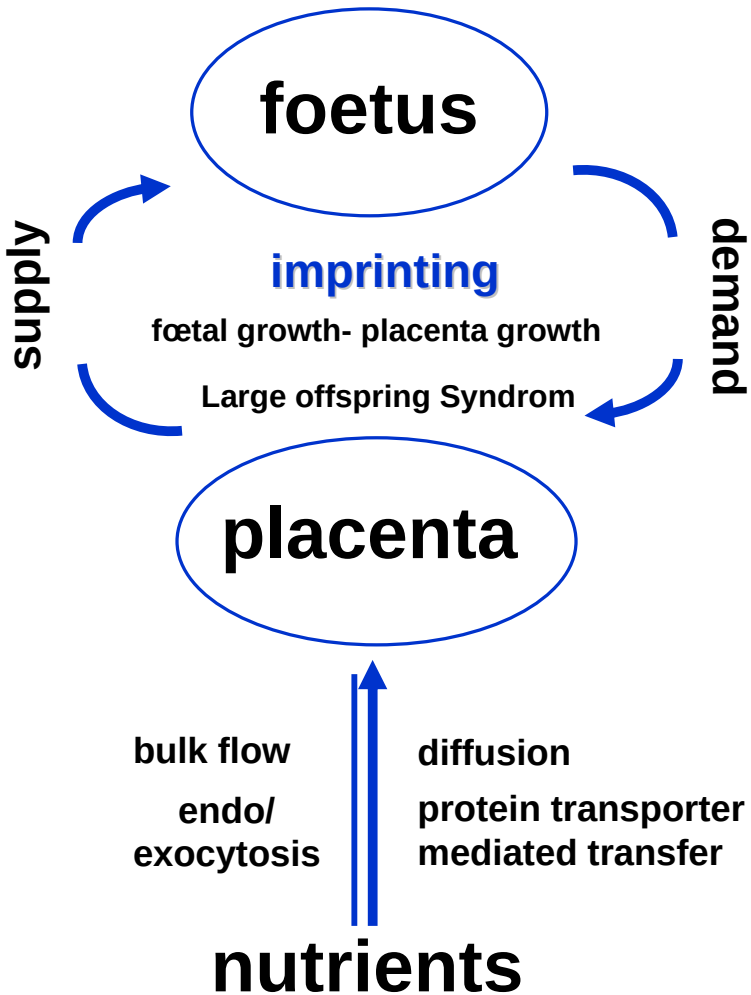
Heyman et al., 2005

D Cloning reveals the ability of living organism to adapt to the perturbations of their environment

- Changes to the microenvironement of a nucleus reveals that nuclear structure and functions can be dramatically reorganised upon nuclear transfer

- Changes to the maternal environment of the developing foetus reveals the importance of foetal programming in the occurrence of adult physiopathologies

Regulation of growth and control of differentiation during gestation



adapted from: Reik et al., 2003
Constancia et al., 2005

conclusion

Cloning and biological robustness:

Robustness: a property that allows a complex living system to maintain its functions despite external and internal perturbations

Kitano, 2004