

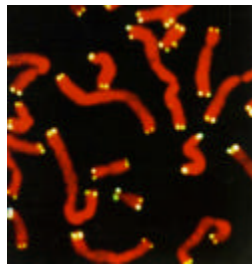
How old is Dolly?

Jie Xu
Dept. of Animal Science
University of Connecticut

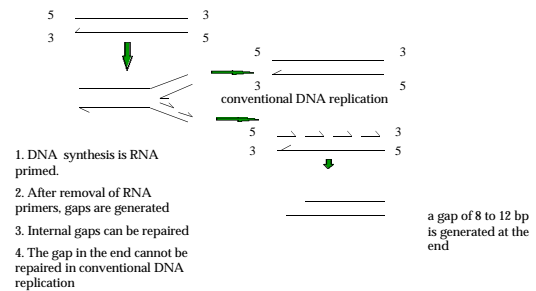
Telomere

- The end structure of Chromosome is called **telomere**
- They are repetitive sequence of TTAGGG
- telomere resides at the end of chromosome, never activated, transcribed
- playing regulatory role

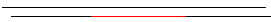
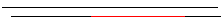
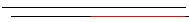
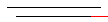
Telomere



Review of DNA replication



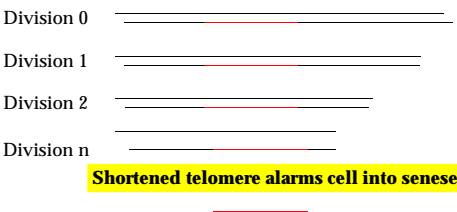
The implication

- Division 0 
 - Division 1 
 - Division 2 
 - Division n  **Your gene damaged!**
- Your important gene

Telomere Functions

- As a buffer for the inevitable loss of DNA by conventional replication
- Signal the cell into senescence stage once reached certain point (Hayflick limit)

Telomere Alarm

-
- 
- Division 0
- Division 1
- Division 2
- Division n
- Shortened telomere alarms cell into senescence**
- Your important gene

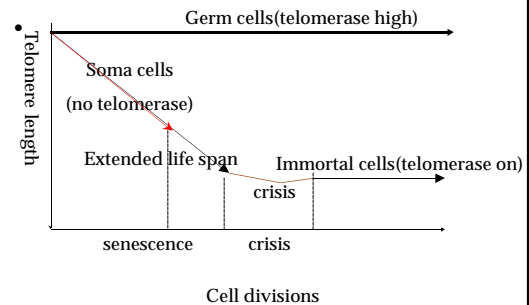
Senescence

- A scientific term for aging
- when cells become senescent:
 - they stop cell divisions
 - their normal functions will cease
 - some may secrete toxic chemicals

Telomerase

- The enzyme that could elongate the telomere length
- not present in most somatic cells
- present in germ cell lines
- present in tumor cells

Cell Senescence



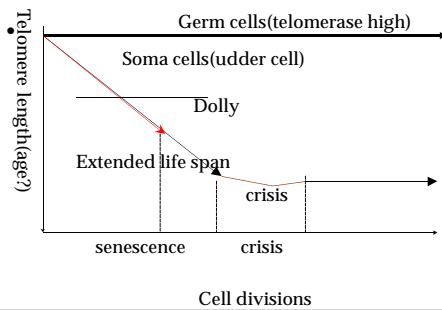
In Normal Reproduction Process

- Sperm and oocyte retain the telomere length (by function of telomerase)
- The offspring will have the same length of telomeres as the parents (theoretically)

In Cloned Animals

- Oocytes are enucleated
- Donor cells are somatic cells. no telomerase activity
- shorter telomere length in these somatic cells compared to sperm/oocyte

Age of Dolly?



Telomere length of cells in Dolly

- Conducted by Shiels et. al. (1999, Nature 399, 316-317)
- comparable to six-year old control

Study by Lanza et. al.

- Cloned cow
- Advanced Cell Technology (Worcester, MA)
- telomeres of clones are longer than age controls

• Science, 2000, 288: 665-669

Study by our group

- 10 clones (six live, 4 dead)
- telomere length similar to age control groups, suggesting successful reprogramming
- telomerase activity detected in early embryos

– Nature Genetics, submitted, 2000

Study by Wakayama et. al.

- Mice
- 6 generations of cloned mice for study
- no signs of premature ageing
- no shortening of telomeres
- in fact, slightly increase

Differences

- Species difference?
- Donor cell type difference?
- Sample cell type difference?
- Others?