

幹細胞研究與再生醫學

Chung-Liang Chien

Department of Anatomy and Cell Biology

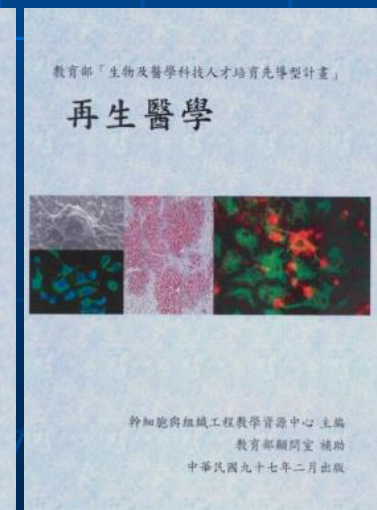
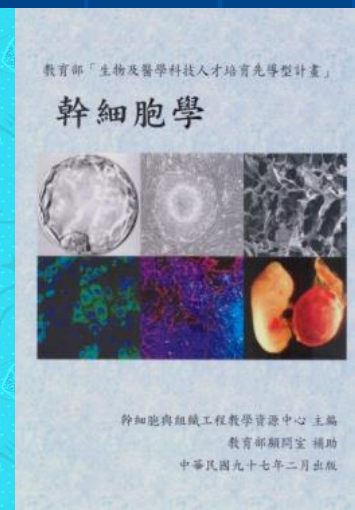
College of Medicine

National Taiwan University

背景說明

幹細胞與再生醫學研究與產學合作之具體成果：

- 建立臺灣人胚胎幹細胞 (Chen et al., 2007, Human Reproduction)
- 臺大醫院骨科部江清泉主任與工研院：「兩相材料軟硬骨關節修復技術」 技術移轉美精技公司 (Exactech)
(臺大醫學院技術移轉案 8 件，總金額超過4000萬元)。
- 幹細胞與組織工程教學資源中心 提供夥伴學校相關服務

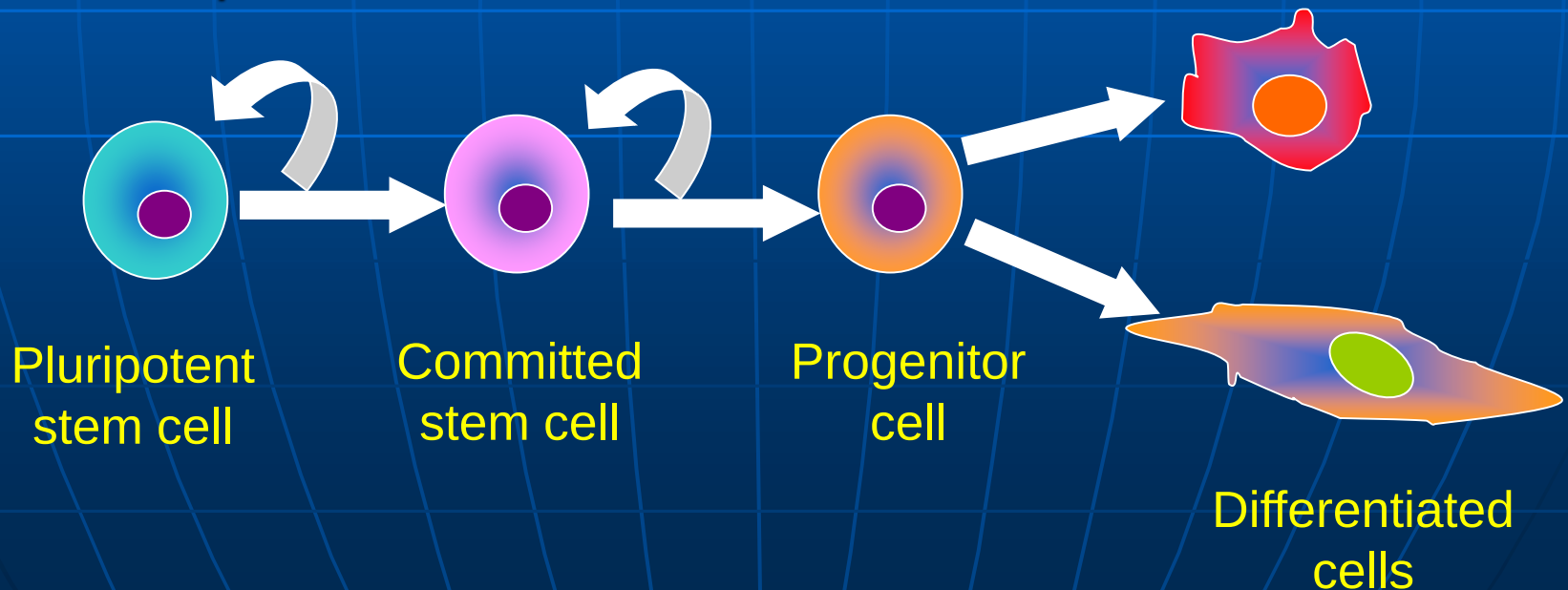


Stem cells

■ Self-renewal

■ Potency

- The capacity to differentiate into specialized cell types
- Totipotent, Pluripotent, Multipotent, and Unipotent



Classes of Stem Cells

Source	Description	Examples
Adult organs	Reservoir of cells partially committed to type of tissue in organ.	Liver, bones, bone marrow, lining of gut, and spermatozoa.
Fetal tissues	Precursor cells more abundant in growing organs; some uncommitted cells.	Heart muscle cells, brain cells, germ cell precursors to sperm and eggs.
Blastocysts	Inner cell mass cells of blastocysts created either by chemical/electrical stimulation of unfertilized eggs to produce parthenotes, or by infertility procedures with sperm and eggs.	Stem cells from parthenotes are under investigation; embryonic stem cells have the potential to give rise to all cell types.
Nuclear transplant blastocysts	Derived from eggs stimulated to divide following complete exchange of genetic information.	Under investigation; process related to animal cloning.

Adult Stem cells & Regenerative medicine

1. Bone marrow
2. Adipose tissue
3. Liver
4. Muscle
5. Intestine
6. Brain
7. Gonad
8. Skin

生体内にある体性幹細胞

体性幹細胞



決められた細胞
になら分化
できるよ!

生体内に存在し、分化
能が限定された幹細胞

腸

消化管上皮
幹細胞

骨髄

造血幹細胞
間葉系幹細胞

脳

神経幹細胞

心臓

心筋幹細胞

肝臓

肝幹細胞

精巣・卵巣

生殖幹細胞

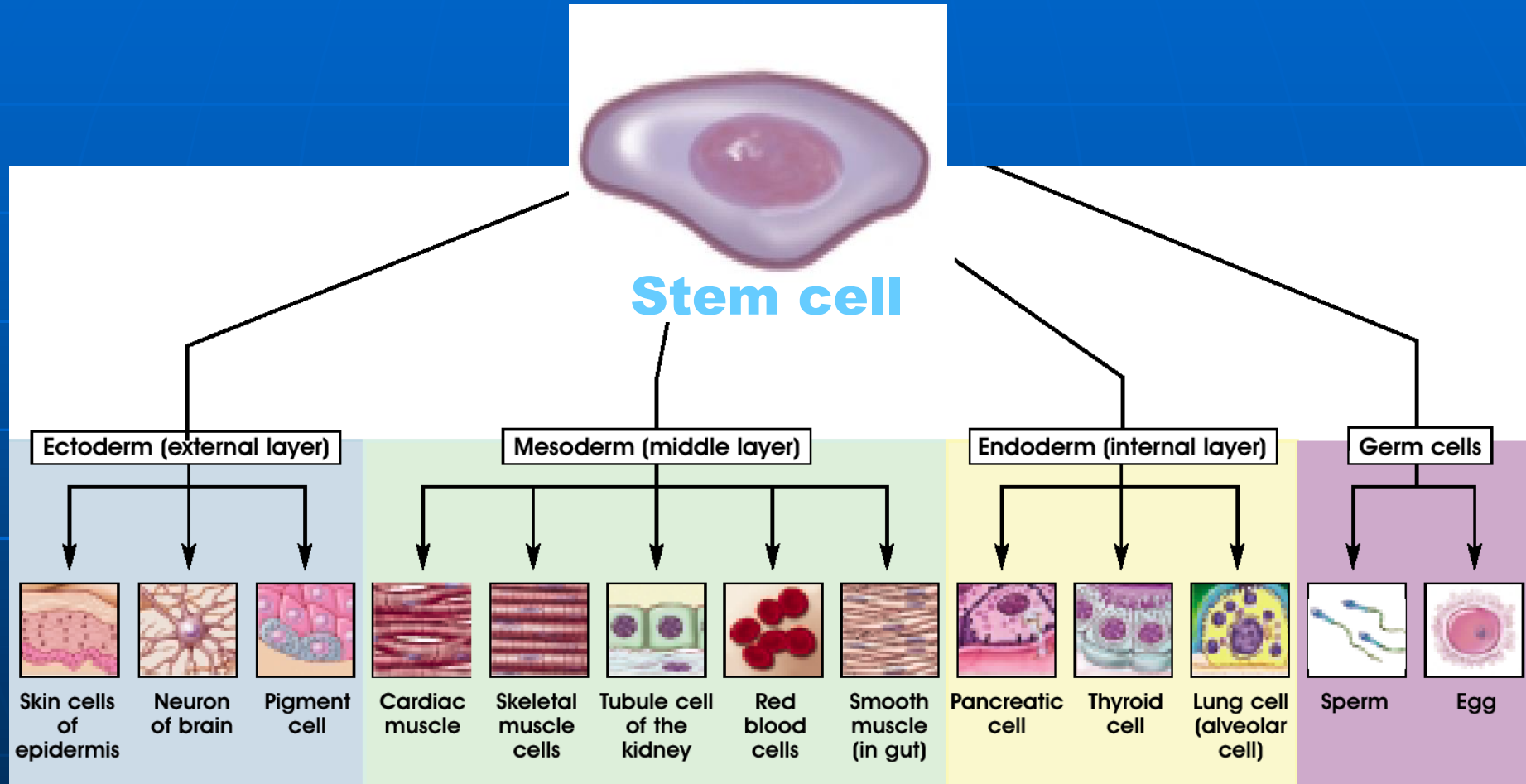
筋肉

骨格筋幹細胞

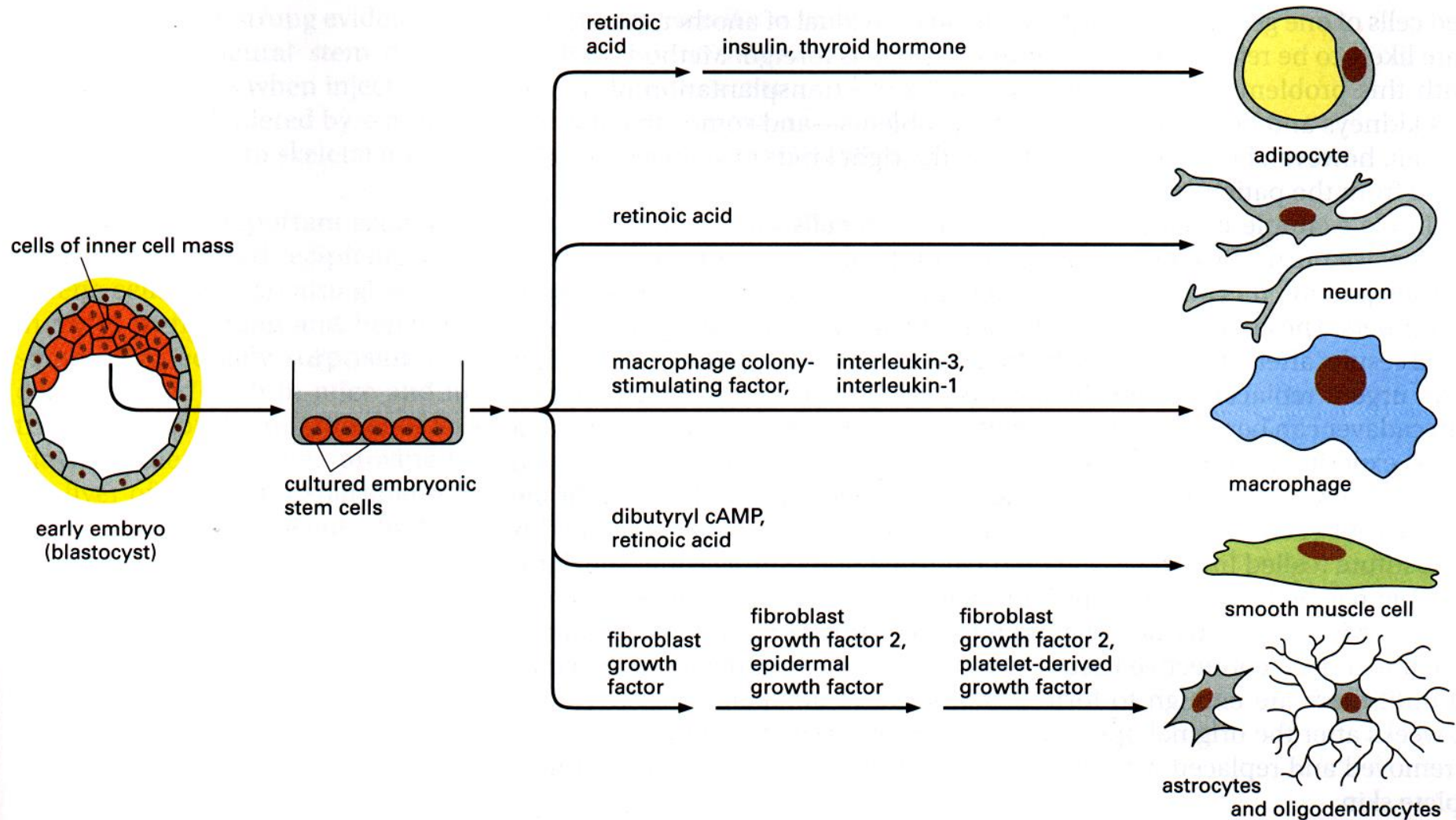


Cell differentiation

With combination of growth differentiation factors



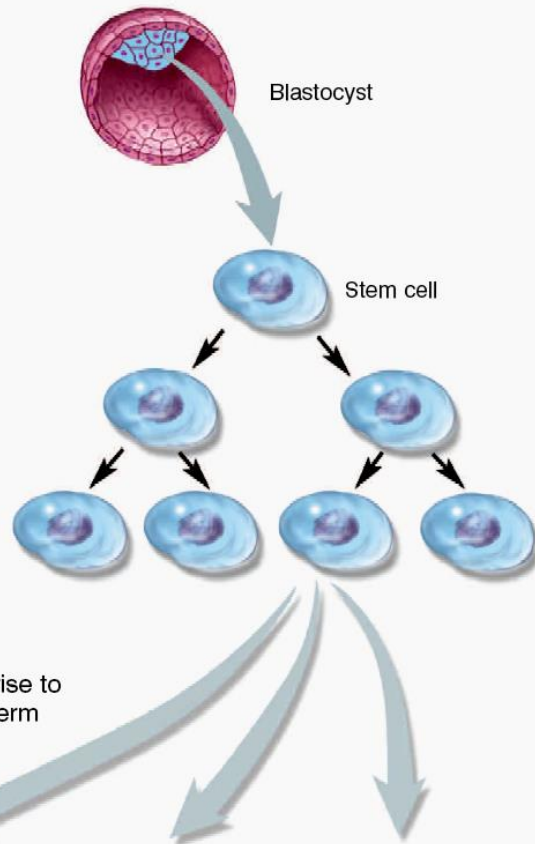
Tissue engineering from ES cells



Characteristics of Embryonic Stem Cells

Application of Stem cells

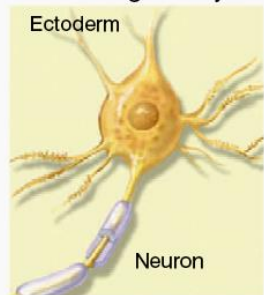
1. Origin:
Derived from pre-implantation or peri-implantation embryo



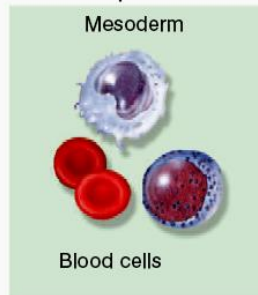
2. Self-Renewal:
The cells can divide to make copies of themselves for a prolonged period of time without differentiating.

3. Pluripotency:
Embryonic stem cells can give rise to cells from all three embryonic germ layers even after being grown in culture for a long time.

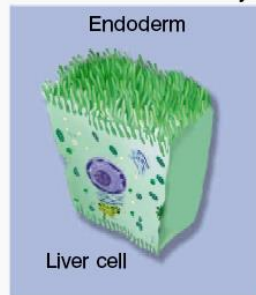
The three germ layers and one example of a cell type derived from each layer:



Ectoderm gives rise to: brain, spinal cord, nerve cells, hair, skin, teeth, sensory cells of eyes, ears, nose, and mouth, and pigment cells.

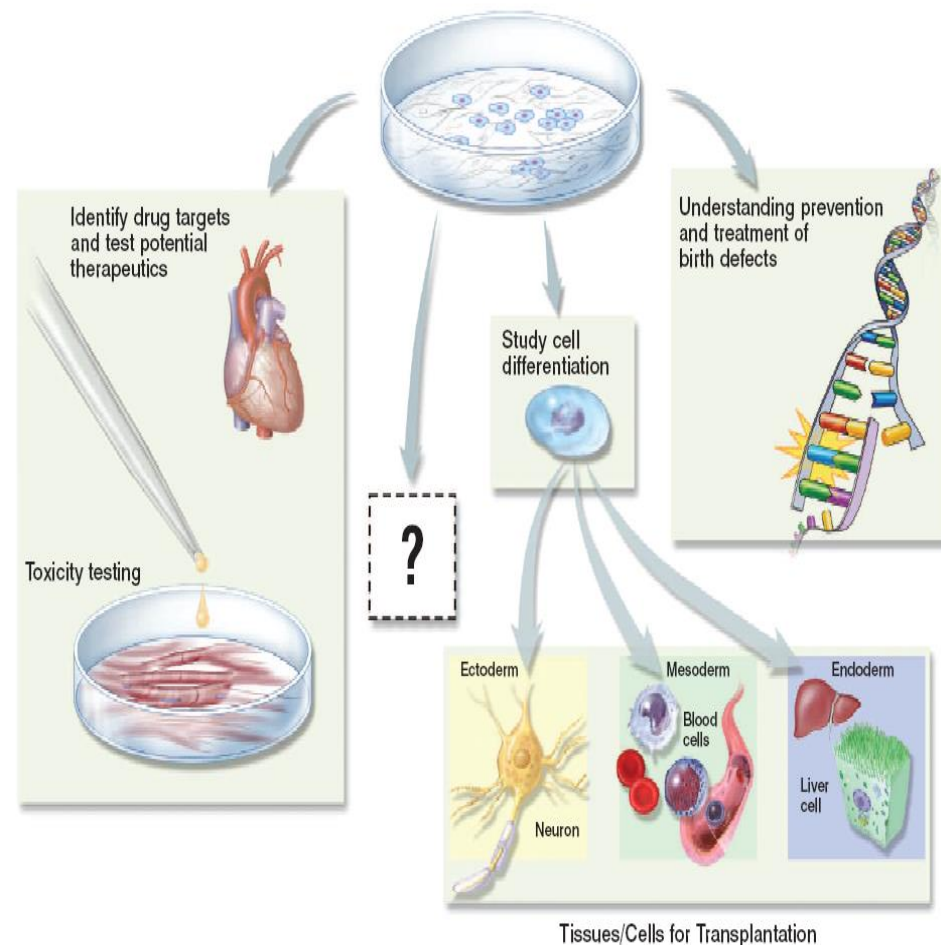


Mesoderm gives rise to: muscles, blood, blood vessels, connective tissues, and the heart.

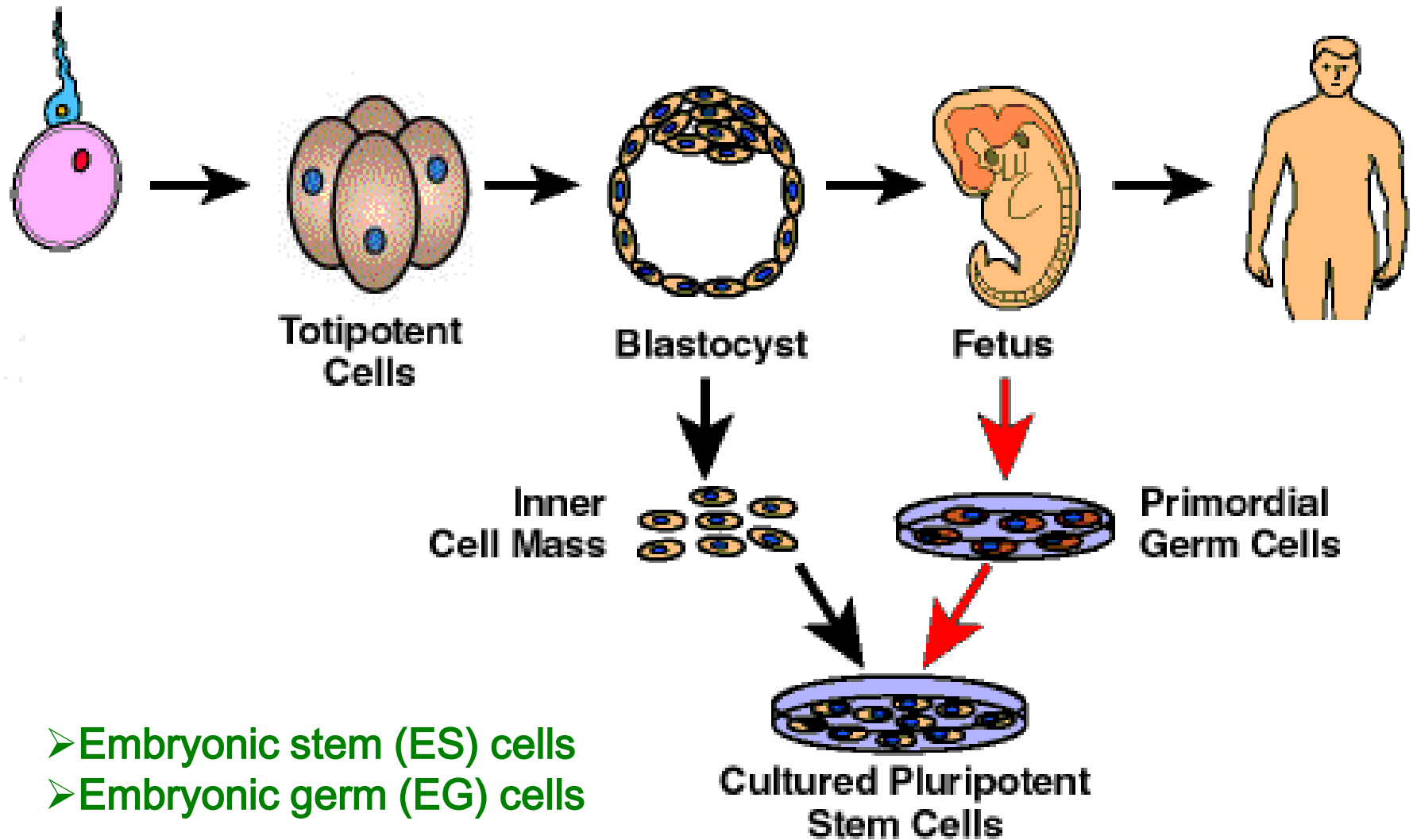


Endoderm gives rise to: the gut (pancreas, stomach, liver, etc.), lungs, bladder, and germ cells (eggs or sperm).

The Promise of Stem Cell Research



Pluripotent stem cells



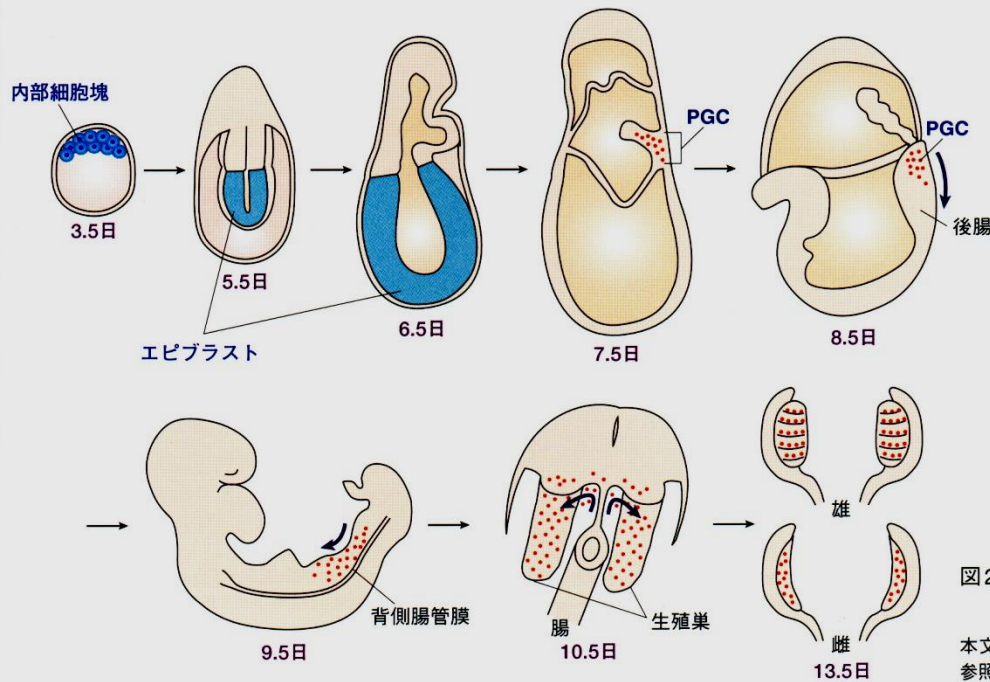
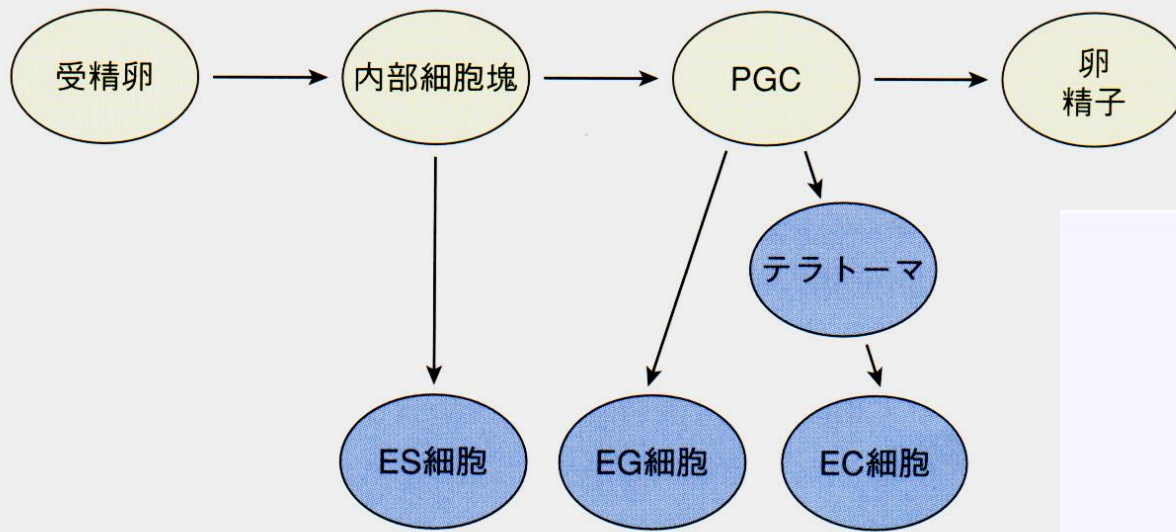
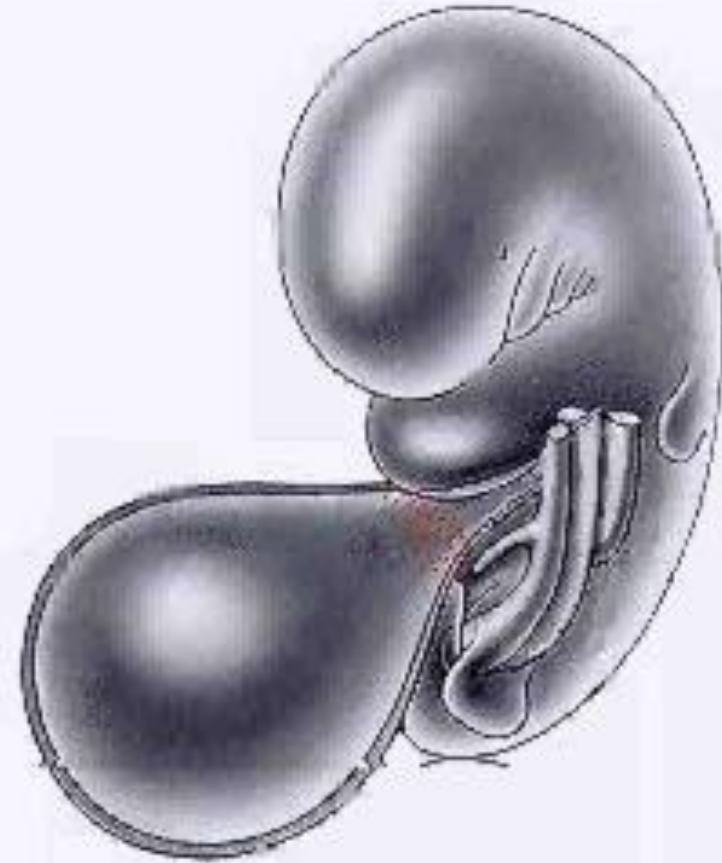


図2. マウス発生における分化多能性細胞とPGC

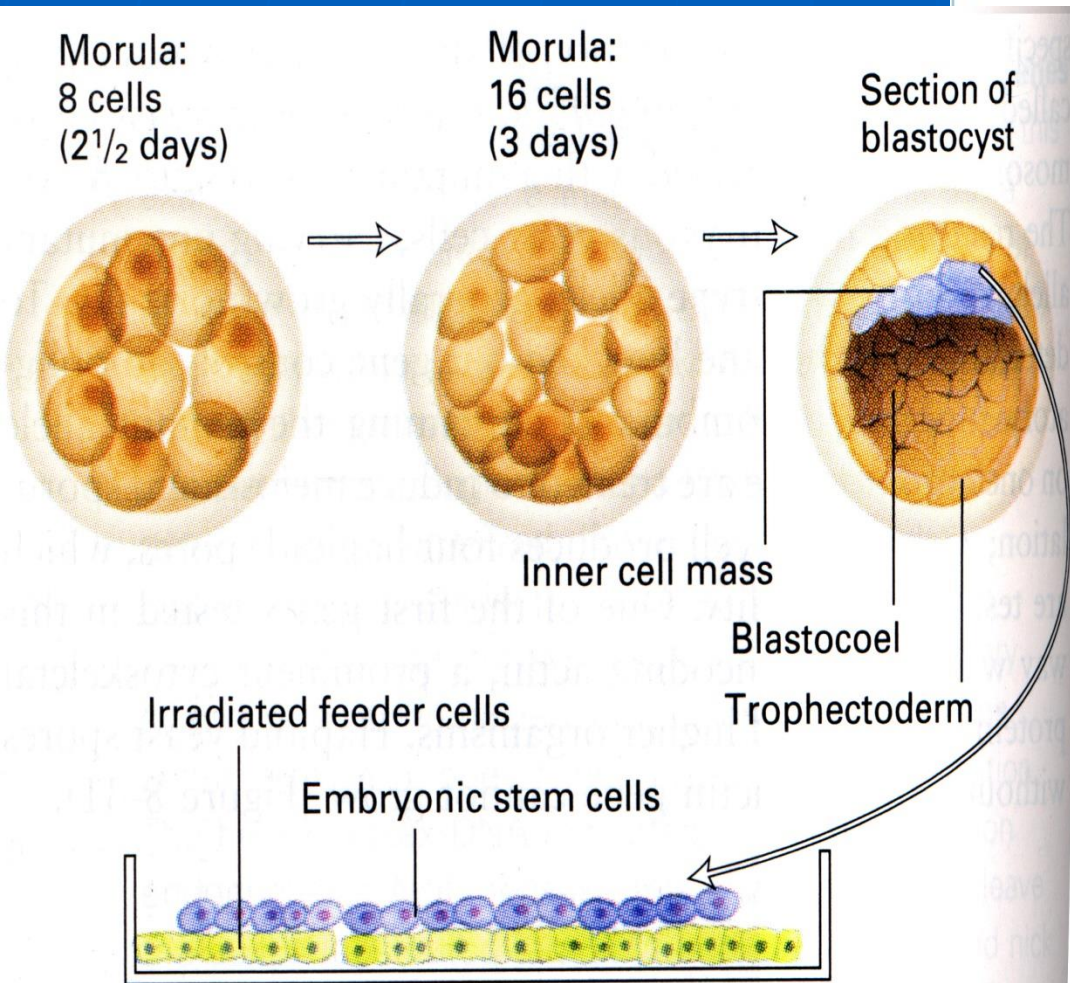
本文「I. 始原生殖細胞 (PGC)」参照。



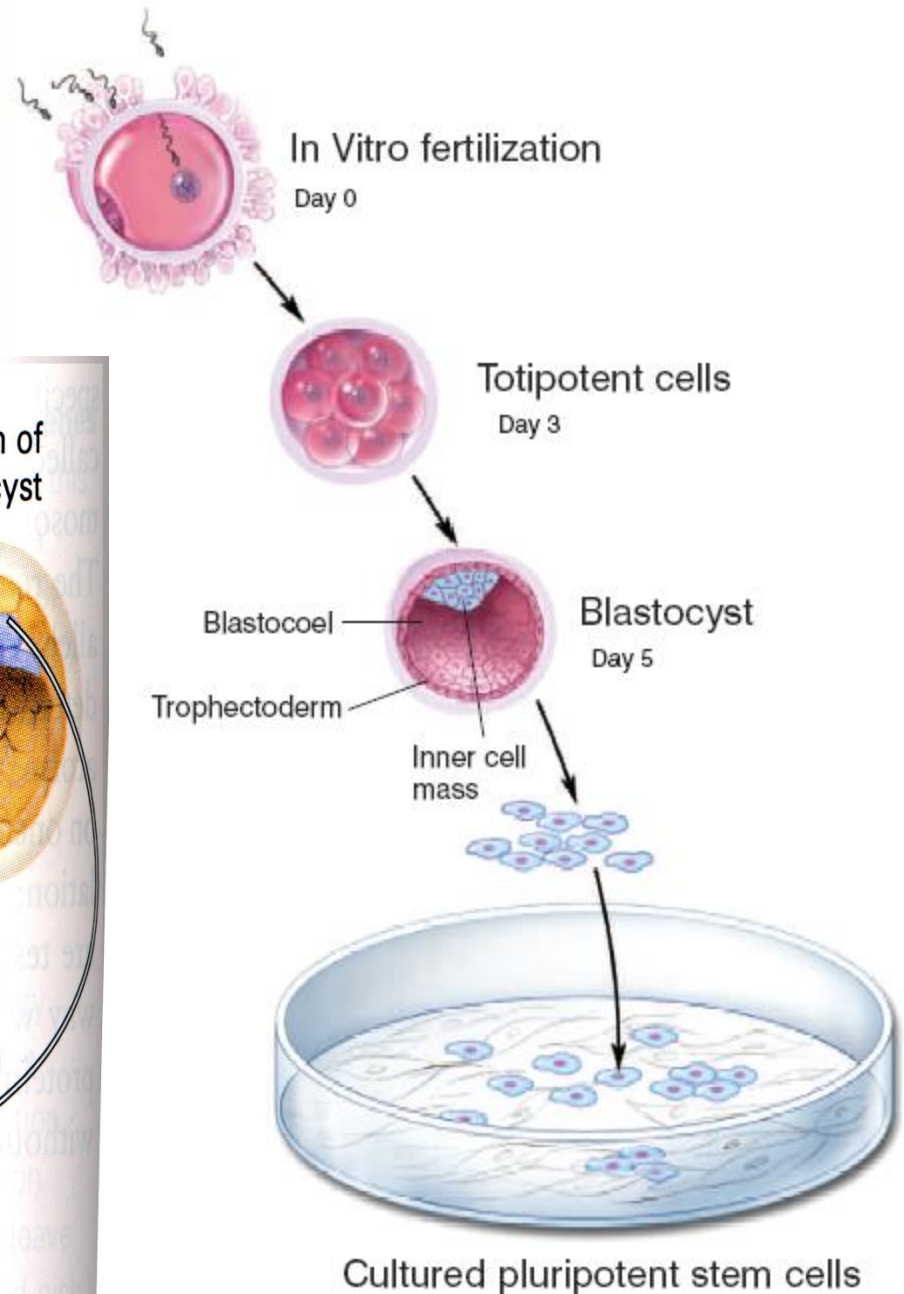
動し、そこで雌雄それぞれの生殖細胞として分化を開始する。

Ⅲ. EG細胞とPGC

How Embryonic Stem (ES) cells are derived



How Human Embryonic Stem Cells Are Derived



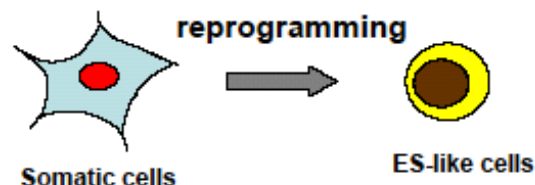


Institute for Frontier Medical Sciences, Kyoto University **Yamanaka's Lab.**

京都大学再生医科学研究所 再生統御学研究部門
再生誘導研究分野 (山中研究室)

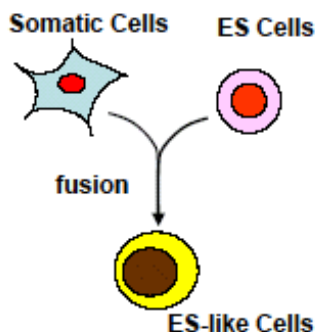
Department of Stem Cell Biology Since 2004

ES-like Cells by Reprogramming

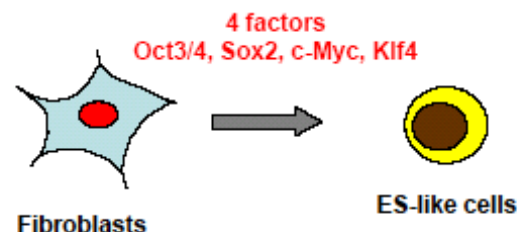


Reprogramming factors

Reprogramming Factors Do Exist

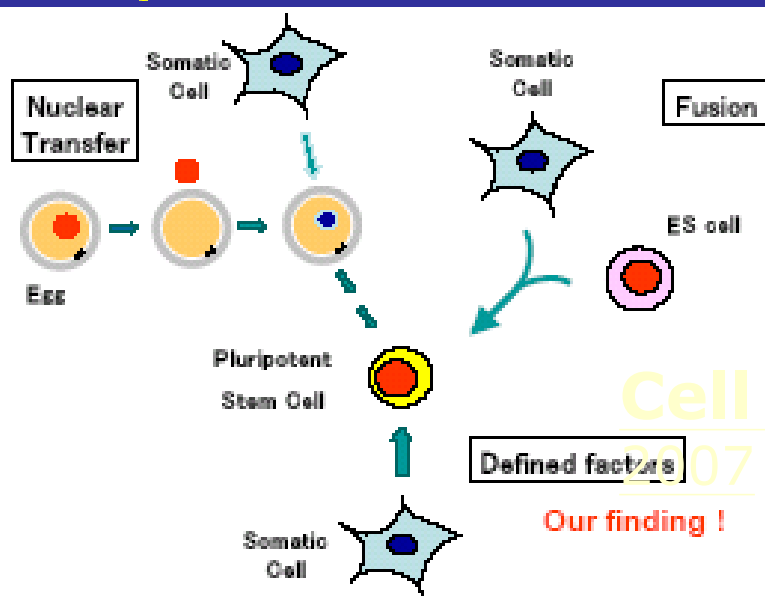


Evaluation of Candidates



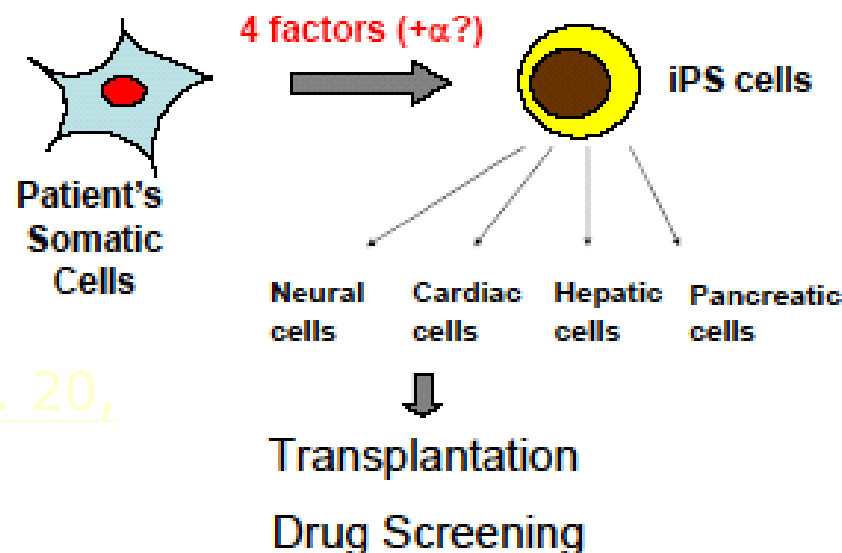
iPS cells
(Induced pluripotent stem cell)

Comparison to Other Methods



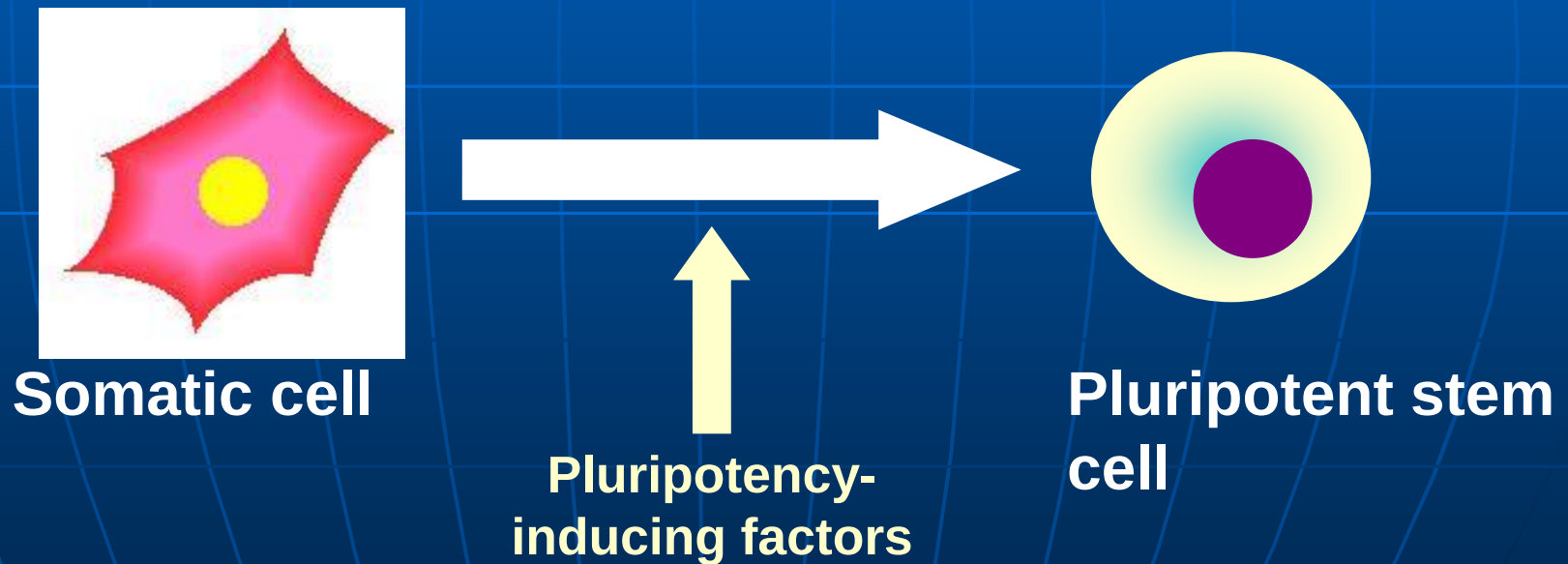
Cell Nov. 20, 2007

Future Plans

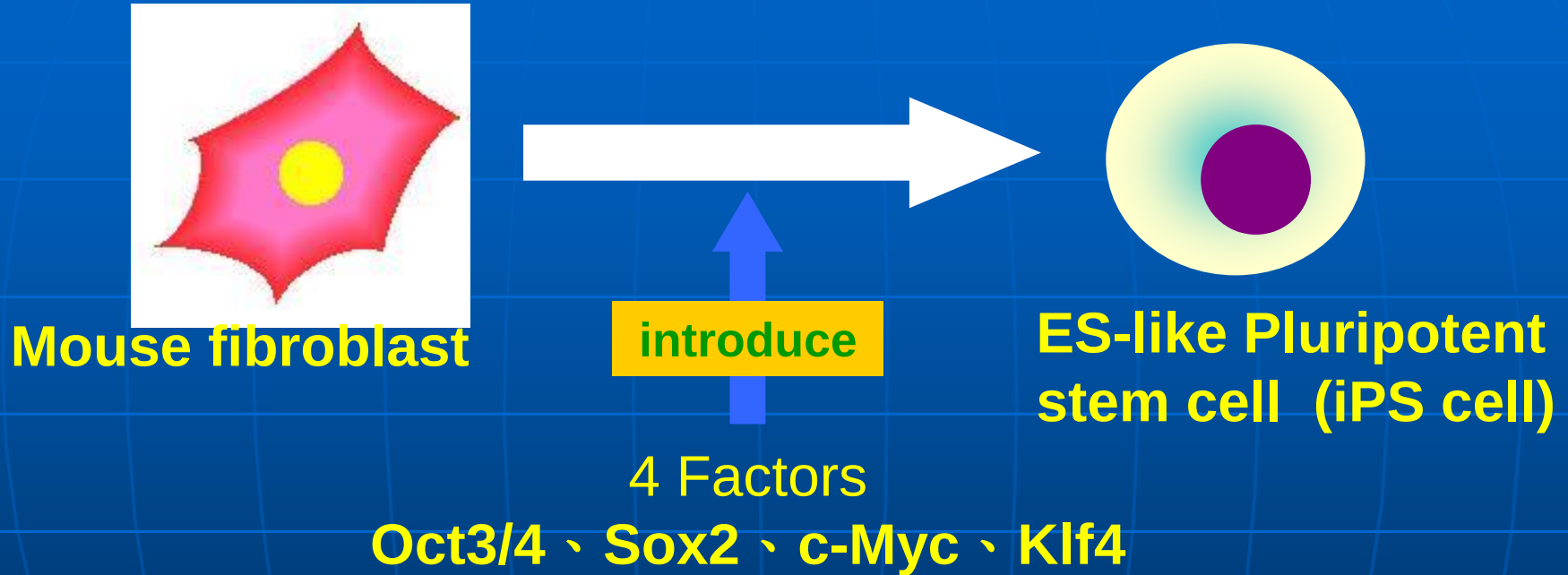


Induced Pluripotent Stem Cells (iPS cells)

- A type of pluripotent stem cell artificially derived from a non-pluripotent cell by inserting certain genes.

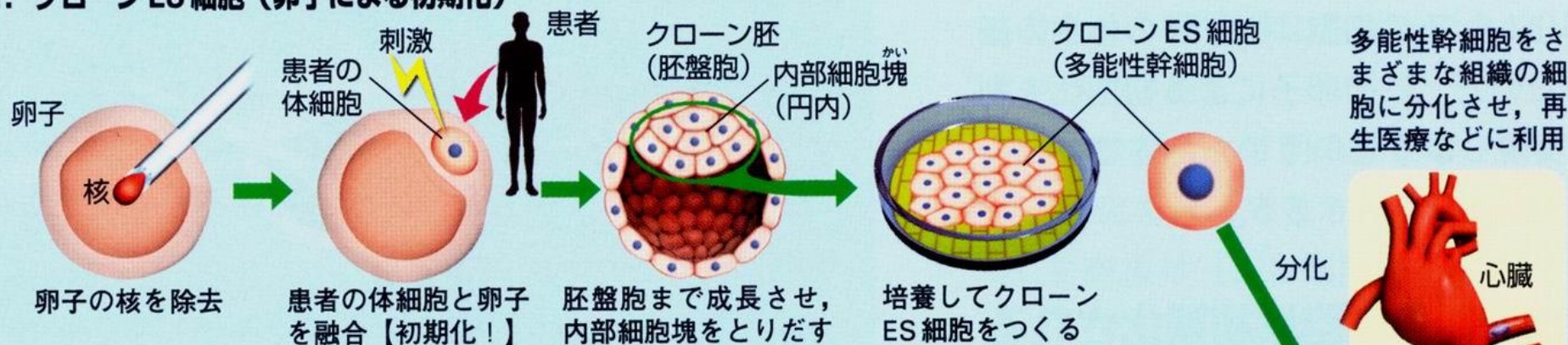


Induced Pluripotent Stem (iPS) Cells in Mouse

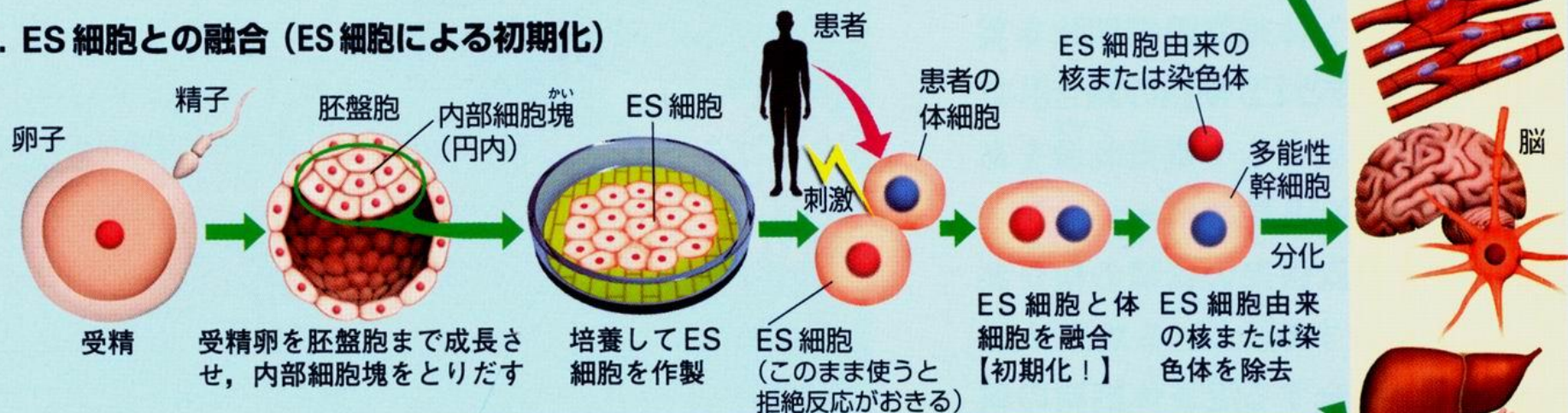


- K. Takahashi, S. Yamanaka, *Cell* **126**, 663 (2006).
- K. Okita, T. Ichisaka, S. Yamanaka, *Nature* **448**, 313 (2007).

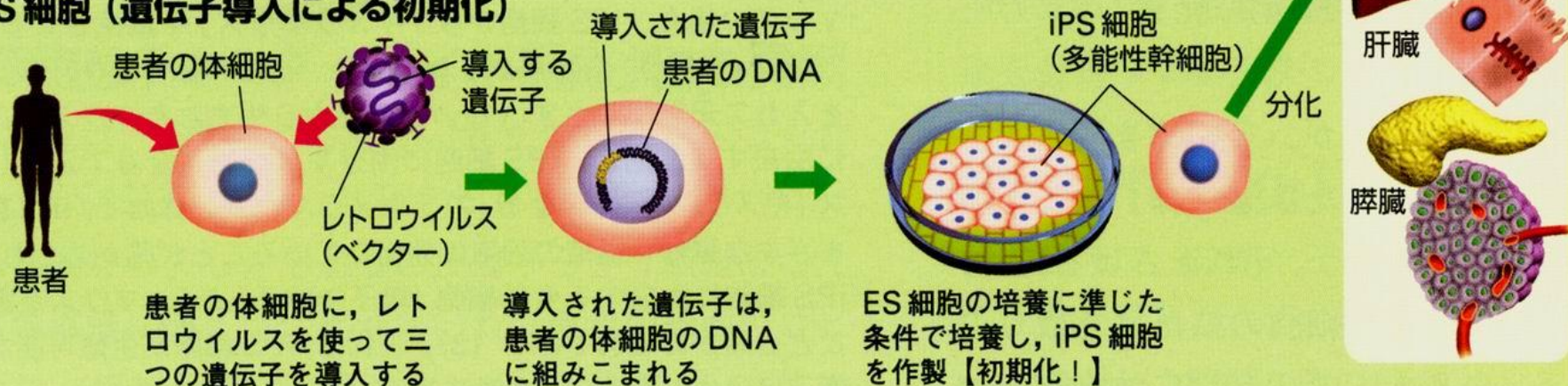
1. クローンES細胞 (卵子による初期化)

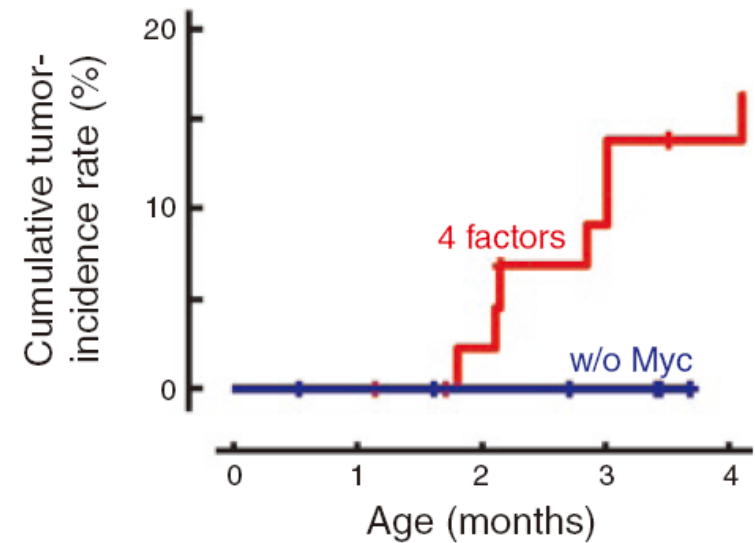


2. ES細胞との融合 (ES細胞による初期化)



3. iPS細胞 (遺伝子導入による初期化)

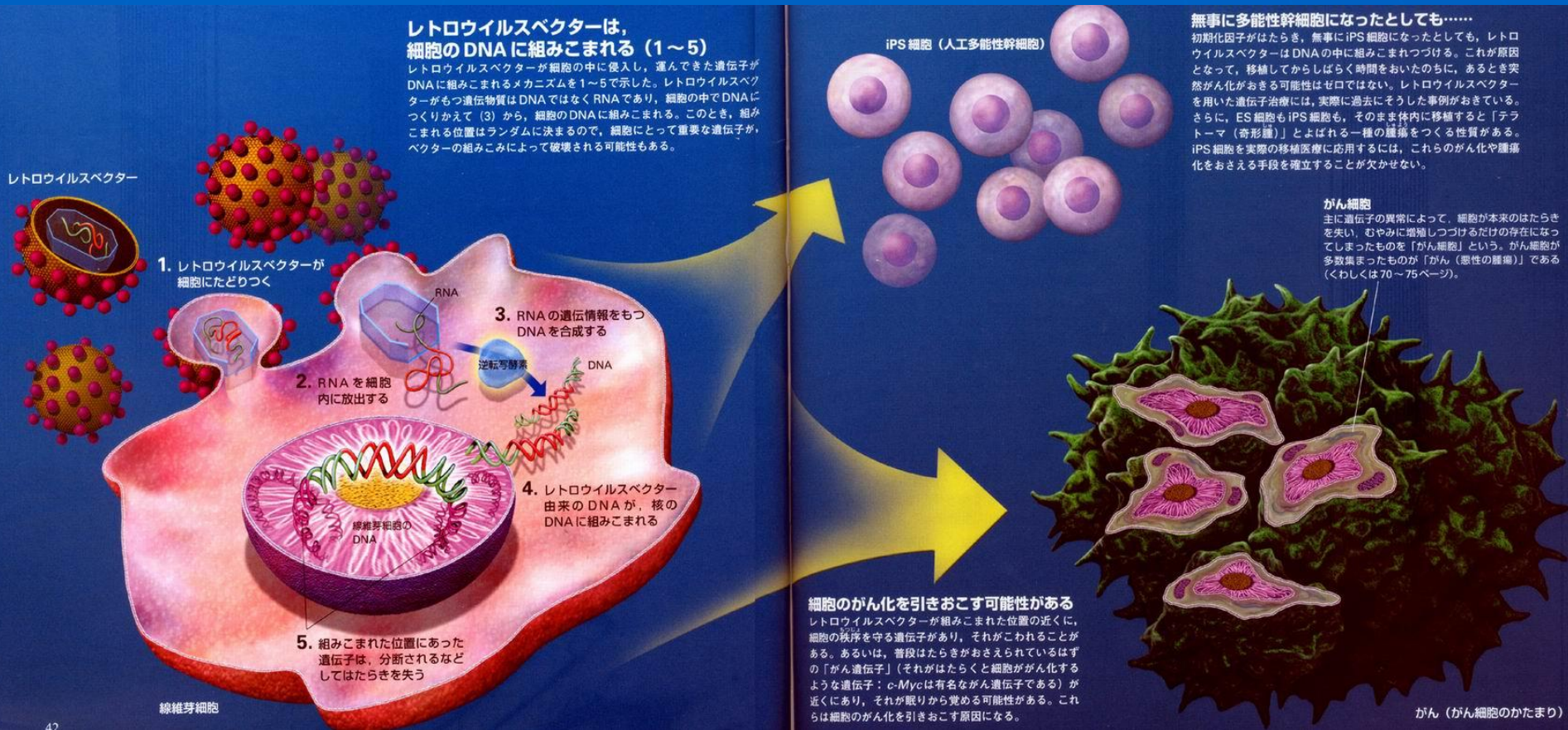




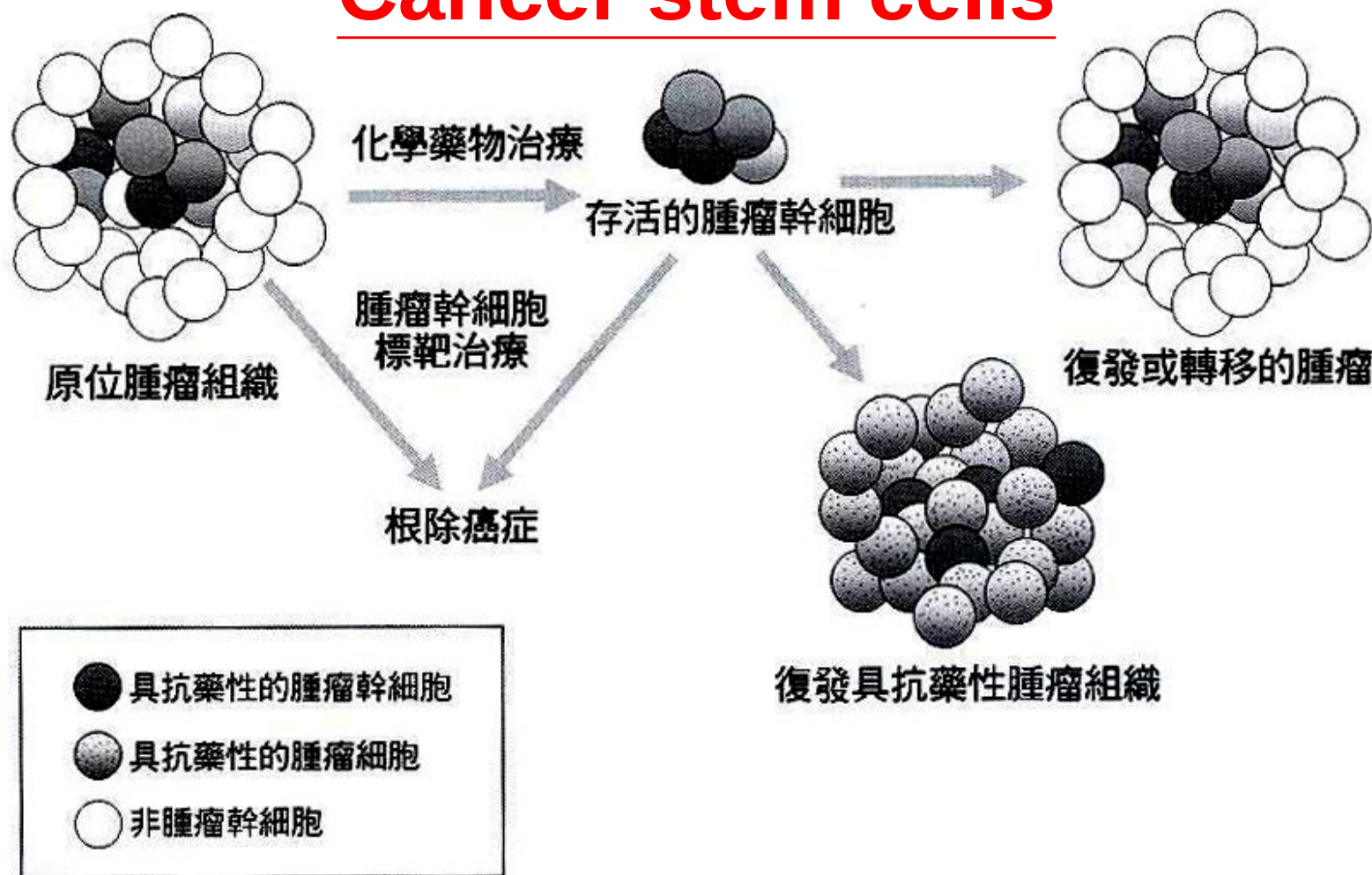
Generation of induced pluripotent stem cells without Myc from mouse and human fibroblasts

Masato Nakagawa^{1,5}, Michiyo Koyanagi^{1,5}, Koji Tanabe¹, Kazutoshi Takahashi¹, Tomoko Ichisaka^{1,2}, Takashi Aoi¹, Keisuke Okita¹, Yuji Mochiduki¹, Nanako Takizawa¹ & Shinya Yamanaka^{1,2,3,4}

iPS cells vs. Tumor cells



Cancer stem cells



科學月刊 457期 (2009/ 7) page 537; 沈家寧等

圖一：癌細胞裡有一小群細胞，具有幹細胞特徵，不但對放射治療、化學治療的抵抗力比正常腫瘤細胞強，同時又可以慢慢分裂出可以長得很快的腫瘤細胞，為了開發更好的診斷及治療癌症的方法，當務之急就是去深入了解癌症幹細胞的特性，並利用這些特性去發展殲滅癌症幹細胞的策略。



觸控代表研發藥物A處理



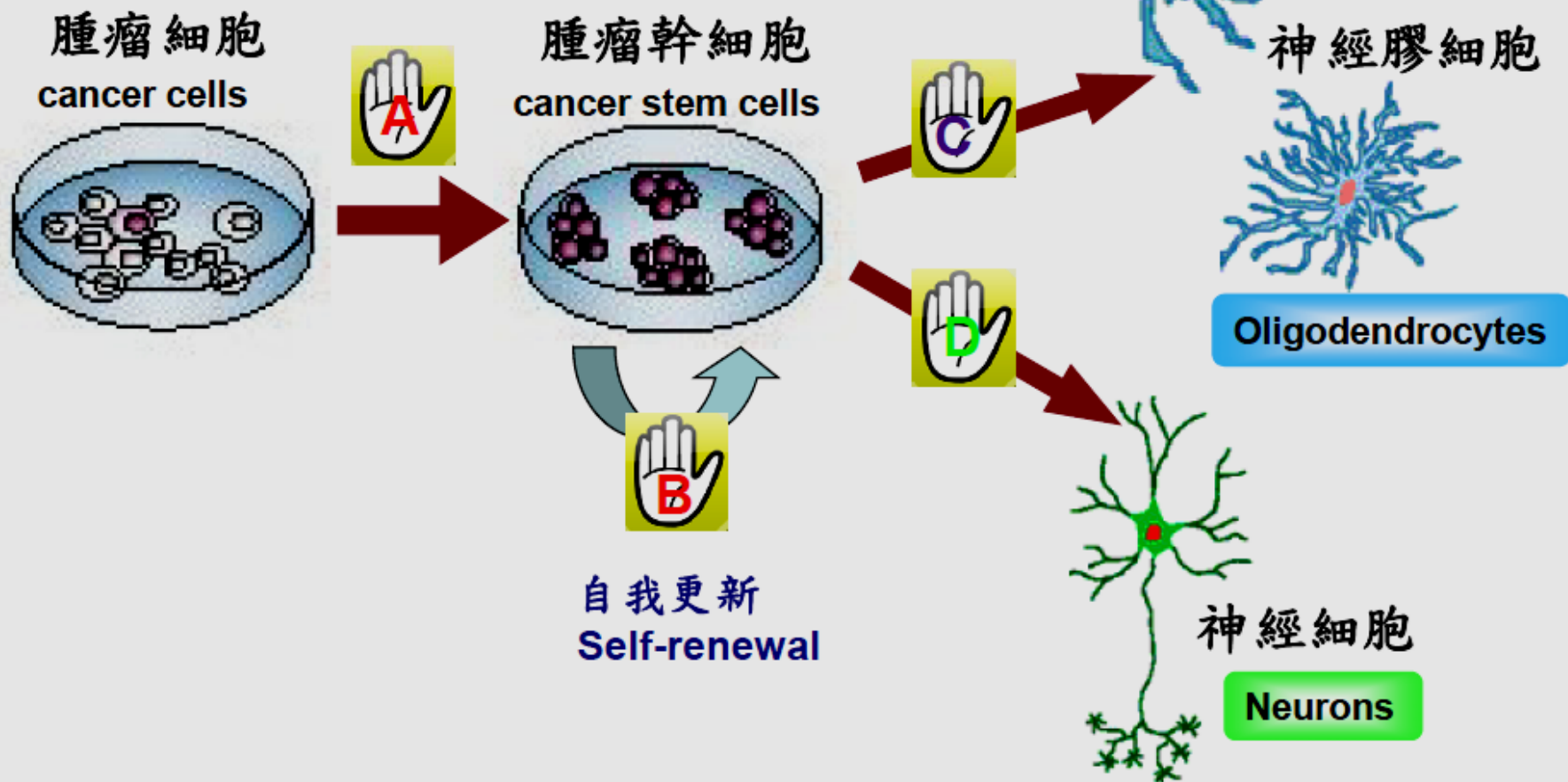
觸控代表研發藥物B處理



觸控代表研發藥物C處理



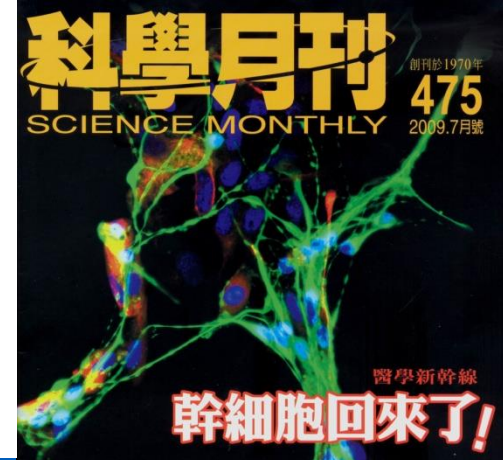
觸控代表研發藥物D處理



認識幹細胞與大眾教育

在這個日新月異的時代，對於富有潛力，但卻普遍缺乏推廣教育的幹細胞，社會大眾應該有更進一步的認知與理解。

錢宗良



- 我兒子有先天性心臟病，臺灣是否有醫師可以利用「幹細胞」來治療？
- 「幹細胞」真能治療脊髓損傷嗎？
- 臍帶血是否值得儲存？

日本京都大學附設醫院細胞治療研究中心

前川平 (Professor Taira Maekawa) 主任

- 幹細胞治療糖尿病
- 每次療程至少**300**萬日幣
- 未必每次都有成效

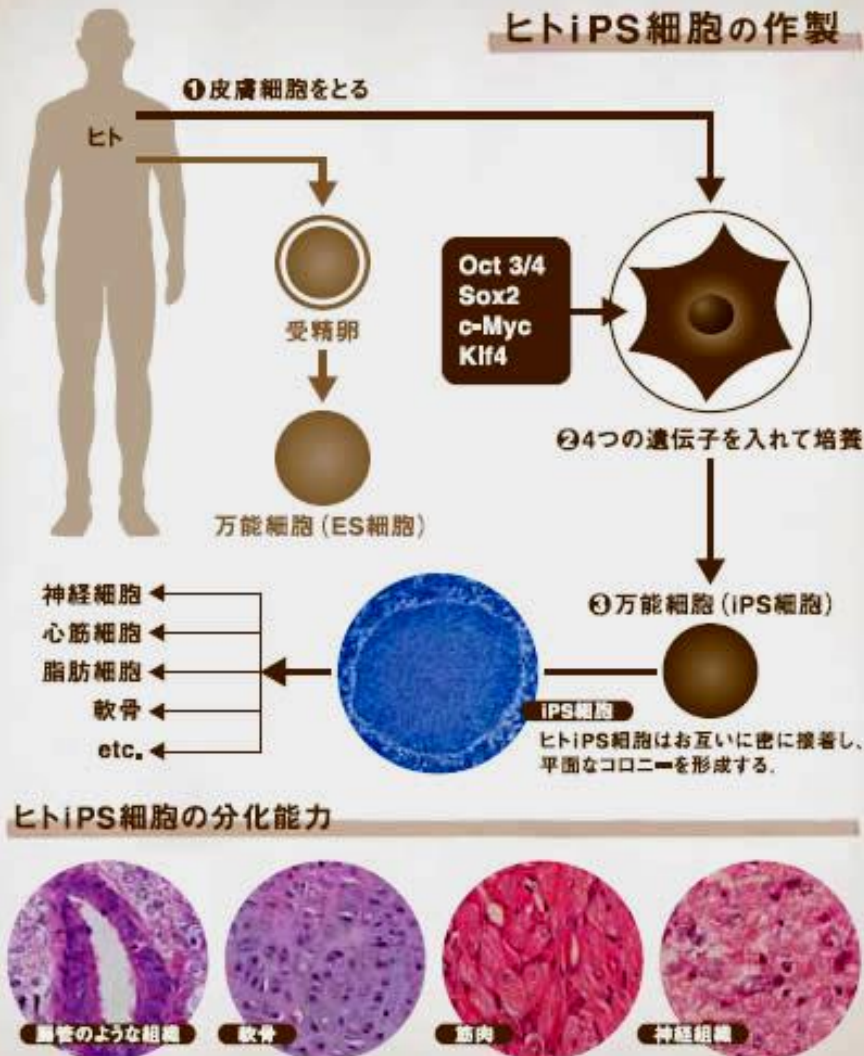


國外幹細胞研究現況

國別	大學/設立研究機構	研究重點
美國	哈佛大學 Harvard Stem Cell Institute	Cardiovascular, Nervous System and Diabetes Disease, Cancer Stem Cell, Tissue Engineering
	史丹佛大學 hESC, Center for Human Embryonic Stem Cell Research and Education	Mature Tissue or Organ Stem Cell, Human Embryonic Stem Cell, Cancer Stem Cell
英國	劍橋大學 Cambridge Stem Cell Initiative	Pluripotent Stem Cell, Adult Stem Cell , Hematopoietic Stem Cell, Cancer Stem Cell
	牛津大學 The Oxford Stem Cell Institute	Embryonic Stem Cell , Adult Stem Cell , Hematopoietic Stem Cell , Cancer Stem Cell
日本	京都大學 Center for iPS Research and Application, Stem Cell Research Center	iPS, Stem Cell Differentiation, Stem Cell engineering, Stem Cell Processing
	東京大學 Center for Stem Cell Biology and Regenerative Medicine	iPS, Hematopoietic Stem Cell, Human Embryonic Stem Cell, Liver Stem Cell

International Symposium on induced Pluripotent Stem (iPS) Cell Research: Frontier and Future (Kyoto, 2008)

Dr. Shinya Yamanaka



Sir Martin Evans (2007 Nobel Laurent)



細胞移植治療的開發情形 (JST/CRDS) (JST 2007年戰略報告書)

註： IND: Investigational New Drug Application 試驗中新藥申請

用途	企業名	國家	來源、 利用之細胞	病患對象	階段	備註
血液 疾病	Gamida-Cell Ltd. (www.gamida-cell.com)	以色列	臍帶血來源、造 血幹細胞	血液惡性腫瘤	II	孤兒藥 指定
	Osiris Therapeutics Inc. (www.osiris.com)	美 MD	骨髓來源、間葉 系幹細胞	急性移植排斥 反應症	II	孤兒藥 指定
	ViaCell Inc. (www.viacellinc.com)	美 MA	臍帶血來源、造 血幹細胞	血液惡性腫瘤	II	
心臟 貧血	Athersys Inc. (www.athersys.com)	美 OH	骨髓來源、多能 性前驅細胞	急性心肌梗塞	預計 2007申 請IND	
	Angioblast Systems (www.angioblast.com)	美 NY	骨髓來源、間葉 系前驅細胞	慢性心貧血	I	
	BioHeart Inc. (www.bioheartinc.com)	美 FY	自身骨骼肌來源、 肌原細胞	鬱血性心不全	III I	歐洲
	Osiris Therapeutics Inc. (www.osiris.com)	美 MD	骨髓來源、間葉 系幹細胞	急性心肌梗塞	I	
	Arteriocyte Inc. (www.arteriocyte.com)	美 OH	自身骨髓來源 、CD133+細胞	慢性心貧血	I	

細胞移植治療的開發情形 (JST/CRDS) (JST 2007年戰略報告書)

用途	企業名稱	國家	來源、 利用之細胞	病患對象	階段	備註
整形外科 相關 疾病	Aastrom Biosciences Inc. (www.aastrom.com)	美 MI	骨髓來源、間葉 系幹細胞	骨髓修復	I	
	Mesoblast Ltd. (www.mesoblast.com)	澳洲	骨髓來源、間葉 系幹細胞	骨骼、軟 骨修復	I	澳洲
	Osiris Therapeutics Inc. (www.osiris.com)	美 MD	骨髓來源、間葉 系幹細胞	軟骨修復	I	
神經 疾病	ReNeuron Group Plc. (www.reneuron.com)	英	胎兒來源幹細胞	腦中風	2007申 請IND	
	Stem Cell Inc. (www.stemcellsinc.com)	美 CA	胎兒來源神經幹 細胞	Batten 病	I	
	Geron Corporation (www.geron.com)	美 CA	ES細胞來源之寡 突前驅細胞	脊髓損傷	2007申 請IND	

註：IND: Investigational New Drug Application 試驗中新藥申請

重點發展領域



1. 五項重點研究：

- 幹細胞的分離，培養與分化技術
- 幹細胞的表現機制與流程控制
- 基因外(epigenetic)調節與體細胞核核轉移的技術研發
- 動物移植模型、生醫奈米、與組織工程相關技術的建置
- 誘導式多能性幹細胞(iPS cells) 相關之分析研究

2. 三種應用技術：

- 以動物複製與異體移植模型；
- 藥物研發；
- 細胞治療的試驗

3. 台灣幹細胞醫療或學術既有特色與強項

幹細胞跨領域及轉譯醫學應用

- 奈米生醫材料：細胞分化及細胞毒性測試
- 生物反應器與組織工程
 1. 生物反應器(Bioreactor): 幹細胞之標準化量產
 2. 組織工程: 人工器官(Artificial Organs)
- 幹細胞治療與再生醫學應用
 1. 神經退化疾病與神經損傷 (Neural stem cells)
 2. 軟骨修復與再生 (Chondroblasts and 3D reconstruction)
 3. 血液腫瘤之細胞療法 (Hemopoietic stem cells)
 4. 心肌梗塞之細胞療法 (Cardiomyoblasts)
 5. 糖尿病之細胞療法 (Pancreatic islet cells)



未來發展方向

幹細胞研究開發的時間軸

約二十年後
(2030年)

約十年後
(2020年)

現在

臍帶血造血幹細胞治療血液惡性腫瘤
(Israel, Gamida-Cell Ltd., 目前 Phase II)

使用胎兒幹細胞治療中風病患
(UK, ReNeuron Group Plc., 2007 IND申請)

神經幹細胞治療貝登式症 (Batten disease) (USA, Stem Cell Inc. 目前 Phase I)

間葉幹細胞使用於軟骨修復
(USA, Osiris Therapeutics Inc., 目前 Phase I)

骨髓CD133+細胞用於慢性缺血性心臟病患治療
(USA, Arteriocyte Inc., 目前 Phase I)

再生醫學治療的使用、普及

臨床試驗(5年)
• 細胞移植治療
• 幹細胞活化治療

基礎研究 (5年)
• 幹細胞恆定研究 (homeostasis)

以幹細胞為基礎
發展抗老預防醫學

開發預防癌症復發
的藥劑

影響

轉譯醫學—幹細胞及再生醫學領域

Thank you for your attention

