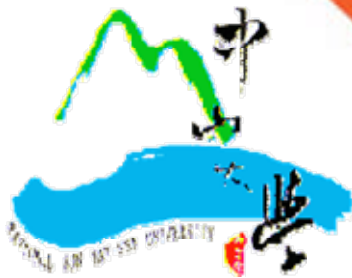




# 第十講 幹細胞原理及其在 生物醫學上的應用

生物科學系  
劉仲康教授



4/5

# Topics:

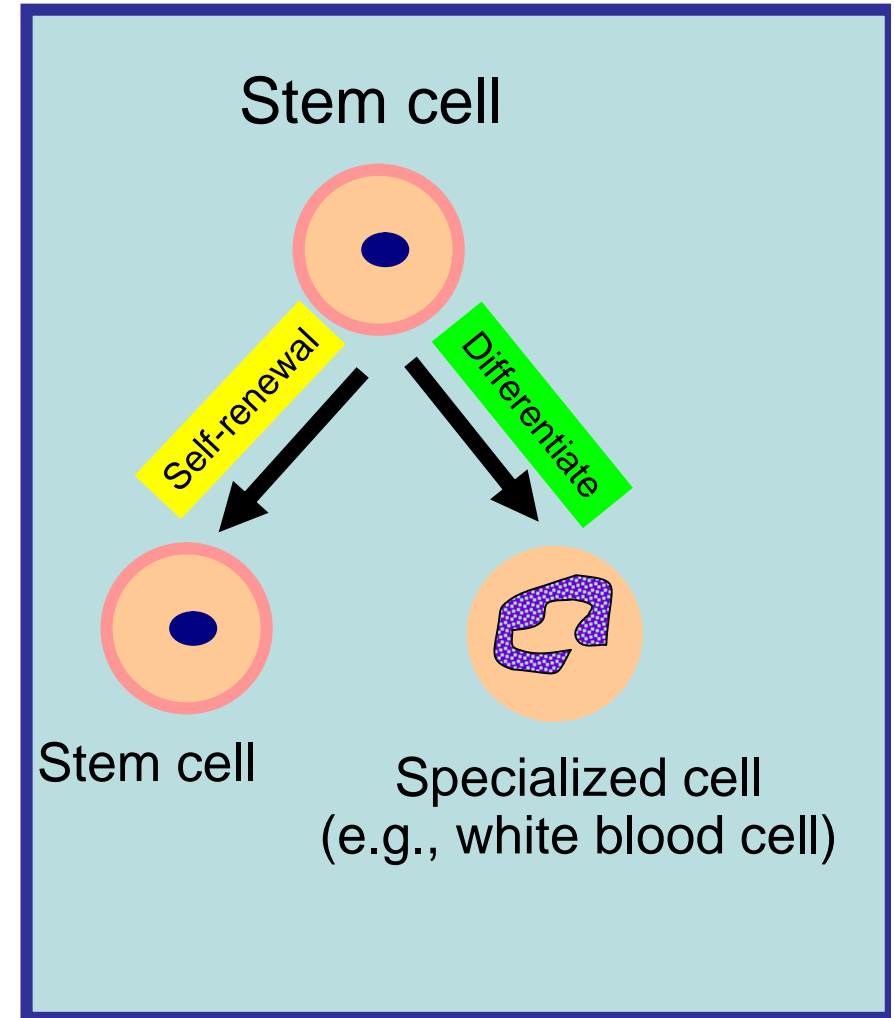
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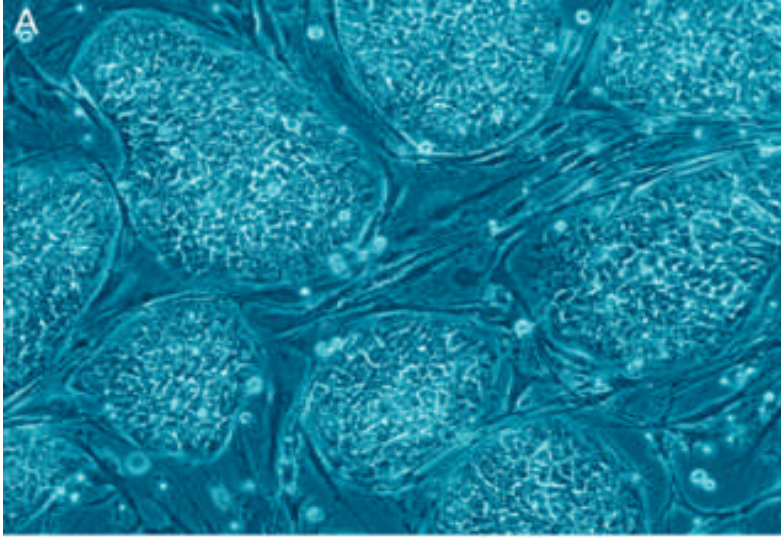
1. What are Stem Cells?
2. Types of Stem Cells
3. Sources of Stem Cells
4. History of Stem Cell/Human Cloning
5. Potential Application of Stem Cell Research
6. Obstacles of Stem Cell Research
7. Ethical Issues on Stem Cell Research

# Stem Cells (幹細胞) - Definition

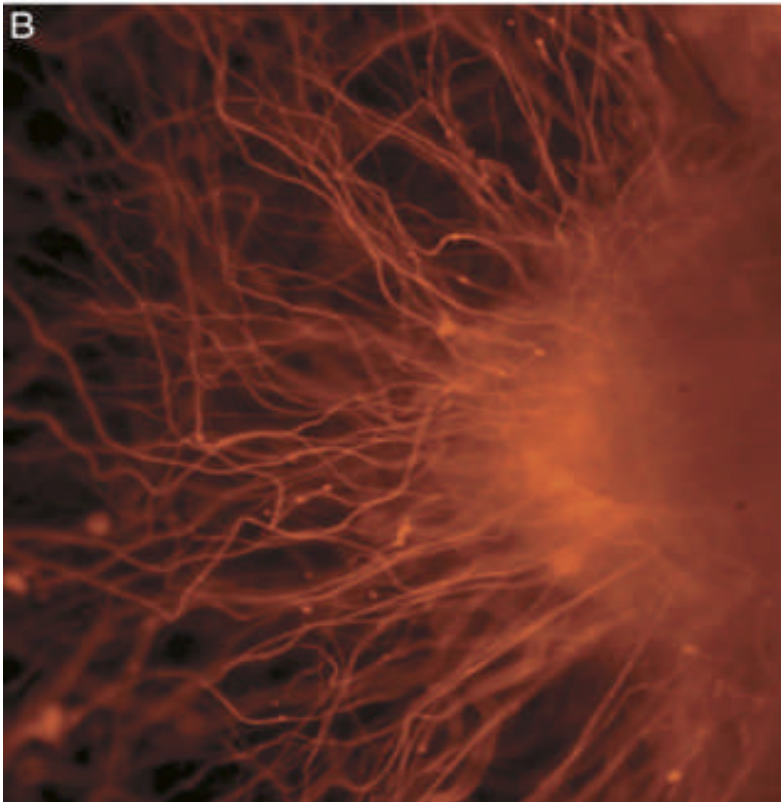
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- **‘Master cells’ (unspecialized)**
- **Capable of dividing and renewing themselves for long periods of time (proliferation and renewal)**
- **Have the potential to give rise to specialized cell types (differentiation 分化)**





← 人類胚胎幹細胞



← 由胚胎幹細胞分化而成的神經元細胞

# The Major Types of Stem Cells

## A. Embryonic Stem Cells (胚胎幹細胞 ESC)

- From blastocysts left over from In-Vitro Fertilization in the laboratory

## B. Fetus Stem Cells (胎兒幹細胞)

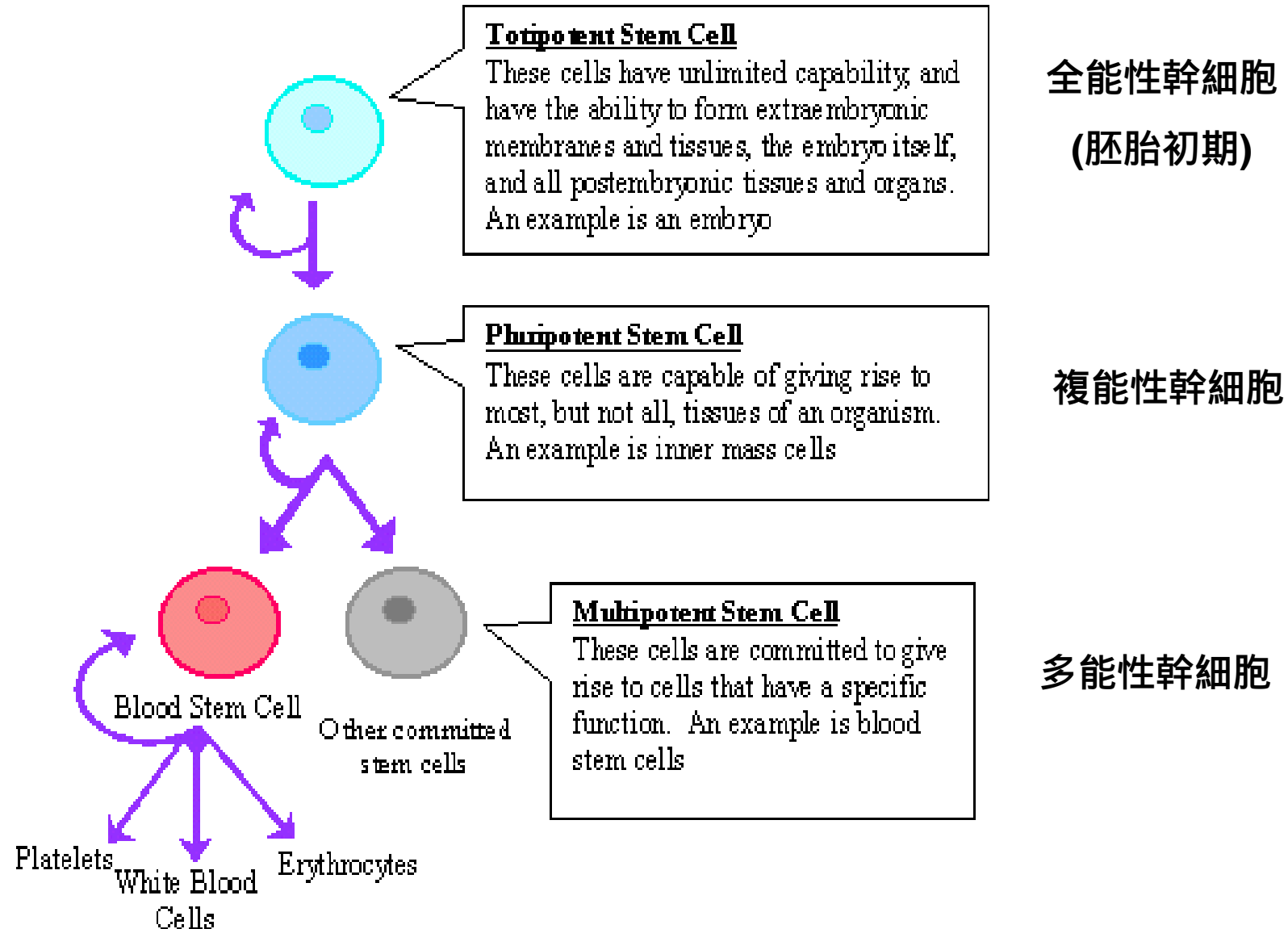
- From aborted fetuses

## C. Umbilical Cord Stem Cells (臍帶幹細胞)

## B. Adult Stem Cells (成體幹細胞)

- Stem cells have been found in the blood, bone marrow, liver, kidney, cornea, dental pulp, umbilical cord, brain, skin, muscle, salivary gland . . . .

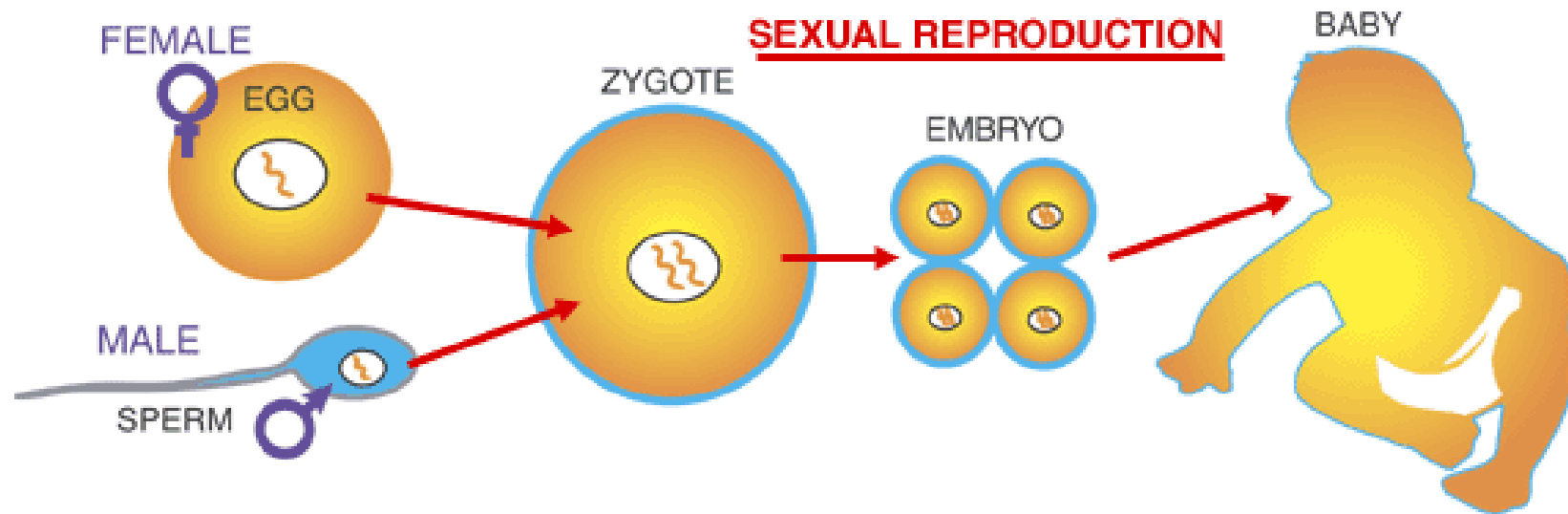
# Stem Cell Differentiation



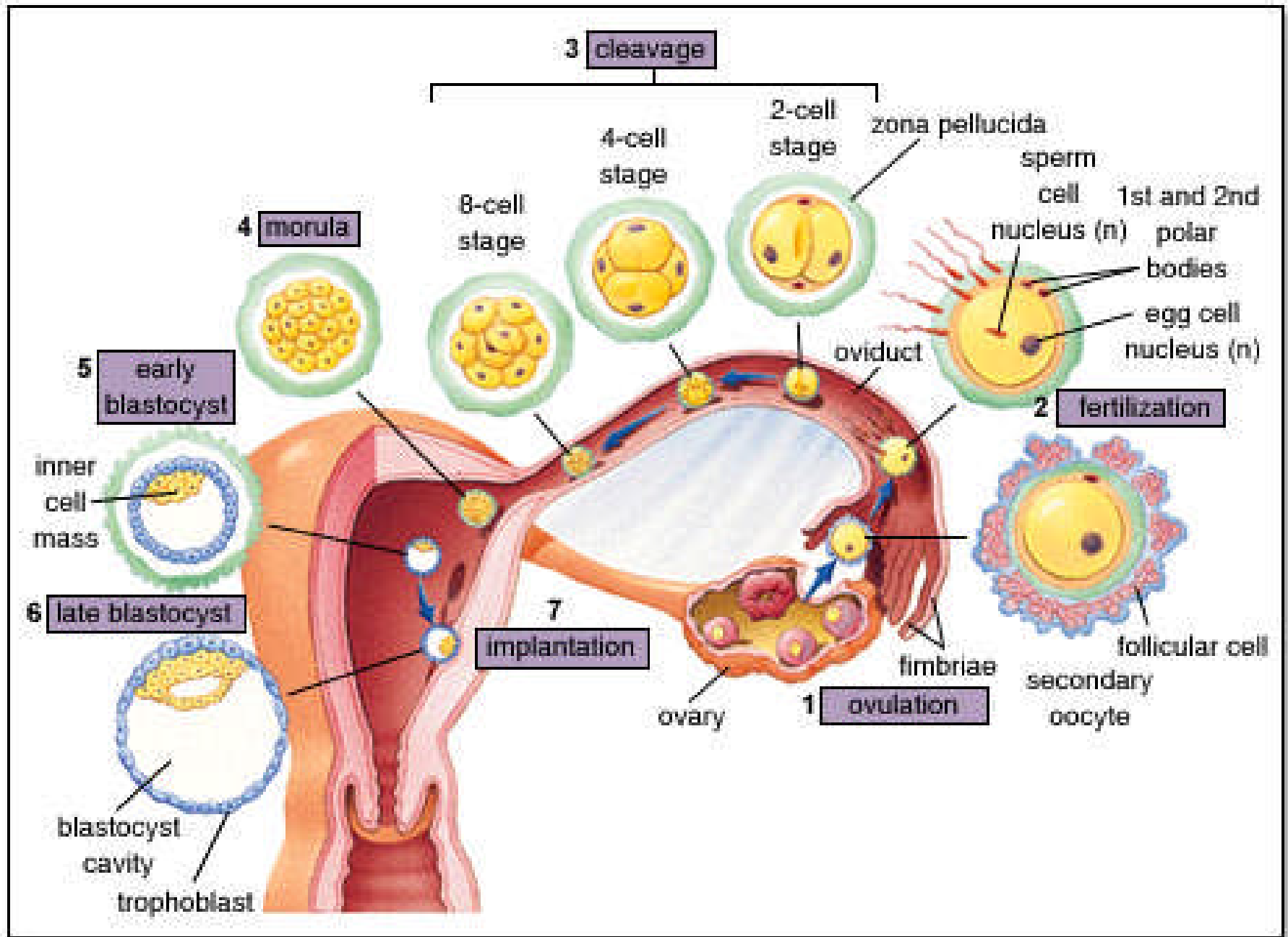
# Advantages and Disadvantages to Embryonic and Adult Stem Cells.

Embryonic S.C.	Adult S.C.
"Pluripotent" (can become any cell)	"Multipotent" ("can become many but not any")
Stable. Can undergo many cell divisions.	Less Stable. Capacity for self-renewal is limited.
Easy to obtain but blastocyst is destroyed.	Difficult to isolate in adult tissue.

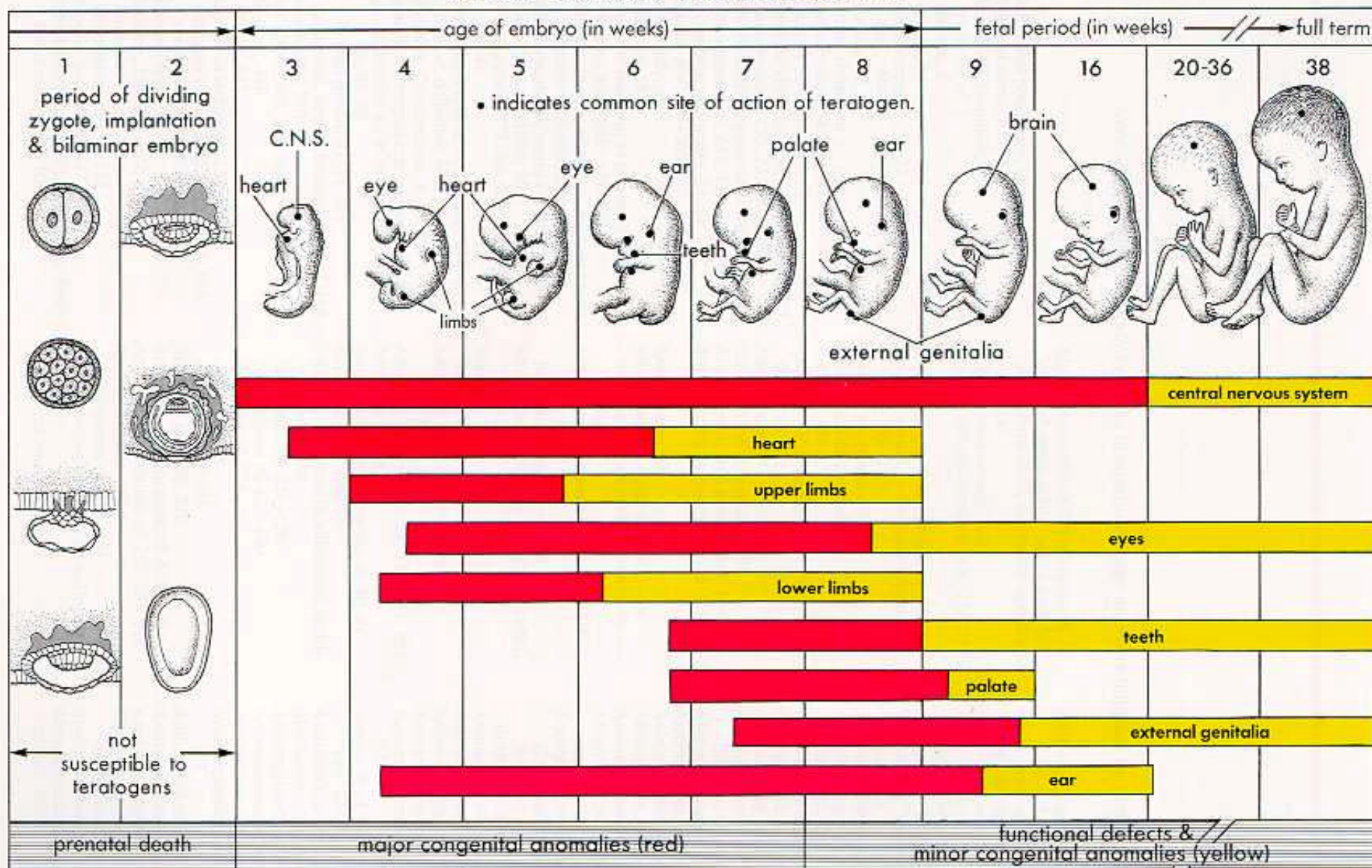
# Sexual Reproduction





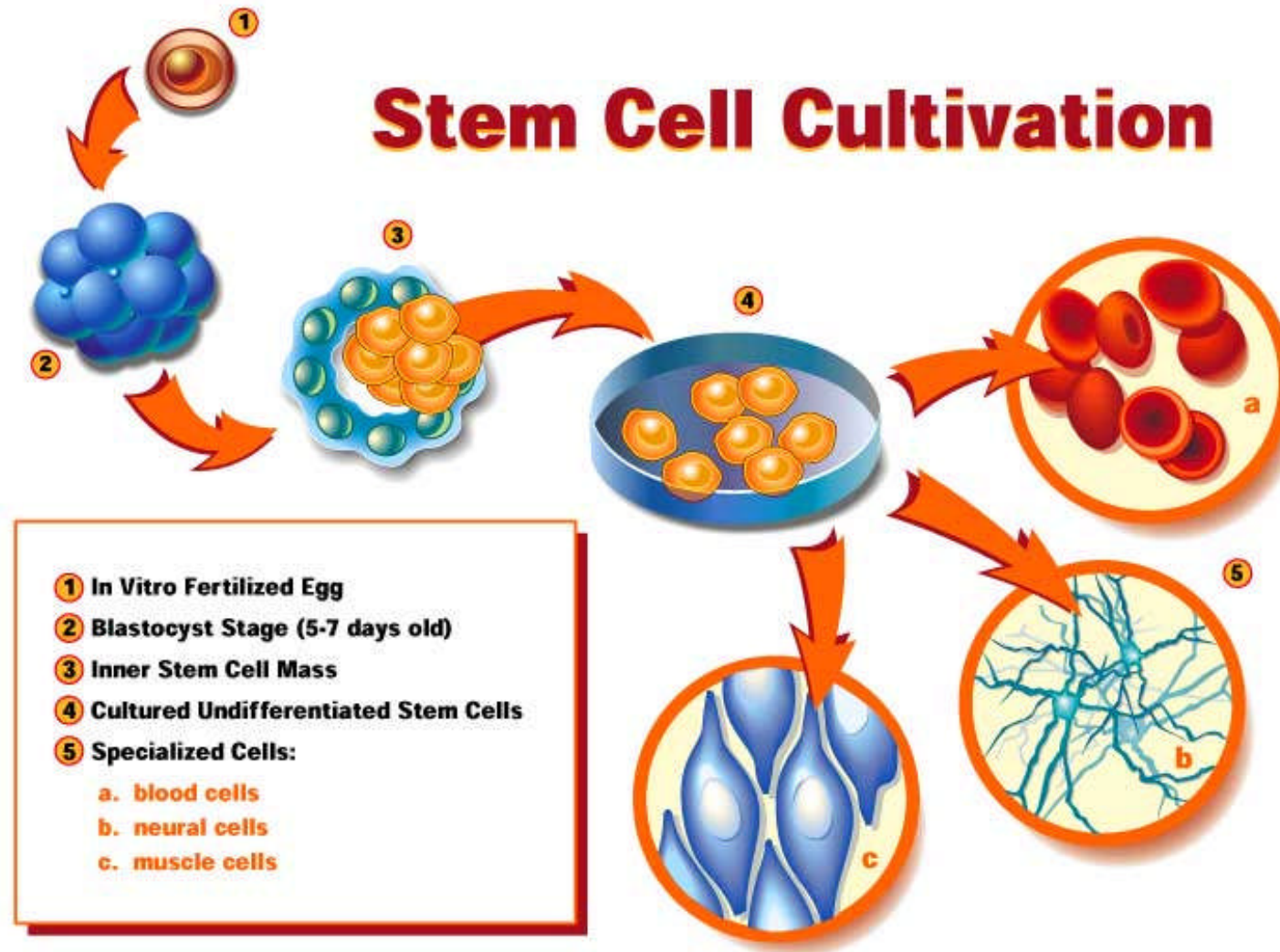


### CRITICAL PERIODS IN HUMAN DEVELOPMENT\*



\* Red indicates highly sensitive periods when teratogens may induce major anomalies.

# Stem Cell Cultivation



# What are the Sources of Fertilized Embryos?

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- Surplus embryos from infertility clinics
- From human cloning

# Sources of Embryos for Deriving ES Cells

## I. From Infertility Clinics

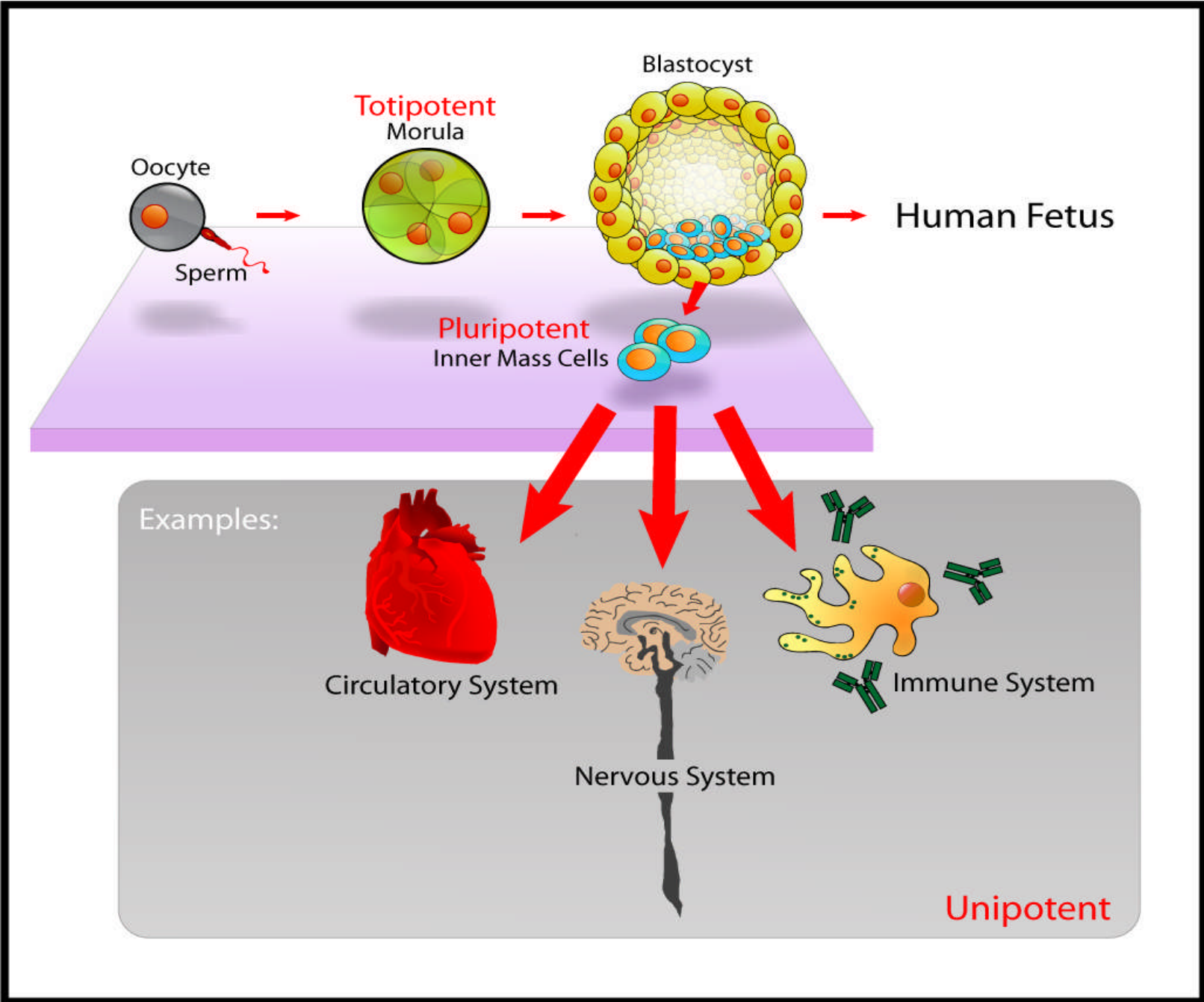
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- Embryos that are created for infertility treatment are often created in excess of the number that is usually needed to achieve a pregnancy.
- If pregnancy is achieved, many parents give up their “surplus” embryos.
- These “surplus embryos” have developed in culture to the **blastocyst stage** and can be harvested for stem cells.

**Ethical issue: Harvesting the inner cell mass destroys the embryos**

# IVF – In Vitro Fertilization

- **Available since 1986**
- **About 100,000 IVF kids in U.S.**
- **Often creates extra embryos**
- **U.S. - About 400,000 frozen embryos (unregulated)**
- **England – 52,000 (regulated by government)**





**2001年8月，美國總統布希針對「人類胚胎幹細胞」的議題，同意美國政府可以有條件地資助幹細胞的研究，但是他限制了胚胎幹細胞來源必須是現有的64株，不可以再取得新的胚胎幹細胞，他認為這樣子就沒有毀掉胚胎的疑慮。**



# 幹細胞引發的道德爭論

✚ 在美國幹細胞的研究，經布希批准宣布聯邦基金可以用來支持這樣的研究，但只限於利用現存的六十四個幹細胞株。

✚ 宗教團體、反墮胎人士及衛道團體已發出嚴正聲明指出，任何毀損人類胚胎的研究均無法取得他們的認同。

# 研究胚胎幹細胞 是不道德的？

**胚胎**

是生命的起源

**墮胎**

本身就是一種殺人的行為，所以使用其胚胎遺體來進行研究在根源上根本就是道德的行為。

由人工受精技術（*in vitro fertilization*）  
來看幹細胞引發的道德爭論。

## 人工授精

利用性荷爾蒙刺激女性的卵巢而促使其  
排出約十數個卵子，再將這些卵子與男性  
的精子進行受精。當受精卵發育到適當階  
段時再將2-5個受精卵移植入母體子宮使  
其繼續發育成胎兒。

## 正 方

在人工授精中將有多餘的受精卵，支持胚胎幹細胞研究的人認為這些多餘的胚胎**本來就會被棄置**，與其如此，還不如在獲得當事人同意的情形下將其利用來從事幹細胞的研究培養，以應用於臨床醫療。



## 反 方

反對胚胎幹細胞研究的人士認為，儘管幹細胞來源已獲得當事人同意，但是**因為從具有生命的胚胎中取出幹細胞後，整個胚胎也就會跟著死亡，因而幹細胞的研究本質上就是終止生命，就是不道德的。**

## 由歷史觀點來看

以胚胎來進行實驗是否具有爭議往往卻隨著實驗本身的成效而有微妙的差異。

人工受精技術開發初期，人們不確定這技術是否會成功，因而也受到大量批判，認為是違反自然的行為，而當這技術證明確實可用來解決不孕症的問題，甚可用來篩選基因遺傳疾病，社會上爭議的聲音幾乎已經聽不見。

# Sources of Embryos for Deriving ES Cells

## II. From Human Cloning

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**Are there human clones?**  
**Yes – Identical Twins**

# Cloning Defined

- **What is cloning?**
  - **Asexual reproduction**
- **Examples**
  - **Bacteria, fungus**
  - **Plants – cutting – potato**
  - **Farm animals**

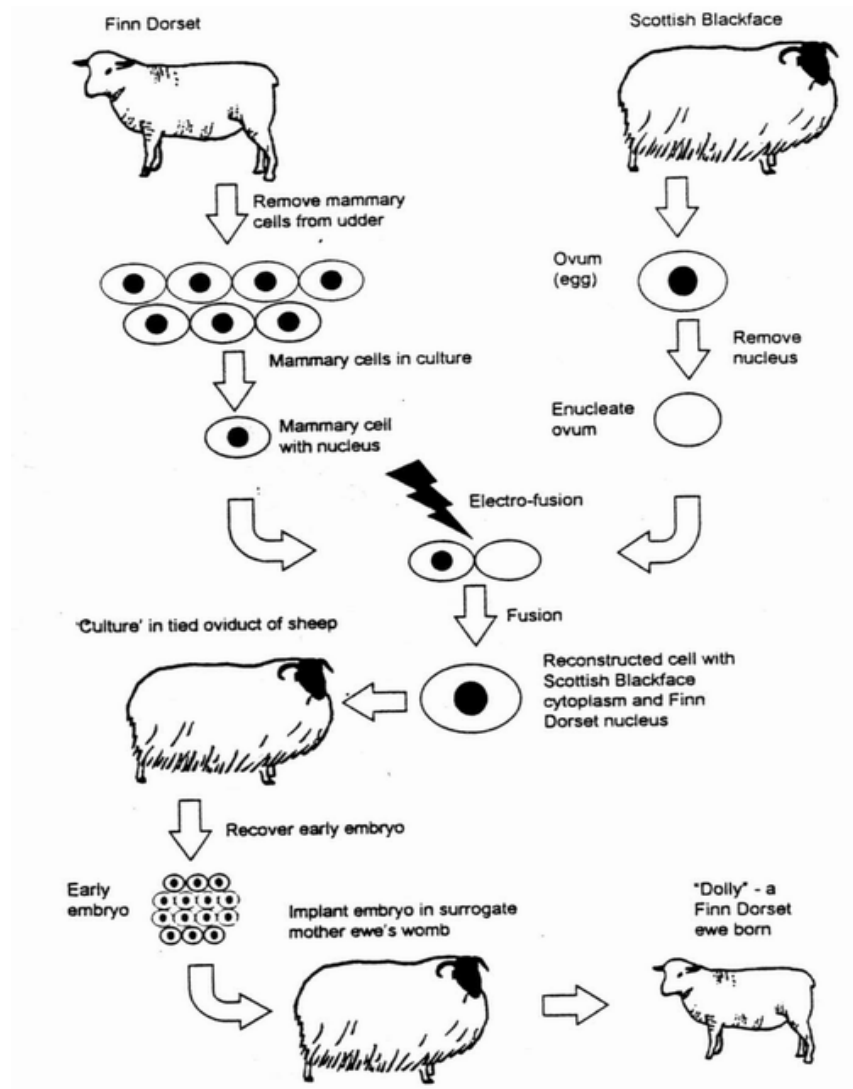
# 複製動物

- 1997年2月27日英國Roslin研究所科學家於Nature雜誌上首先發表複製羊桃莉(Dolly)複製成功

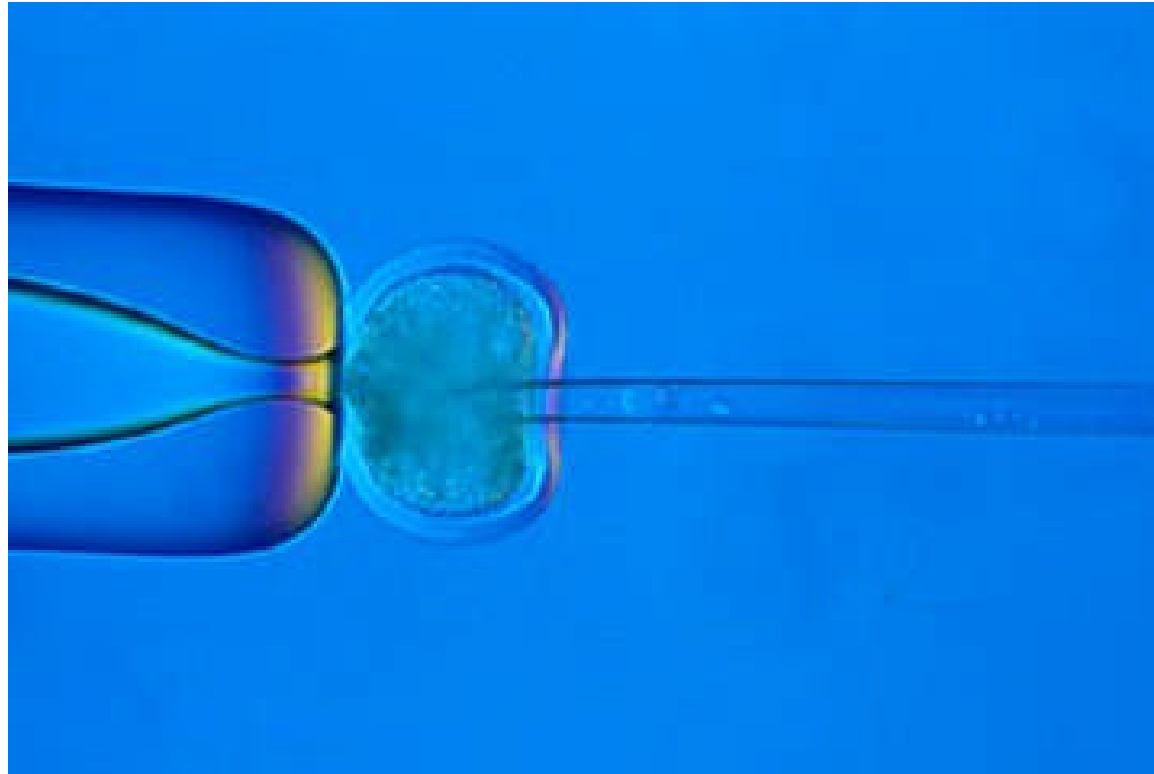




# 複製羊技術

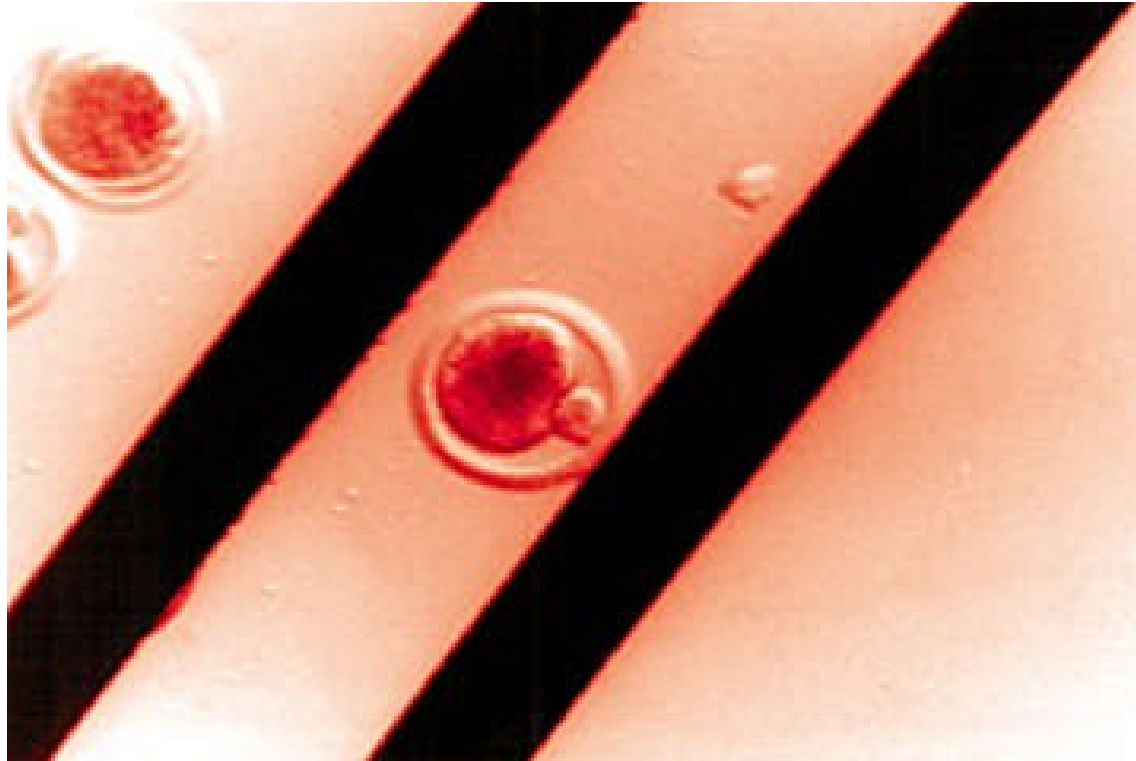


# Removing Nucleus



**Removing the maternal nucleus before  
nuclear transfer**

# Nuclear transfer



**Nuclear transfer embryo about to be activated**

# Sources of Embryos for Deriving ES Cells

## II. From Human Cloning

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- Human cloning is the process of using asexual reproduction to replicate an organism.
- The method employed is called **somatic cell nuclear transfer (SCNT)** and results in the creation of a new organism by way of fusion, as opposed to fertilization.

# Sources of Embryos for Deriving ES Cells

## II. From Human Cloning

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- SCNT consists of removing the nucleus of an unfertilized egg and replacing it with the nucleus of a somatic cell from the donor to be cloned.
- A somatic cell, such as a skin or white blood cell, contains the donor's DNA or genetic code.

# Sources of Embryos for Deriving ES Cells

## II. From Human Cloning

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- Then, instead of fertilization, a small electric pulse is applied to cause the cells to fuse and divide.
- If successful, the result is a newly cloned individual who begins the same process of human development that we all experienced.

# 複製人技術引發爭議

**SPACEDAILY**  
YOUR PORTAL TO SPACE

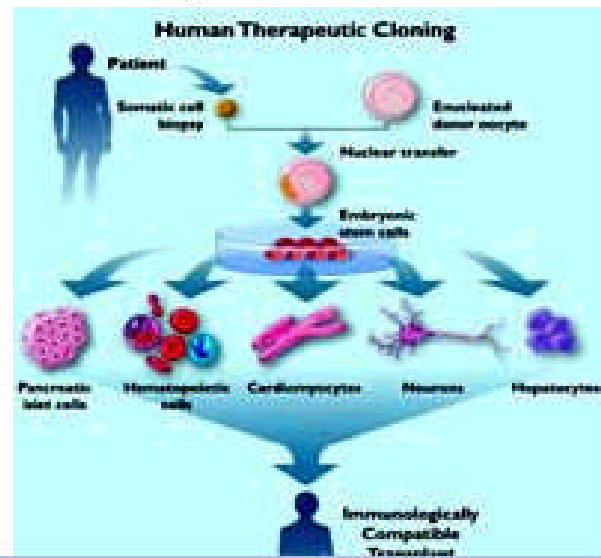
CLONE SPACE

## US Academy Wants Ban On Human Cloning But Hails Therapeutic Use

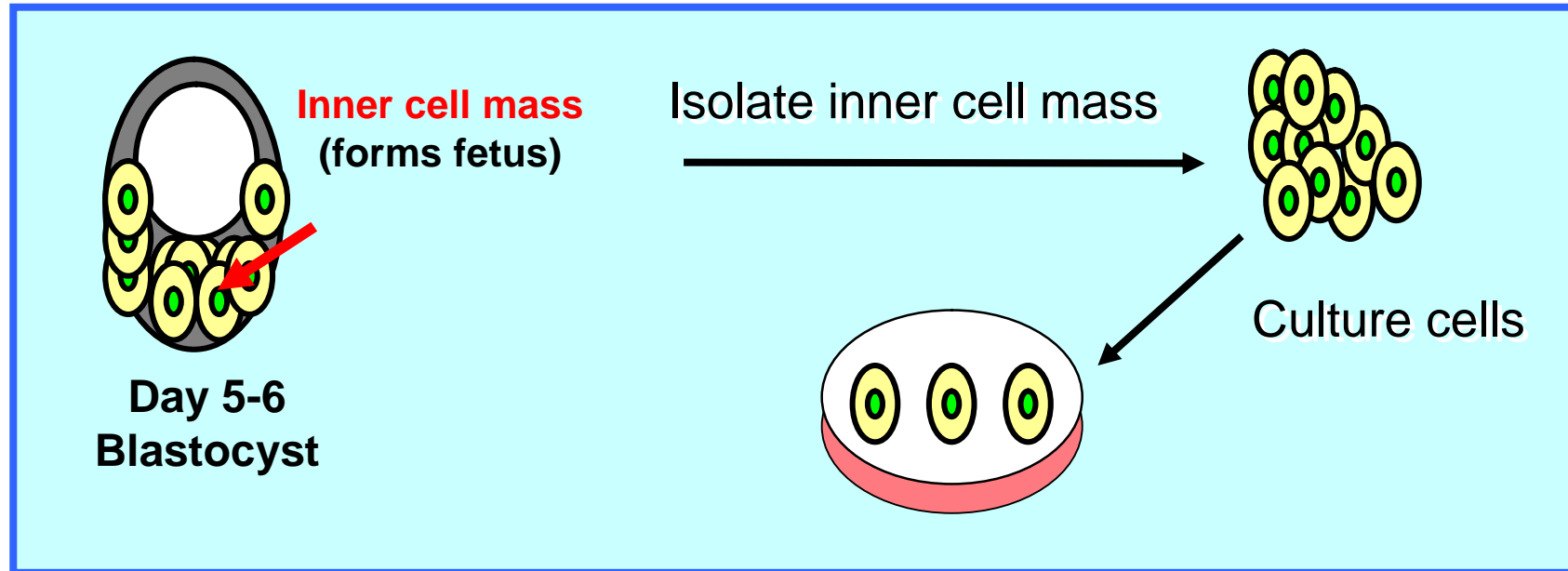
by Maxim Kniazkov

Washington (AFP) Jan 19, 2002

A blue-ribbon panel sponsored by the US National Academy of Sciences called Friday for a strict ban on human cloning but -- in stark disagreement with the Bush administration -- backed creation of new stem cell lines for



# History of Human Embryonic Stem Cell Research



- In 1998, **James Thomson (University of Wisconsin-Madison)** isolated cells from the inner cell mass of the blastocyst, and developed the first human embryonic stem cell line in culture.



# History of Human Embryonic Stem Cell Research

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- In 1998, **John Gearhart (Johns Hopkins University)** derived human embryonic germ cells from cells in fetal gonadal tissue in culture.

Aborted fetus

# History of Animal Cloning (Somatic Cell Nuclear Transfer)

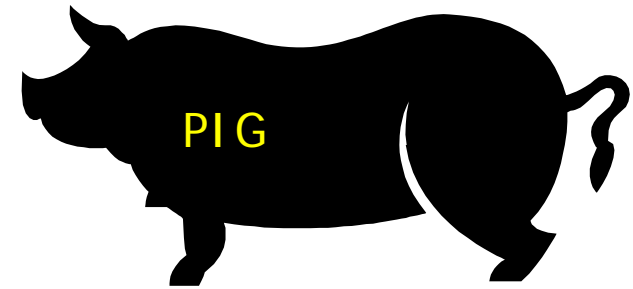
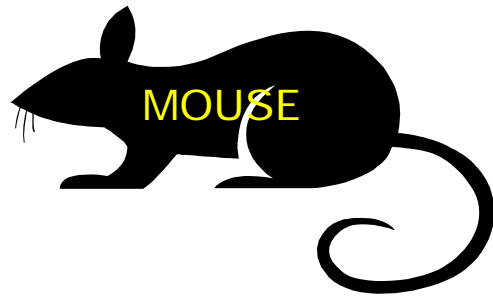
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- 1996 – **Dolly,**  
**the sheep,** was  
the **first**  
**mammal** cloned  
from adult cells.

# History of Animal Cloning

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- Since then, animals including mice (1998), cows (1998), pigs (2000), cats (2001), rabbits (2002), and dogs (2005) were successfully cloned.



# How Successful Was Animal Cloning? **Very low (~1-3%)**

Dolly ( <b>sheep</b> )	1 live birth out of 29 cloned embryos	3%
Cloned <b>mice</b>	31 live births out of 2468 cloned embryos	1%
Cloned <b>pigs</b>	5 live births out of 335 cloned embryos	1%
Cloned <b>goats</b>	3 live births out of 85 cloned embryos	3%
Cloned <b>cattle</b>	30 live births out of 496 cloned embryos	6%
Cloned <b>cat</b>	1 live birth out of 87 cloned embryos	1%
Cloned <b>rabbits</b>	6 live births out of 371 of cloned embryos	1%

# First Success of Human Embryo Cloning

- In 2001, the first cloned human embryo created by US researchers died at the 4-6 cell stage — **too early to obtain embryonic stem cells.**

**CNN.com / SCI-TECH**

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## Human embryo created through cloning

November 26, 2001 Posted: 12:33 PM EST (1733 GMT)



WASHINGTON (CNN) -- Scientists at a technology company said Sunday they have created human embryos through cloning, drawing criticism from President Bush and lawmakers and raising new ethical questions.

Advanced Cell Technology Inc. of Worcester, Massachusetts, said the experiment was aimed not at creating a human being but at mining the embryo for stem cells used to treat disease.

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# First Success of Human Embryo Cloning

- On February 12, 2004, South Korean scientists, Dr. Woo Suk Hwang and Dr. Shin Young Moon of Seoul National University, reported the successful creation of **30 cloned human embryos developed** to the **blastocyst stage** and then destroyed by stem cell extraction, **yielding one embryonic stem cell line.**

**CNN INTERNATIONAL .com**

> **BREAKING NEWS** Gustav weakens to tropical storm over Louisiana War [CNN.com](#).

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## HEALTH

### Scientists 'cloned human embryos'

Stems cells extracted to be used for medical research

Friday, February 13, 2004 Posted: 0250 GMT (10:50 AM HKT)

SEOUL, South Korea (CNN) -- South Korean researchers reported Thursday they have created human embryos through cloning and extracted embryonic stem cells, the universal cells that scientists expect will result in breakthroughs in medical research.

Hanyang University professor Hwang Yoon-Young said, "Our research team has successfully culled stem cells from



A microscopic photo released by Seoul National University shows eight of the cloned embryos.

# How Many Human Embryonic Stem Cell Lines are There?

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- The actual number of human embryonic stem cell lines is a matter of some debate.
- To date, **more than 100** human embryonic stem cell lines have been derived worldwide.
- However, most of those lines are not adequately characterized yet.
- Only 22 cell lines are eligible for federal funding in the USA.

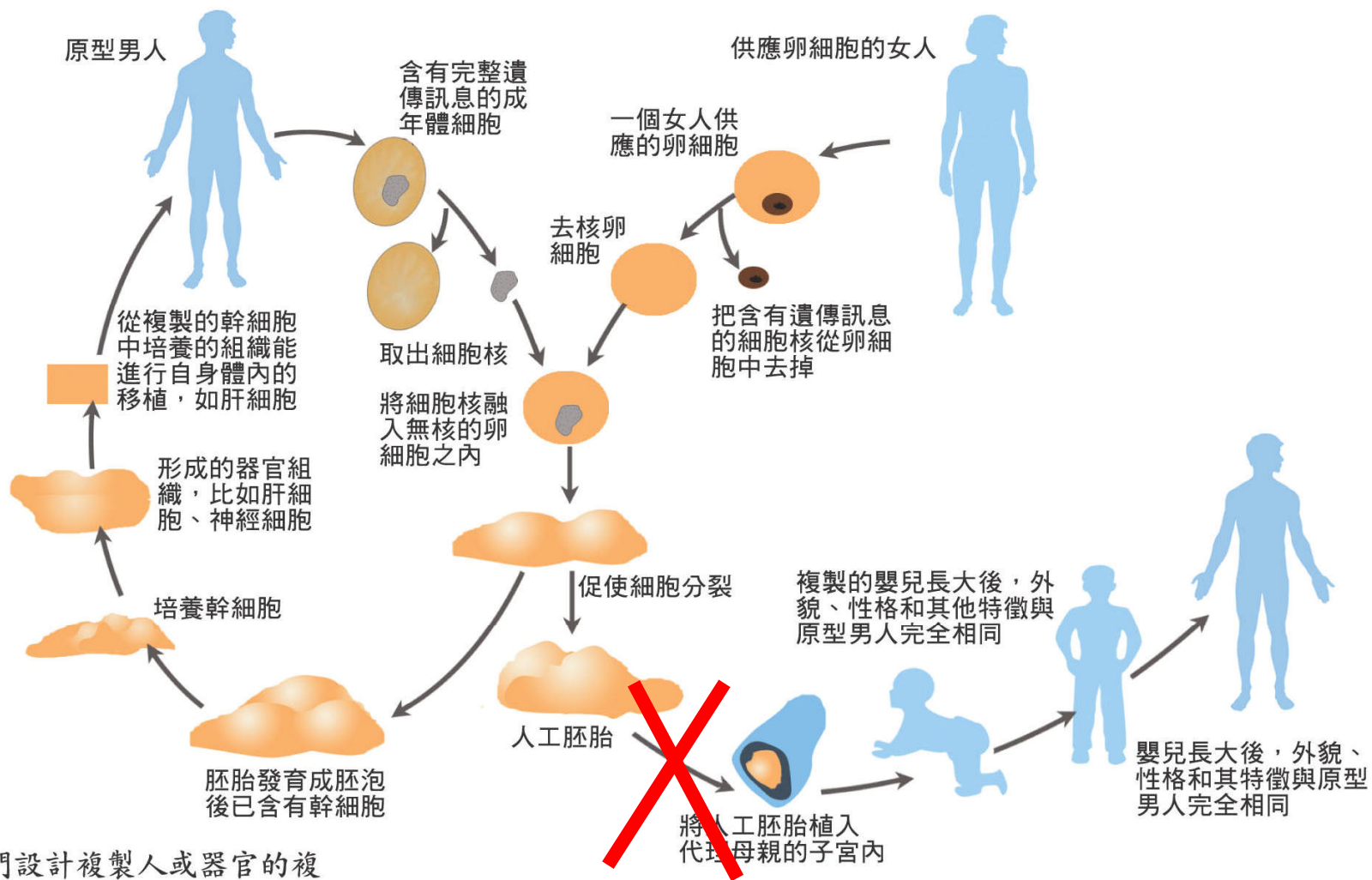
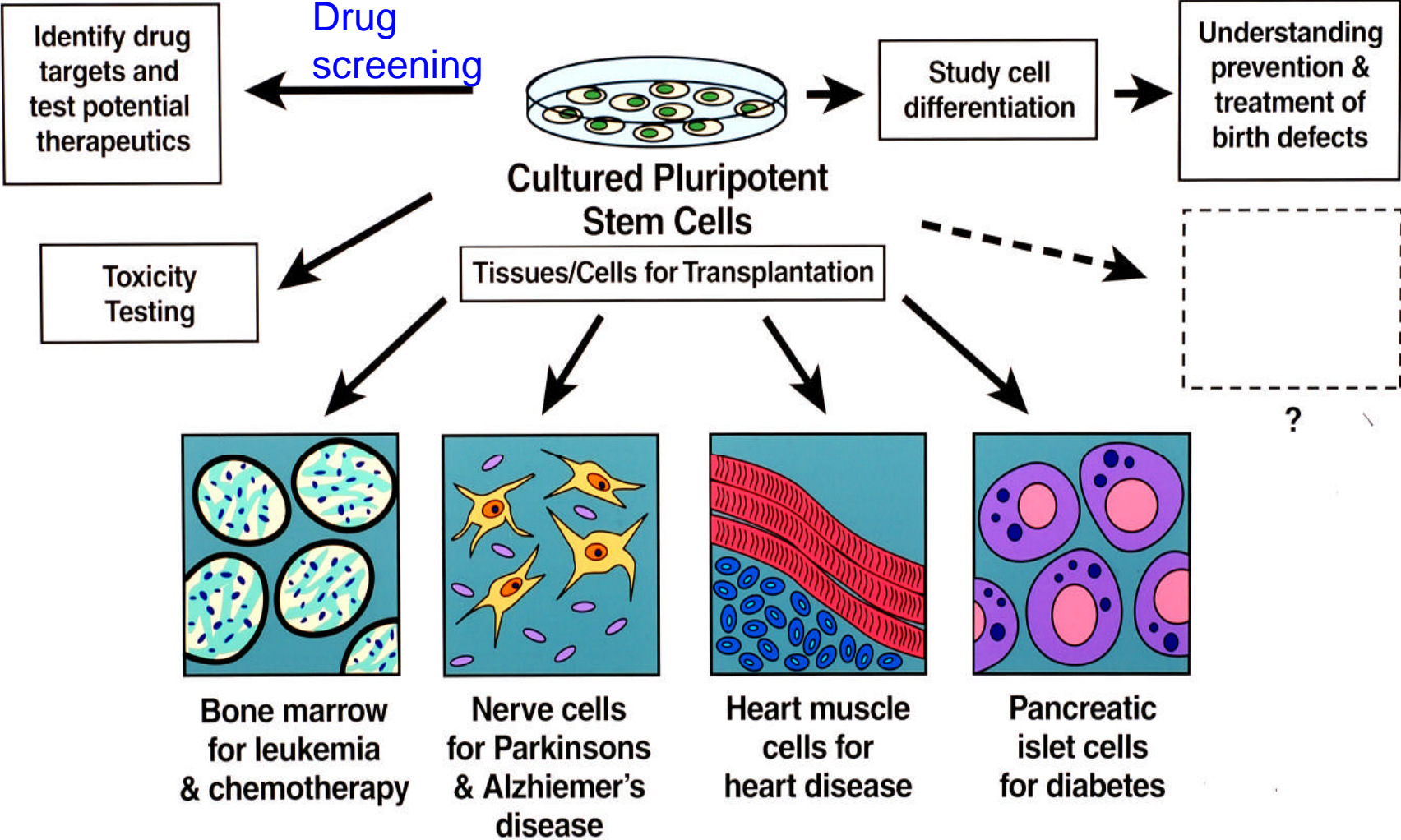


圖 12-28 專門設計複製人或器官的複製技術與步驟



# The Promise of Stem Cell Research



# How Does Cell Therapy Work?

- Stem cells can be used to generate healthy and functioning specialized cells, which can then replace diseased or dysfunctional cells.
- It is similar to the process of organ transplantation only the treatment consists of **transplanting cells instead of organs.**



# How Does Cell Therapy Work?

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- **Bone marrow transplants** are an example of cell therapy in which the stem cells in a donor's marrow are used to replace the blood cells of the victims of leukemia.
- Cell therapy is also being used in experiments to **graft new skin cells** to treat serious burn victims, and to **grow new corneas** for the sight-impaired.
- **In all of these uses, the goal is for the healthy cells to become integrated into the body and begin to function like the patient's own cells.**

## 未來幹細胞或許可以用來治療以下常見疾病

Parkinson's disease (巴金森氏症)

Alzheimer's disease (老人癡呆症)

Spinal cord injury (脊髓損傷)

Stroke (中風)

Burns (燒傷)

Diabetes (糖尿病)

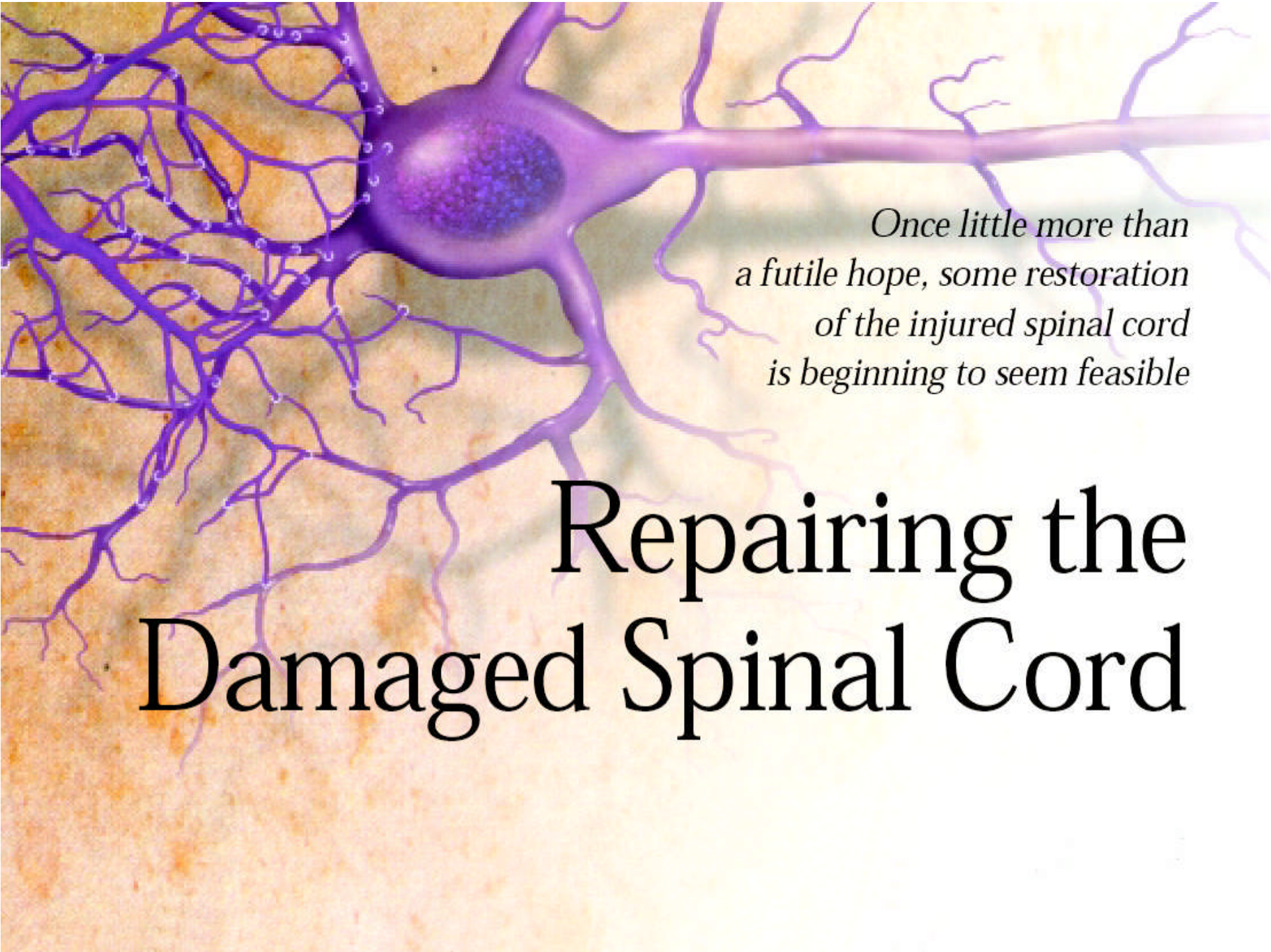
Liver failure (肝衰竭)

Heart disease (心臟病)

Osteoarthritis (骨關節炎)

Rheumatoid arthritis (風濕性關節炎)

End-stage kidney disease (末期腎臟病變)



*Once little more than  
a futile hope, some restoration  
of the injured spinal cord  
is beginning to seem feasible*

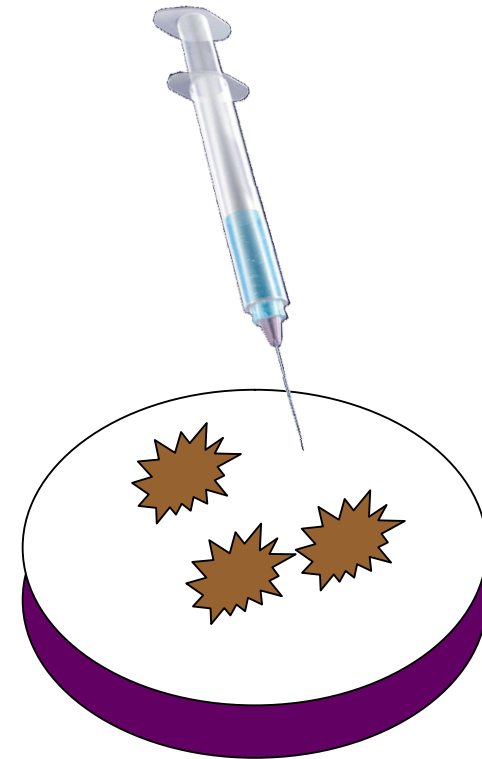
# Repairing the Damaged Spinal Cord



# Drug Testing (Screening)

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- Stem cells could allow scientists to test new drugs using human cell line which could speed up new drug development.
- Only drugs that were safe and had beneficial effects in cell line testing would graduate to whole animal or human testing.
- It would allow quicker and safer development of new drugs.



# Obstacles of Stem Cell Research

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- **How to find the right type of stem cells?**
- **How to put the stem cells into the right place?**
- **Will the stem cells perform the desired function in the body?**
- **Differentiation protocols for many cell types have not been developed.**



# Divergent Religious View on Research and Clinical Use of ESC

Religions	Embryonic Stem Cell (ESC) Research
Catholic 天主教徒	<b>Prohibited</b> (life begins at conception)
Muslim 伊斯蘭教信徒	<b>Acceptable</b> (fetus has moral existence only at the end of the 4 <sup>th</sup> month)
Jewish 猶太人	<b>Acceptable</b> (embryo has no moral status until 40 days)
Buddhist 佛教徒	<b>Prohibited</b> (life begins at conception)

# Ethical Considerations of Stem Cell Research

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- **When does human life/personhood begin?**
- **Adult stem cells or embryonic stem cells?**

# Religious Debate over Harvesting Embryonic Stem Cells

---

## The pro-life group generally believes that:

- Personhood happens at, or shortly after, conception.
- Thus, they consider the removal of stem cells from an embryo -- a procedure which kills the stem cells -- to be a form of murder of a human being.
- They argue that no potential health benefits to even hundreds of millions of people can justify the murder of other humans.



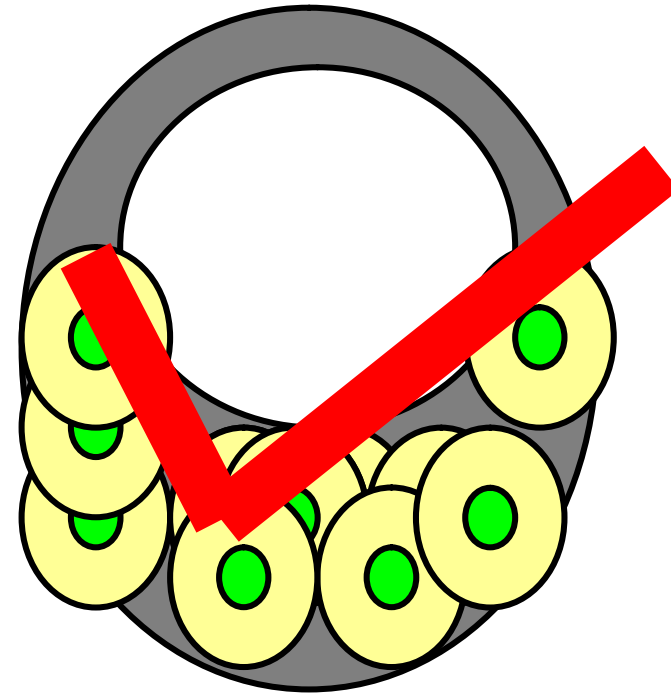
**Day 5-6  
Blastocyst**

# Religious Debate over Harvesting Embryonic Stem Cells

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## The pro-choice group generally believes that:

- Personhood is attained much later in pregnancy, perhaps when the fetal brain develops consciousness during the third trimester.
- Thus, extracting stem cells from an five or ten-day old pre-embryo is not murder.
- Killing a pre-embryo, which is only a potential human being, is justified if it has the potential to cure diseases and extend the lives of people.



**Day 5-6  
Blastocyst**

# Pros and Cons of Using Adult Stem Cell

---

## Pros

- Do not require the killing of an embryo.
- Adult stem cell research is more advanced because of its four decade head start over embryo stem cell studies.

## Cons

- Difficult to obtain, grow slower, and are less robust when compared to cells extracted from embryos.
- Stem cells for all cell and tissue types have not yet been found in the adult human.
- Stem cells in adults are often present in only minute quantities, are difficult to isolate and purify, and their numbers may decrease with age.

# Pros and Cons of Using Embryonic Stem Cell

---

## Pros

- Stem cells can potentially develop into all cell types.

## Cons

- Require the killing of an embryo.
- Difficult to develop and maintain.
- Unstable and mutate in culture.
- Pure embryonic stem cells cultures are difficult to obtain.

# Human Embryonic Stem Cells are Difficult to Develop and Maintain - The South Korean Experiment

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- **Sixteen South Korean women** received hormonal treatment to trigger them to release many eggs at one time.
- Then, the eggs were retrieved through a surgical procedure.
- A total of 242 eggs were used in the experiment.
- Researchers used the same cloning method that created Dolly, the sheep: *somatic cell nuclear transfer*.
- **Of the 242 eggs used in the cloning process, 30 reached the blastocyst (5-7 day) stage.**
- **Twenty embryos were harvested for stem cells, forming one usable embryonic stem cell line.**

# Embryonic Stem Cells are Unstable and Mutate in Culture

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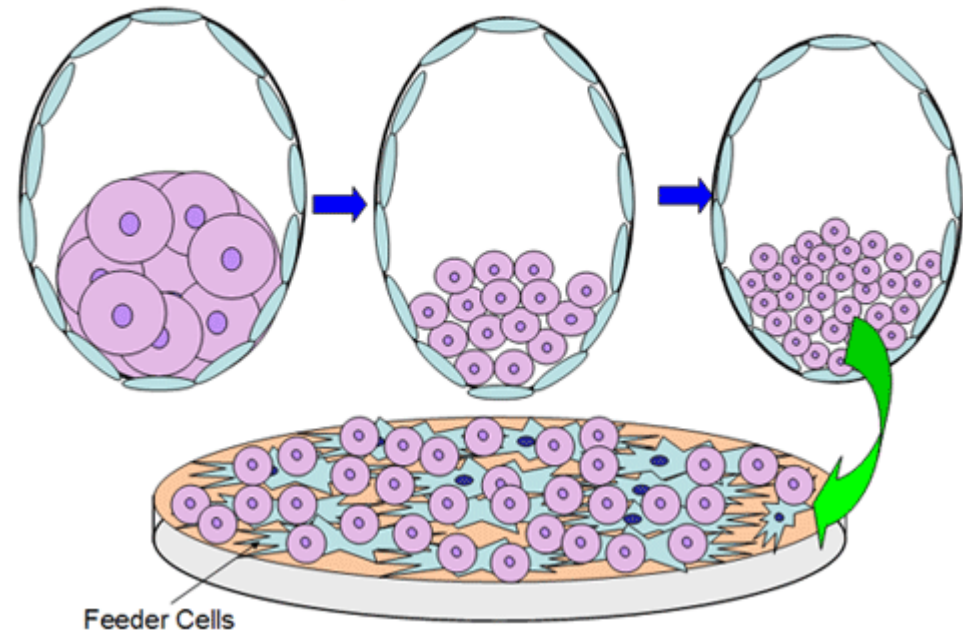
- Like ordinary cells, stem cells accumulate significant numbers of **mutations** over time, including several that could cause them to become tumors.



# Pure Embryonic Stem Cells Cultures are Difficult to Obtain

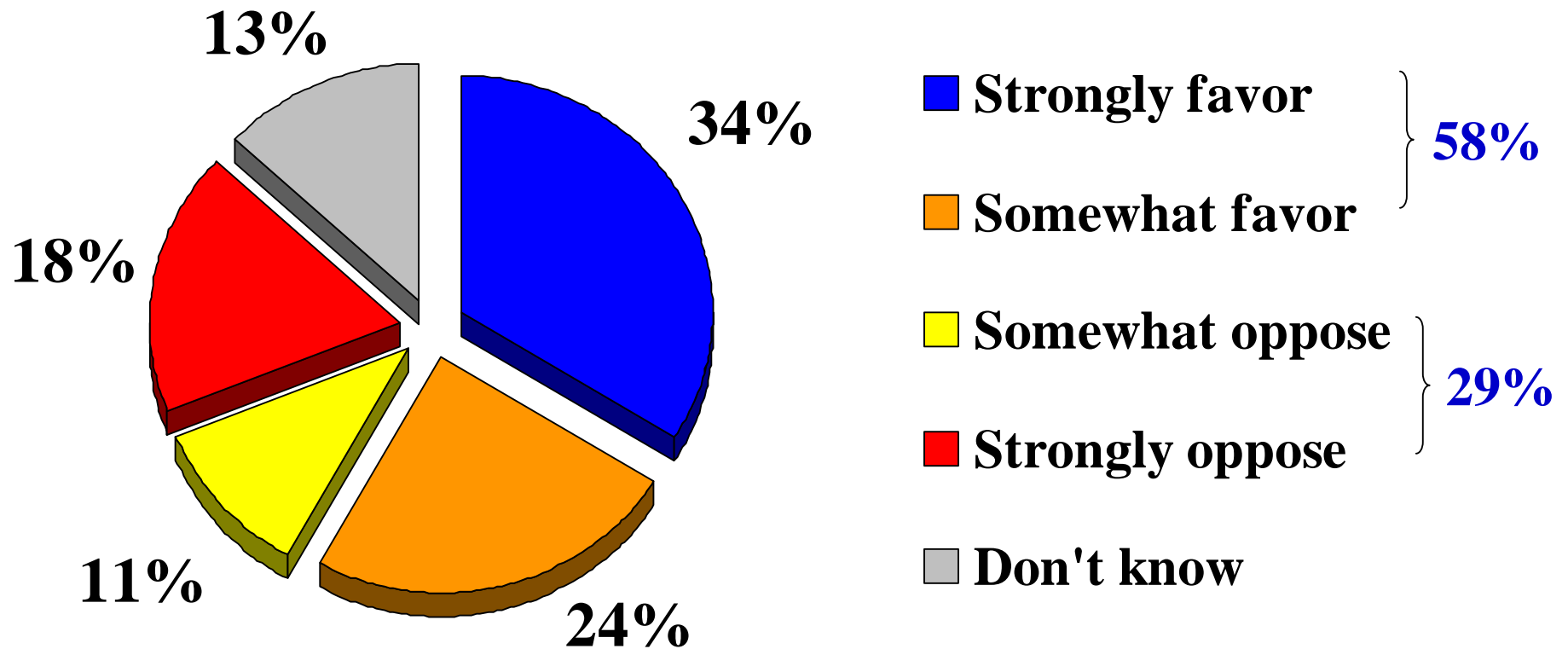
- **Some embryonic stem cell lines approved for research are no longer "pure" human lines since being exposed to mouse "feeder" cells to help keep them viable.**

**Figure 1B: Blastocyst Harvested and then Expanded *In Vitro***



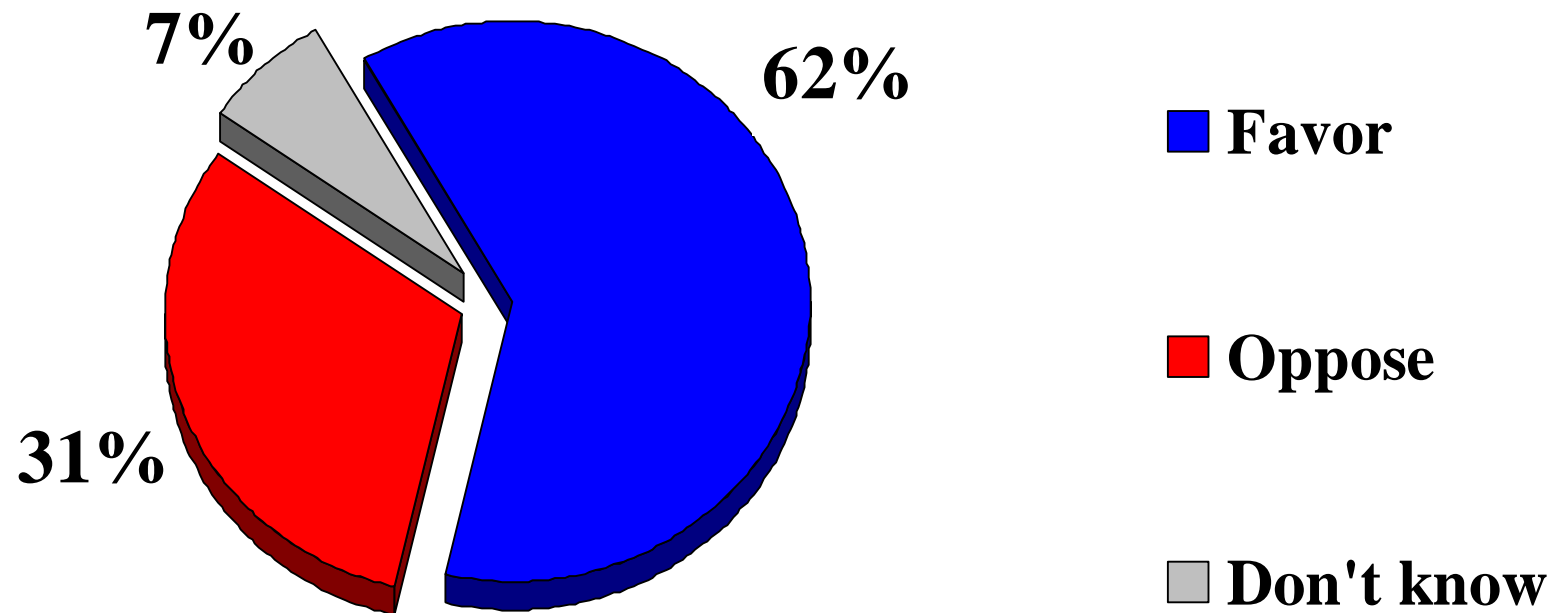
# A Majority of Americans Favor Embryonic Stem Cell Research

Do you favor or oppose medical research using embryonic stem cells?



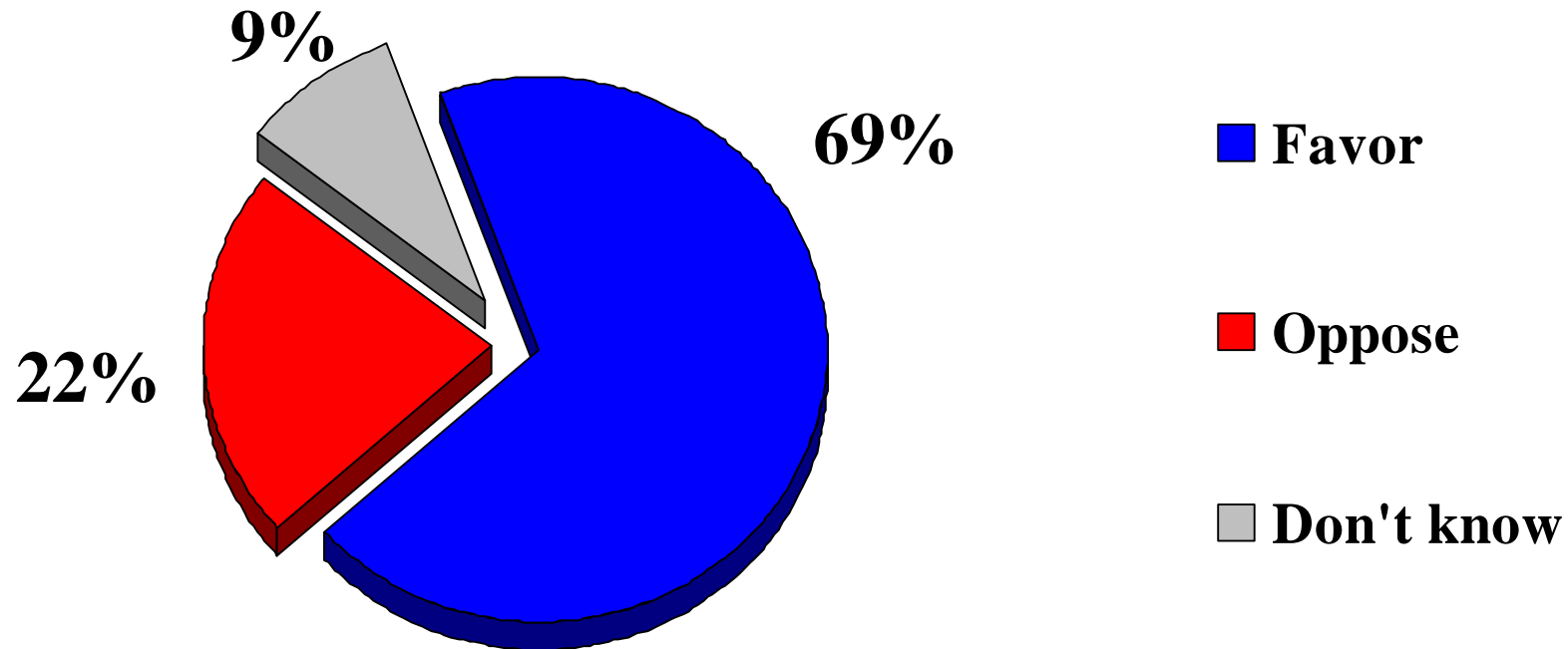
# A Majority of Americans Favor Research Using Donated Eggs from Fertility Clinics

Scientists can extract embryonic stem cells from fertilized eggs that are voluntarily donated by fertility clinic patients. These fertilized eggs would otherwise be discarded. Knowing this, do you favor or oppose embryonic research?



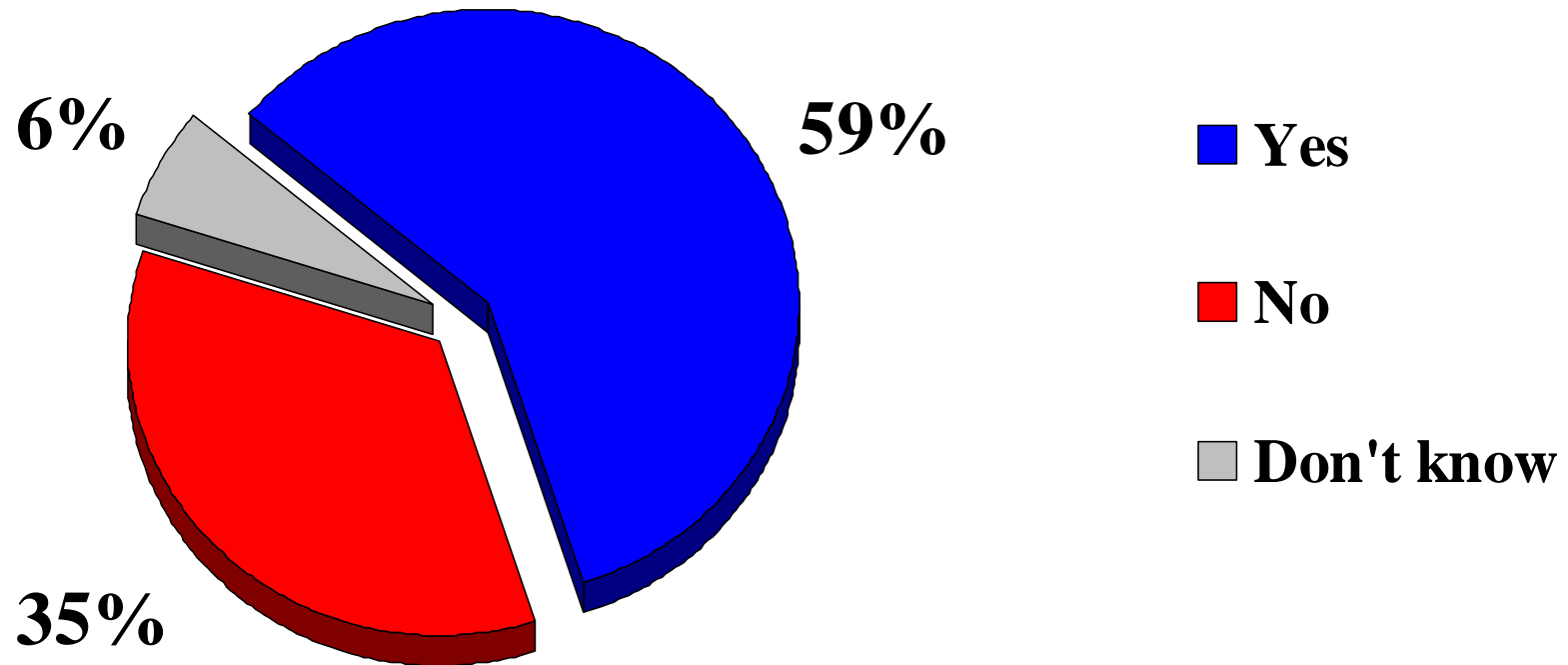
# A Majority of Americans Favor Cloning Technology to Make Embryonic Stem Cells

Scientists can now make embryonic stem cells for medical research by merging an unfertilized egg with a skin cell, for example. In other words, no fertilization takes place and there is no merger of egg and sperm. Knowing this, do you favor or oppose embryonic stem cell research?



# Therapeutic Cloning Should Be Allowed

Therapeutic cloning is the use of cloning technology to help in the search for possible cures and treatments for diseases and disabilities. Do you think that research into therapeutic cloning should be allowed?



# USA National Regulation

- **2001 - President Bush restricts federal funding for embryonic stem-cell research**
- **Federal funding only for existing stem cell lines**
- **Many consider inadequate**

# International Legislation

- **South Korea – refined nuclear transfer or therapeutic cloning**
- **China – supports research**
- **Singapore – stem cell research a national priority**
- **Israel – leaders stem cell disease**
- **Great Britain – leader Dolly – active support of research**
- **Japan – supports research**

# Summary of Policies Defined Around the World

<b>Countries</b>	<b>Human Embryo Cloning (=creating embryo)</b>	<b>Use of Stem Cell Lines</b>	<b>Use of Superfluous Embryos</b>
France, Spain	Prohibited	Authorized	Authorized
Italy, Austria, Ireland	Prohibited	Prohibited	Prohibited
U.K. Denmark	Authorized	Authorized	Authorized
Israel, Sweden, Belgium, India	Prohibited	Authorized	Authorized
Germany	Prohibited	Authorized (imported)	Authorized
U.S.A.	Prohibited (public) Free (private)	Authorized under restricted condition (public) Free (private)	Authorized (in most states)
Canada	Prohibited	Under consideration	Under consideration
Japan, Netherlands, Korea	Authorized	Authorized	Authorized
Australia	Currently prohibited but under consideration	Authorized	Authorized



國別	法律是否明文禁止複製人 (reproductive cloning)	法律是否允許以下列來源進行研究			相關主管部會	專門的全國性委員會
		幹細胞	人類胚胎	墮胎的胚胎		
丹麥	禁止	可	可	可	健康與研究部	丹麥倫理委員會
芬蘭	禁止	可	可	可	社會事務與健康部	全國健康看護諮詢委員會下的子委員會
挪威	禁止	無法律規範	不允許	正立法當中	健康與社會事務部	全國研究倫理委員會
瑞典	禁止	不允許	可	可	健康、社會事務與教育部	無全國性的機構,只有地區性的倫理委員會
英國	禁止	可	可	可	健康部門	人工受精、胚胎授權與人類基因委員會
法國	禁止	可	不允許	可	勞動與社會事務部	健康與生命科學倫理的全國性諮詢委員會
德國	禁止	無法律規範	不允許	可	聯邦健康部	無全國性的機構,只有地區性的倫理委員會
荷蘭	正立法中	正立法中	正立法中	正立法中	健康、福利與運動部	與人類事務研究有關的中央
瑞士	禁止	無法律規範	無法律規範	無法律規範	聯邦司法局	
西班牙	禁止	可	可	可	健康部	會

瑞士(2004/11/29)就一項允許對人類胚胎幹細胞進行醫學研究的法律舉行複決公投，有三分之二選民投下贊成票。