

# Current Development and Ethical Issues in Stem Cell Research and Applications

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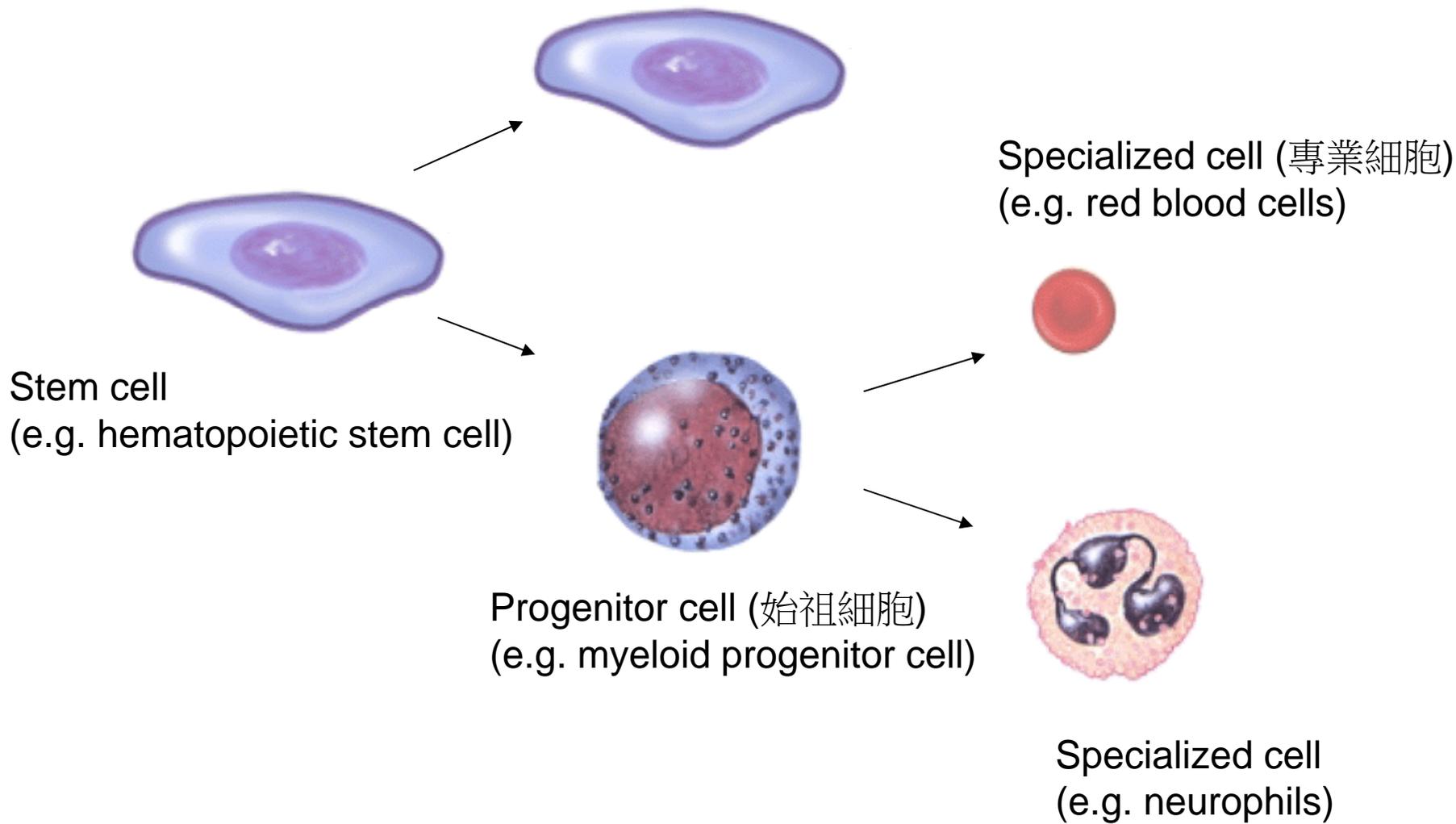
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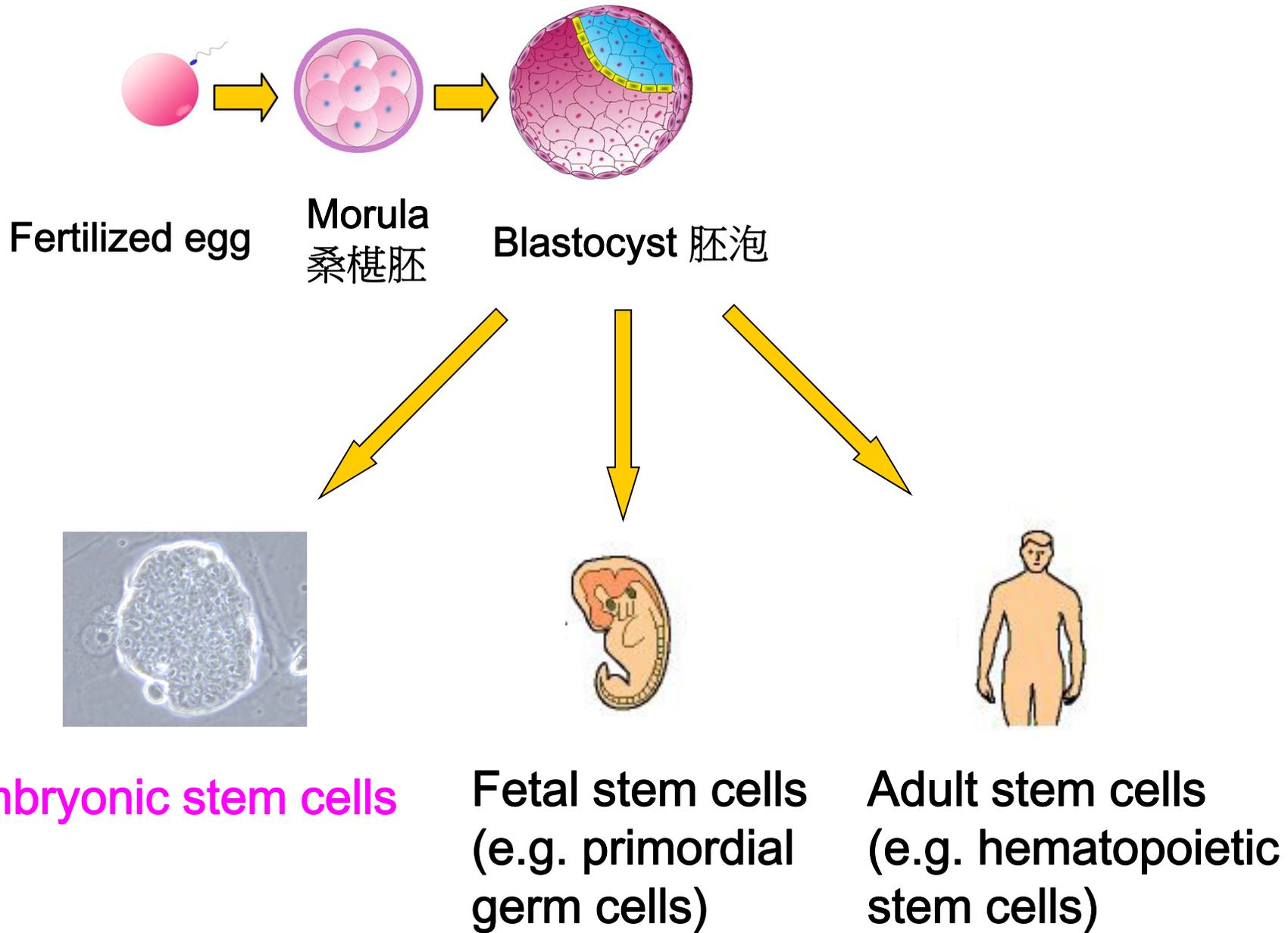
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# What are stem cells (幹細胞)?

1. unspecialized cells
2. renew themselves for long periods through cell division (self-renewal)
3. under certain physiologic or experimental conditions, they can be induced to become specialized/ differentiated cells (e.g. cardiac cells, insulin-secreting cells)





**Stem Cell Sources**



# Types of stem cells

## Totipotent (全能)

- potential is total; it gives rise to cells in ectoderm, mesoderm and endoderm and eventually all the different types of cells in the body, e.g. fertilized eggs

## Pluripotent (萬能)

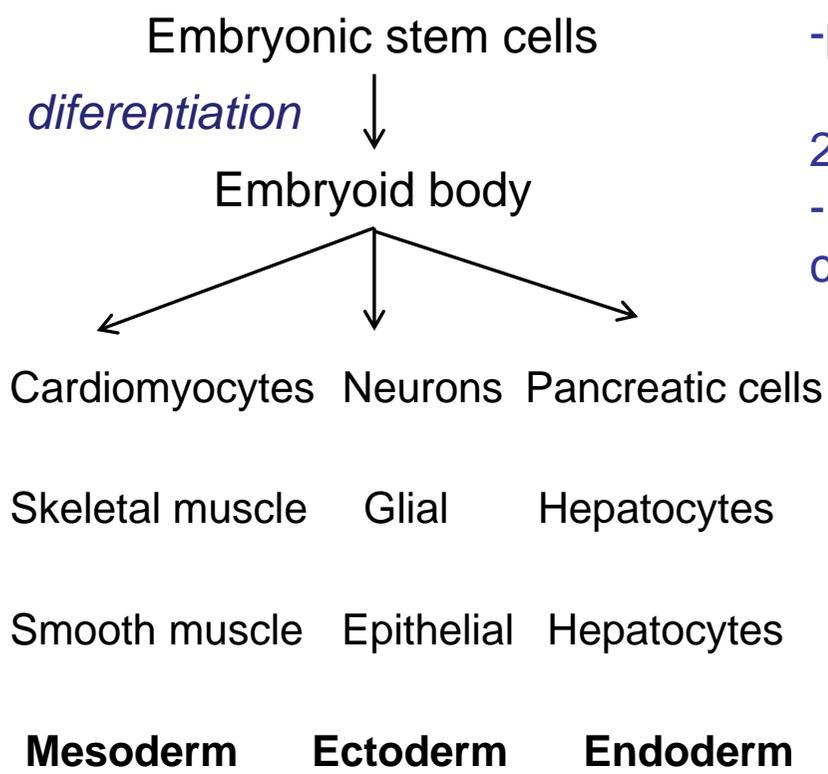
- give rise to any type of cells in the body except those needed to develop a fetus, e.g. the extra-embryonic tissue  
- e.g. embryonic stem cells (胚胎幹細胞)

## Multipotent (多能)

- give rise to a small number of different cell types, typically generate the cell types of the tissue in which they reside  
- e.g. hematopoietic stem cells (造血幹細胞)

## Unipotent (單能)

- Give rise to only one cell type



1. **Self-renewal**  
 -proliferate indefinitely in culture

2. **Pluripotency**  
 - ability to differentiate into ALL kinds of cells in our body

\* Unlimited supply of **HUMAN** cells for transplantation & basic medical science research

# History of stem cell research

- 1868 First used to describe as the unicellular ancestor of all multicellular organisms and as the fertilized egg that gives rise to all cells of the organism.
- 1886 Described the parts of plant that grow and regenerate.
- 1909 Introduced the idea that blood cells come from the same ancestor cell.
- 1957 E. Donnall Thomas in Seattle carried out the first human bone marrow transplantation.
- 1963 Scientists found that different blood cells are from a special class of cells, which provides the first evidence of blood stem cells.
- 1981 Pluripotent stem cells were derived from the embryos of mice.

# History of stem cell research

- 1989 Mice with a gene missing (knock-out mice) were created by manipulating embryonic stem cells.
- 1997 Scientists discovered that leukemia comes from the same stem cells that make the blood cells (the concept of cancer stem cells).
- 1998 Creation of the first batch of human embryonic stem cells.
- 2003 The conversion of stem cells from mice into germ cells and eventually sperm cells that are able to fertilize egg cells.
- 2006 Japanese scientists Shinya Yamanaka and Kazutoshi Takahashi created rodent induced pluripotent cells (iPS).
- 2008 Scientists were able to turn a rodent pancreatic exocrine cell into an insulin-producing cell, skipping the creating iPS cells.

# History of stem cell research

- 2009 USA FDA approved the clinical trial of using stem cells for spinal cord injuries.
- 2012 Two patients received implants of retinal pigment cells made from human embryonic stem cells had improvement in vision
- 2013 Scientists in Japan created human liver from stem cells.
- 2013 Scientists in the Netherlands made the first test tube burger.

## **Two ways to obtain embryonic stem cells**

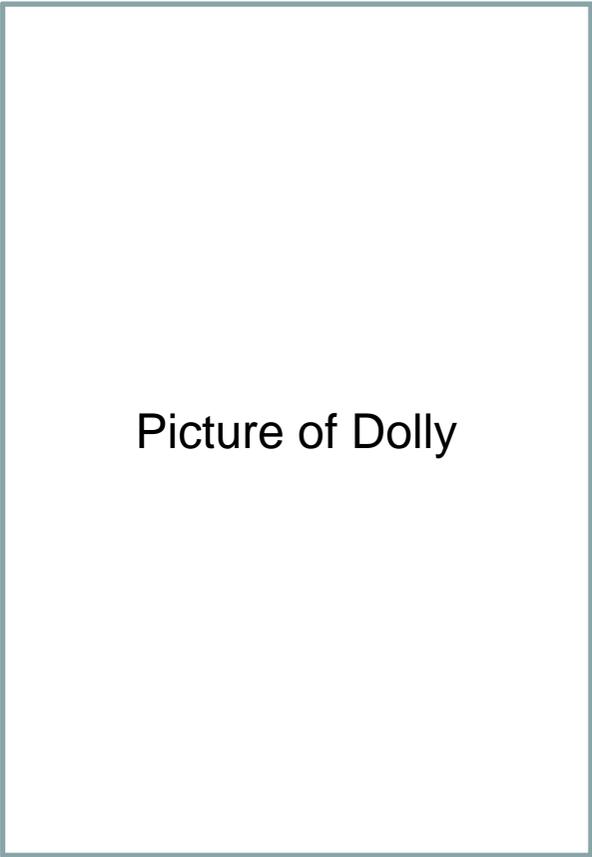
- Sexual Reproduction
- Nuclear Transplantation

<http://magazine-archives.wustl.edu/Spring05/images/p25.gif>

# Nuclear transplantation

## Somatic-cell nuclear transfer (SCNT)

- begins with the same process used to create Dolly, the famous cloned sheep, in 1996.
- A donor cell from a body tissue such as skin is fused with an unfertilized egg from which the nucleus has been removed.
- The egg 'reprograms' the DNA in the donor cell to an embryonic state and divides until it has reached the early, blastocyst stage.
- The cells are then harvested and cultured to create a stable cell line that is genetically matched to the donor and that can become almost any cell type in the body.



Picture of Dolly

<http://edition.cnn.com/2013/05/18/health/stem-cells-cloning/>

# Adult stem cells

- e.g. in epidermal structures (表皮組織), intestinal epithelium (腸上皮), bone marrow (骨髓), adipose tissue (脂肪組織)
- multipotent
- primary roles of adult stem cells in a living organism are to maintain & repair the tissue in which they are found
- reside in a specific area of each tissue where they may remain quiescent (non-dividing) for many years until they are activated by disease or tissue injury

# Adult stem cells

- Where they've been found
  - Brain
  - Blood
  - Cornea
  - Retina
  - Heart
  - Fat
  - Skin
  - Dental pulp
  - Bone marrow
  - Blood vessels
  - Skeletal muscles
  - intestines

- Umbilical cord
  - Cord blood stem cell
    - platelets
    - red blood cells
    - white blood cells
    - mesenchymal cells

- Neural stem cell
  - glial cells
  - neurons

# Induced Pluripotent Stem Cells (iPSCs)

[http://en.wikipedia.org/wiki/Induced\\_pluripotent\\_stem\\_cells](http://en.wikipedia.org/wiki/Induced_pluripotent_stem_cells)

1. Isolate & culture host cells. *e.g.* adult human dermal fibroblasts.
2. Introduce the ES specific genes into the cells.
3. Harvest & culture the cells according to the method for ES cell culture.
4. A subset of the cells generates ES-like colonies, that is, iPS cells.

# Significance

- **iPSCs**

- patient-specific somatic cells

- unlimited supply

- avoid immunorejection

- drug screening

- understanding disease mechanisms

- gene therapy

- tissue/organ engineering

# Plant stem cells

- Found in the root apical meristem (分生組織), shoot apical meristem and vascular system, supply precursor cells to form tissues and organs
- Totipotent
- Can self-renew to maintain the number of stem cells

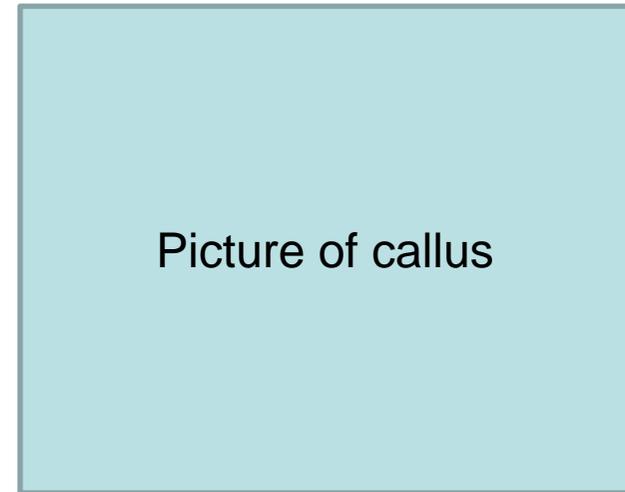
Picture of root tip (10X)

- 1) Meristem;
- 2) Columelle
- 3) Lateral part of the tip;
- 4) Dead Cells;
- 5) Elongation zone

[http://en.wikipedia.org/wiki/Plant\\_stem\\_cell](http://en.wikipedia.org/wiki/Plant_stem_cell)

# Callus (胼胝體)

- somatic cells that undergo dedifferentiation to give rise to totipotent embryogenic cells
- Can be derived from cells of a plant wound and formation induced by plant hormones (somatic embryogenesis)



[http://en.wikipedia.org/wiki/Callus\\_\(cell\\_biology\)](http://en.wikipedia.org/wiki/Callus_(cell_biology))

# Uses of callus (胼胝體)

- **Regeneration (再生)** - Callus can be differentiated to whole plant by adding plant hormones
- **Micropropagation (微繁殖)** – obtaining genetically identical plants
- **Transgenic (轉基因)** - Genes can be inserted into callus, for generating transgenic plants. e.g. for producing proteins, for protecting against pests and pesticides, for growing in harsh conditions

# **Research and applications of stem cells**

# Stem cells in animals

- Stem cells determine the end of agricultural product – manipulation of stem cells allow desired outcomes
- Microinject embryonic stem cells into an embryo
- The stem cells may be genetically manipulated before being used
  - For producing transgenic offsprings

# Stem cells in animals

## **Approach to generate chimeric animals**

Targeted ES cells are injected into blastocysts →  
blastocysts are implanted into mice foster mothers →  
chimeric mice offspring

(<http://www.sabiosciences.com/pathwaymagazine/pathways9/induced-pluripotent-stem-cells-quick-facts.php>)

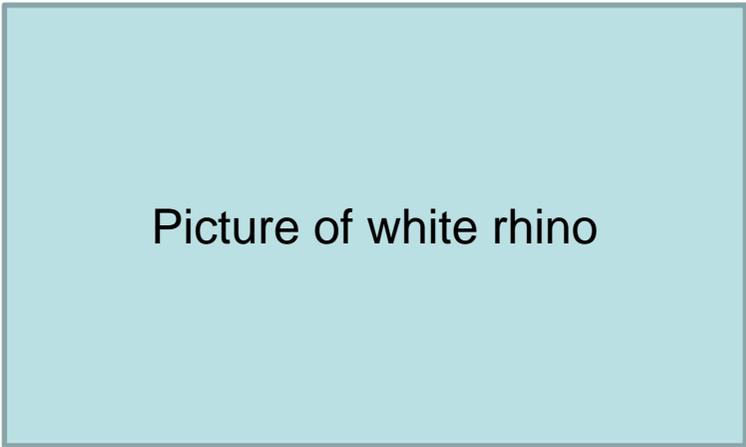
## **Chimeric pigs from induced pluripotent stem cells**

([www.westlaboratory.org/livestock-stem-cells](http://www.westlaboratory.org/livestock-stem-cells))

# The values of stem cells in animals

- Provide models for human diseases and for drug screening
- Produce animals more environmental friendly, e.g. with less methane production
- Increase production of food and nutrients
- For the conservation of endangered species
- Understand the developmental process
- Propagation animals with useful/rare traits
- Manipulating bovine mammary stem cells to increase the yield of milk
- Manipulating the limb development genes in chicken stem cells to generate chicken with four wings and four legs

# Can stem cells rescue endangered species?



Picture of white rhino

Northern white rhino  
(left) – only seven in the  
world

(<http://www.nature.com/news/2011/110904/full/news.2011.517.html>)

- Obtained fibroblasts from the connective tissues
- Able to convert them to iPS by inserting selected genes and then generated different types of cells

## Issues to overcome:

- Little knowledge on the reproductive, which is needed to support assisted reproduction programmes
- Only small number of animals left, not able to find sufficient fostered mother

# The issues of animal rights

- Many philosophers agreed that we should not treat animals badly
- Immanuel Kant: we have moral obligations not to mistreat animals because mistreating them exemplifies, or encourages the development of, bad moral character, and is therefore at odds with our goal of moral self-perfection.
- Tom Regan: animals, being sentient, have the inviolable rights of ends in themselves
- Peter Singer: since animals experience pleasure and pain, it is morally required consider if our actions produces the happiness of the greatest number to them

# The moral acceptability of using animals for stem cell experiments

- Would this cause harm to the animals?
  - Refine the procedure to reduce the suffering
  - Use less sensitive animals
- Would the interests of the animals considered?
  - Give better welfare to the animals
  - Use the most appropriate types of animals
  - Reduce the number of animals
  - Achieve our aim without animals
- Would the work promote greatest happiness of the greatest number?
  - Expected benefits from this experiment

# Stem cell and food

- Burger developed from cow stem cells

How the burgers are grown

- Mail online 5 August 2013

<http://www.dailymail.co.uk/sciencetech/article-2384715/At-tastes-meat--Worlds-test-tube-artificial-beef-Googleburger-gets-GOOD-review-eaten-time.html>

- The 142 g burger costs UKP250,000 to make
- Took three months to grow from 20,000 strips of meat cells
- Add beetroot juice and saffron for the color, mix with salt, breadcrumbs, egg powder to form a patty
- After lightly fried with butter and sunflower oil, it tasted close to meat, but not juicy

# Ethical implications of stem cell burger

- Reasons to support

# Ethical implications of stem cell burger

- Reduce farming activities, which use up a lot of natural resources, e.g. energy, crops, water and causes pollution, e.g. generation of methane gas, feces and waste water
- Lab grown beef would use 45% less energy, produce 96% fewer greenhouse gas emissions, and require 99% less land than farming cattle.
- Reduce cruelty to farm animals, e.g. factory farming, consumption of artificial food, packed transportation in lorries, mass killing
- Make food supply safer

# Ethical implications of stem cell burger

- Reasons to against

# Ethical implications of stem cell burger

- Although overall suffering would be greatly reduced, but still some animals need to be killed to get the cells, the medium for growing cells is an animal product
- Eating food derived from animals cannot reduce the concept of treating animals as property and exploited
- Eating less meat or a plant-based diet would be an easier way to tackle meat shortages

# Ethical implications of stem cell burger

- From consumers' viewpoint:
  - How to make it more authentic, as meat should have different types of cells and blood vessels
  - Can it be affordable?
- Would this be accepted as a 'vegetarian' food, as no animal is killed?

<https://www.youtube.com/watch?v=jJrSdKk3YVY>

# Stem cell and therapies

- Bone marrow transplantation
- Treating spinal cord injuries
- Replacing damaged cells
- Generation of artificial organs
- .....

# Fabricating stem cell data

- Hwang Woo-Suk (黃禹錫), a top scientist in Seoul National University, South Korea, who cloned a number of animals, including dogs in 2005, claimed to generate human embryonic cells through cloning
- He was found to request his female staff to donate eggs and fake data of at least 9 stem cell lines he claimed to have created
- In 2006, he was charged with embezzlement and bioethics law violations
- Sentenced to 2 years suspended prison sentence in 2009

Picture of Hwang Woo-Suk

Picture of Snuppy

Snuppy stands next to the male Afghan hound (left) from which he was cloned (<http://www.npr.org/templates/story/story.php?storyId=4784301>)

# Why did Hwang fabricate the data?

- A highly competitive field
- Success brings high rewards
- The pressure to stay the first
  - The title of ‘Supreme scientist’ in Korea
  - Korean Air called him ‘National treasure’ and offered him free passage for a decade
  - Get virtually unlimited funding
- Research-at-all-cost mentality
  - Work from 6am till midnight
- Hwang confessed: Being too focused on scientific development, I may not have seen all the ethical issues related to my research

# How did this incidence affect others?

- Your opinions please

# How did this incidence affect others?

- Diminish the hope to those who are disabled
- Hit Korea's pride
- Diminish the trust on scientists and biotechnology industry
- Cause an increase in anti-stem cell research

# Do you believe in the followings?

- Doctor has high hopes for new hair-loss treatment
  - 21 February 2013
  - <http://abclocal.go.com/ktrk/story?section=news/local&id=9001937>
- Sales sky-rocket as 'Stem Cell Therapy' anti-aging cream hits Priceline stores!
  - *Sydney Morning Herald*
  - 11 September 2011
- 經絡美顏幹細胞療程
- 干细胞治疗中心
  - <http://www.baike.com/wiki/211%E5%8C%BB%E9%99%A2%E5%B9%B2%E7%BB%86%E8%83%9E%E6%B2%BB%E7%96%97%E4%B8%AD%E5%BF%83>

# References

- <http://www.explorestemcells.co.uk/> - provides general information on stem cells, good for the beginners
- <http://stemcell.childrenshospital.org/about-stem-cells/history/> - records the timeline of stem cell research
- <http://www.nature.com/news/2011/110904/full/news.2011.517.html> - about the use of stem cells to rescue endangered animals
- [http://en.wikipedia.org/wiki/Hwang\\_Woo-suk](http://en.wikipedia.org/wiki/Hwang_Woo-suk) - an introduction on Hwang Woo Suk

~ The End ~