PRINCIPE FELIPE
CENTRO DE INVESTIGACION

fundación fIVI

CÉLULAS MADRE

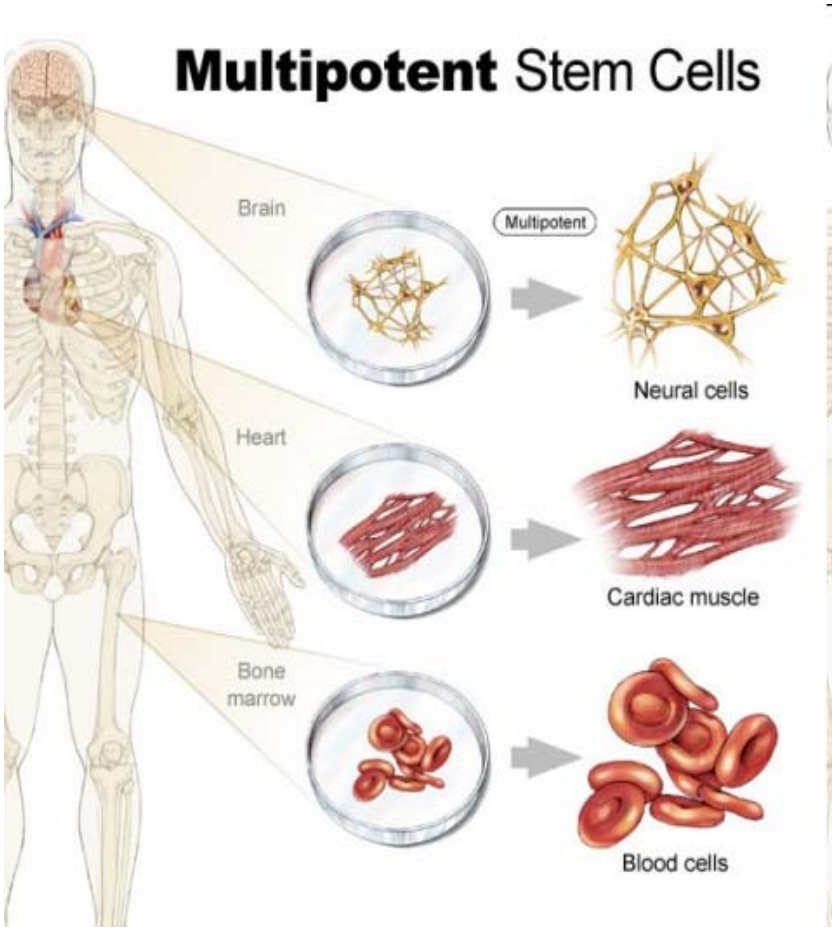
Carlos Simón Vallés MD, Ph.D

7 CONGRESO NACIONAL DE ENFERMERIA QUIRÚRGICA
9 Jornadas AEQCV
10-12 Marzo, Valencia

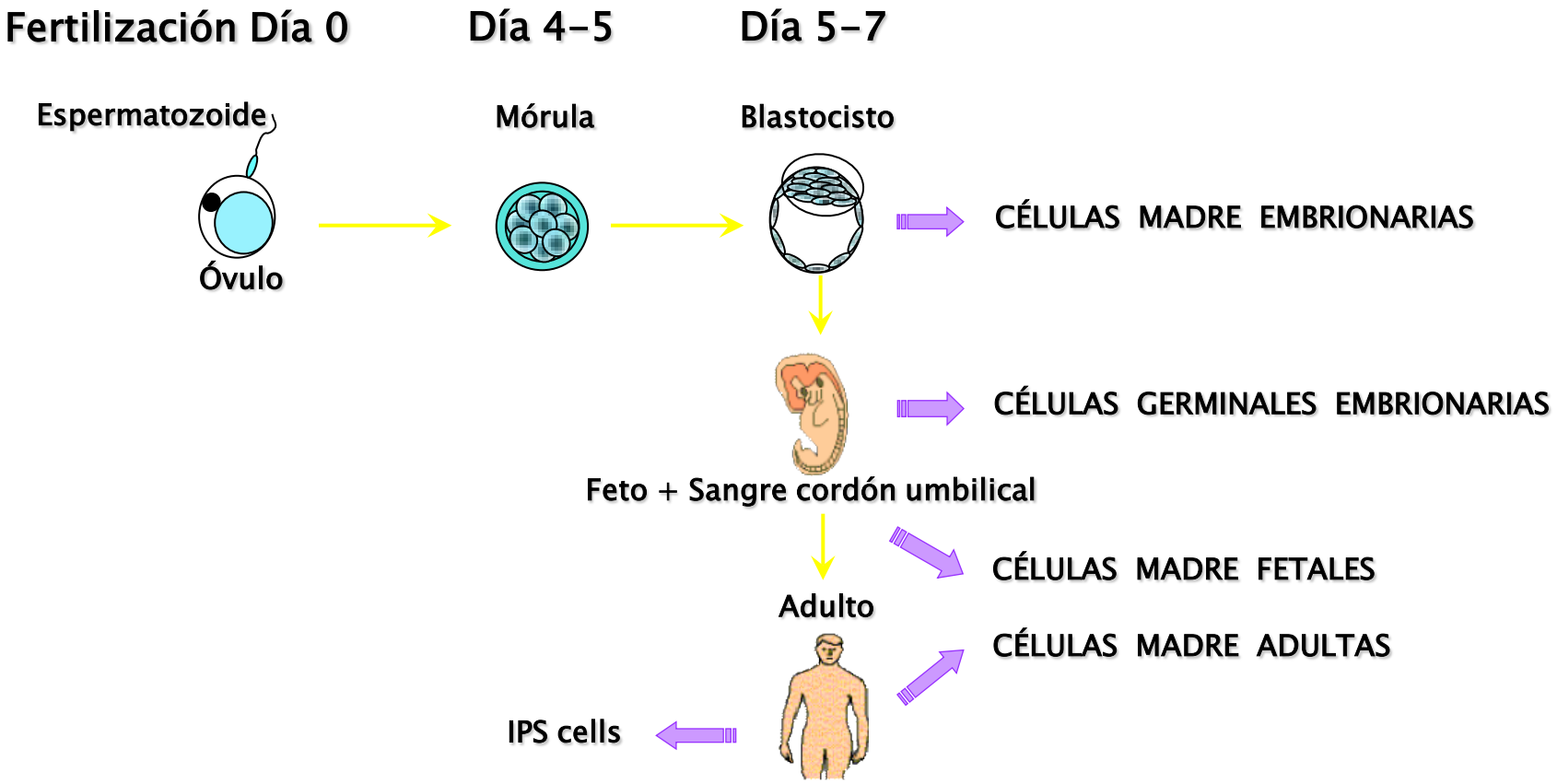
BANCO DE LÍNEAS CELULARES

¿Qué son las células madre?

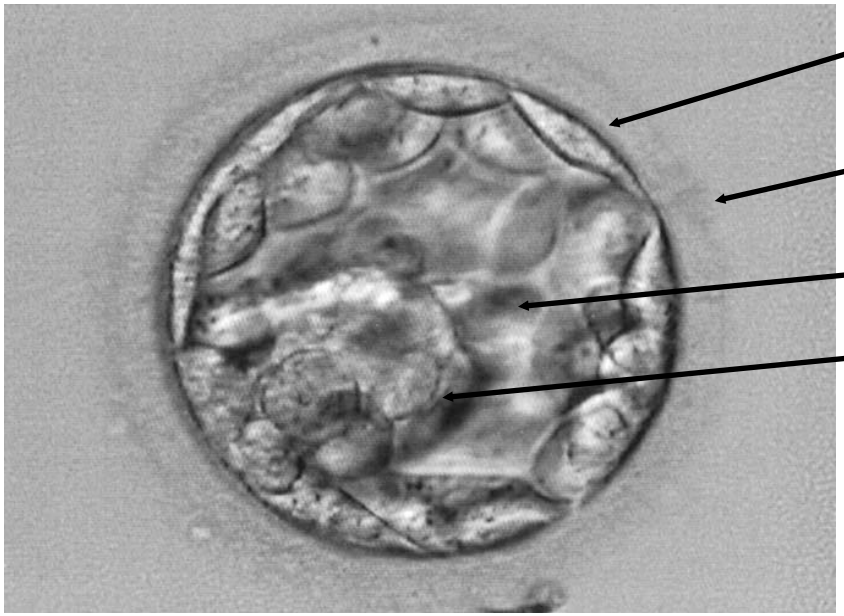
- Totipotencia: Cigoto
- Pluripotencia: Células madre embrionarias
- Multipotencia: Células madre adultas

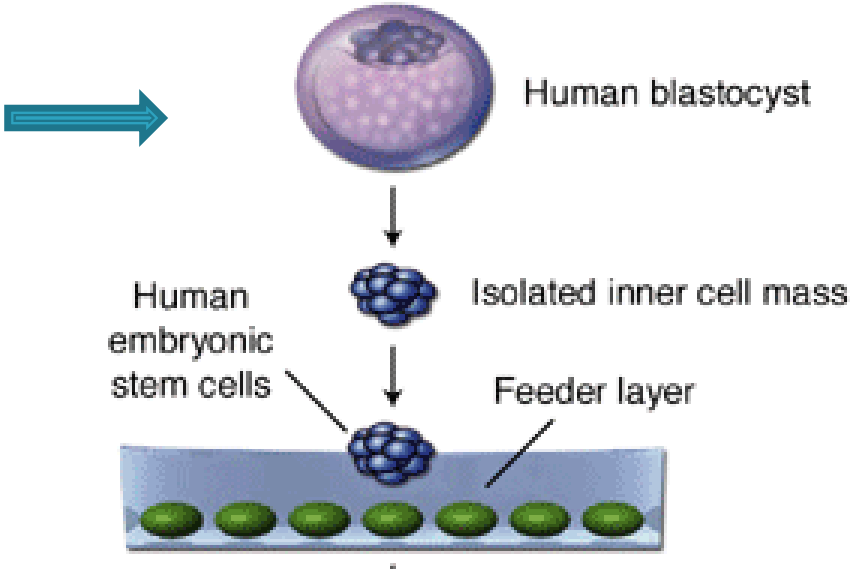


¿Qué son las células madre?

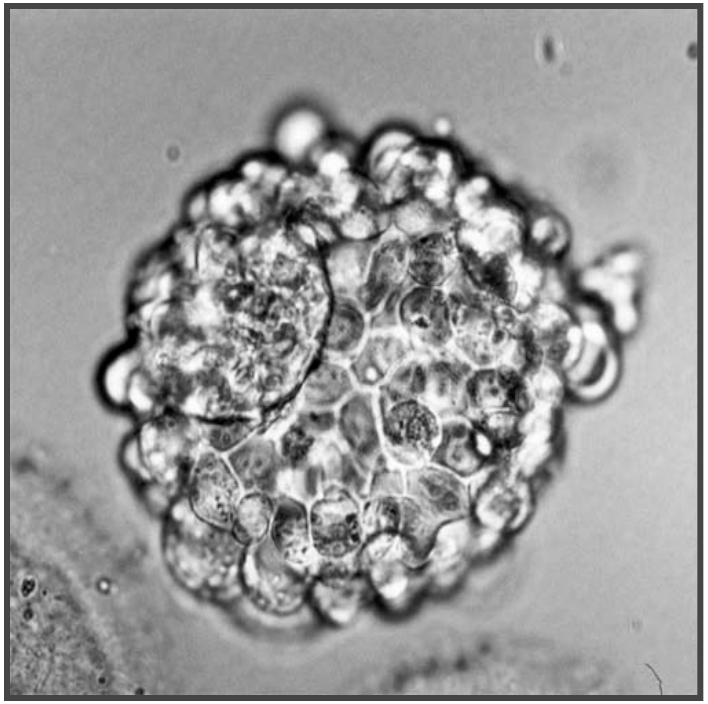


Células Madre Embrionarias

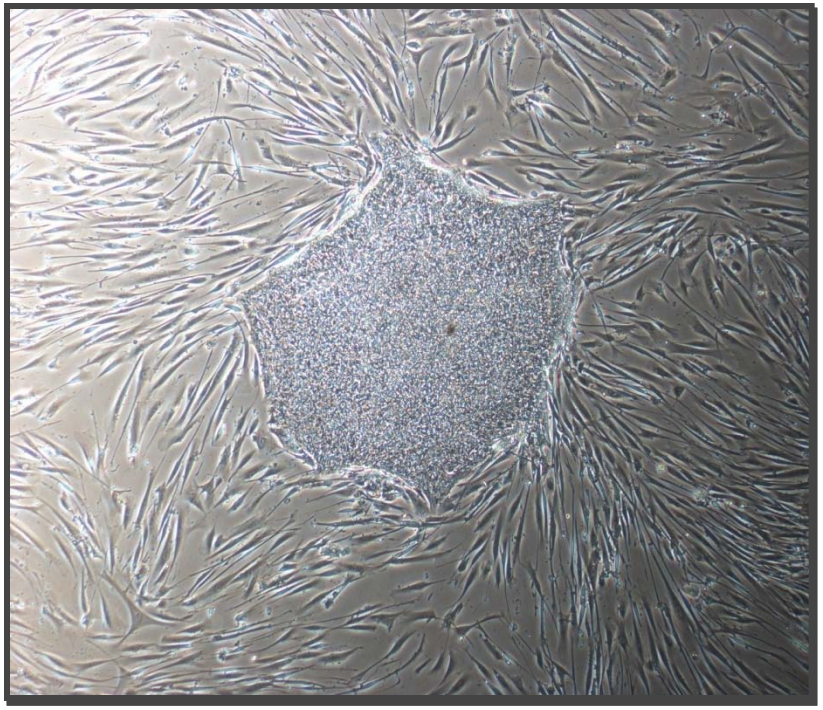




Células Madre Embrionarias



Masa Celular Interna

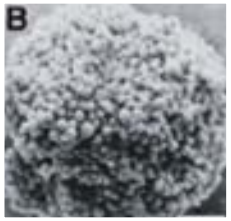


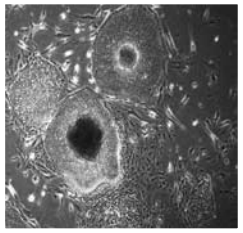
Colonia de hESC

Células Madre Embrionarias

hESC

Cuerpos embrionarios



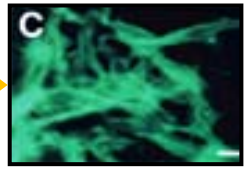


Monocapa

Ovocitos

Esperma

Línea germinal

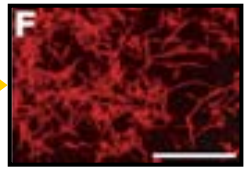


Cardiomyocitos

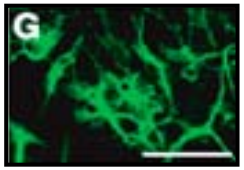
Músculo estriado

Músculo liso

Mesodermo



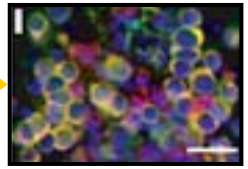
Neuronas



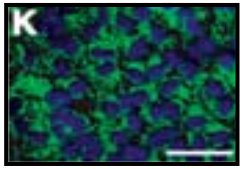
Glia

Epitelio

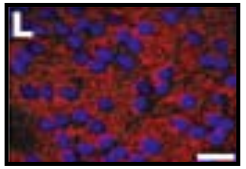
Ectodermo



Céls. pancreáticas



Sangre

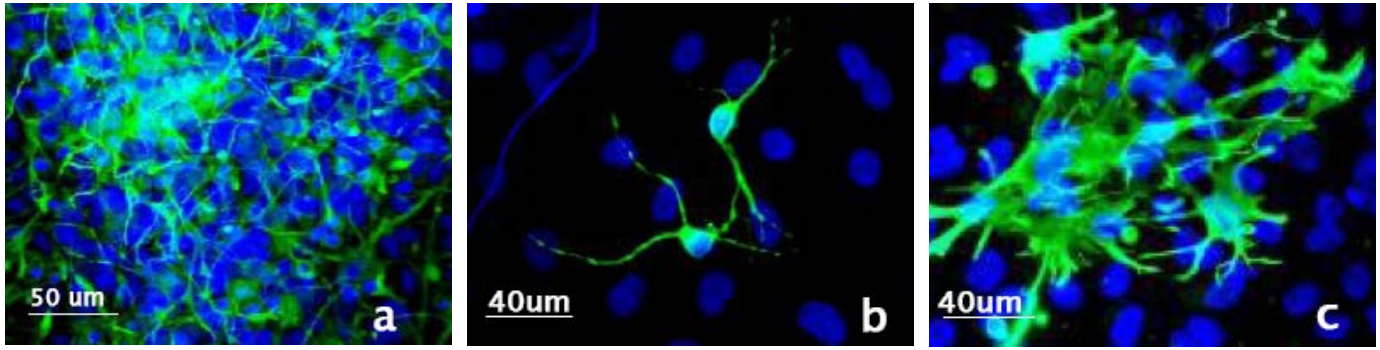


Hepatocitos

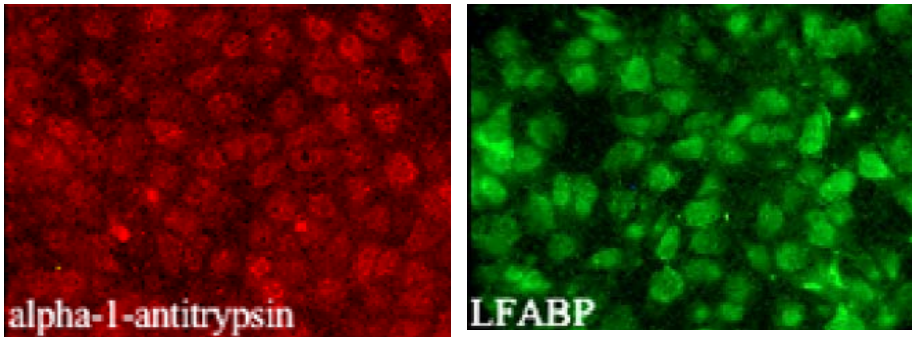
Endodermo

Células Madre Embrionarias

EJEMPLOS DE DIFERENCIACIÓN DIRIGIDA



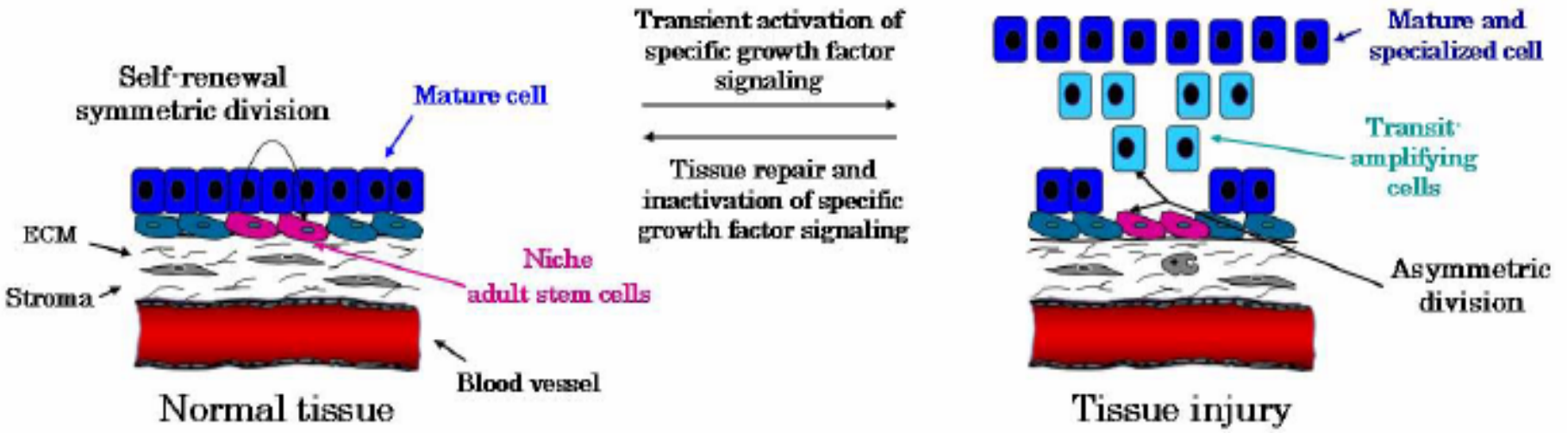
Células Neuronales: Adición de NGF



Hepatocitos: Adición de HGF

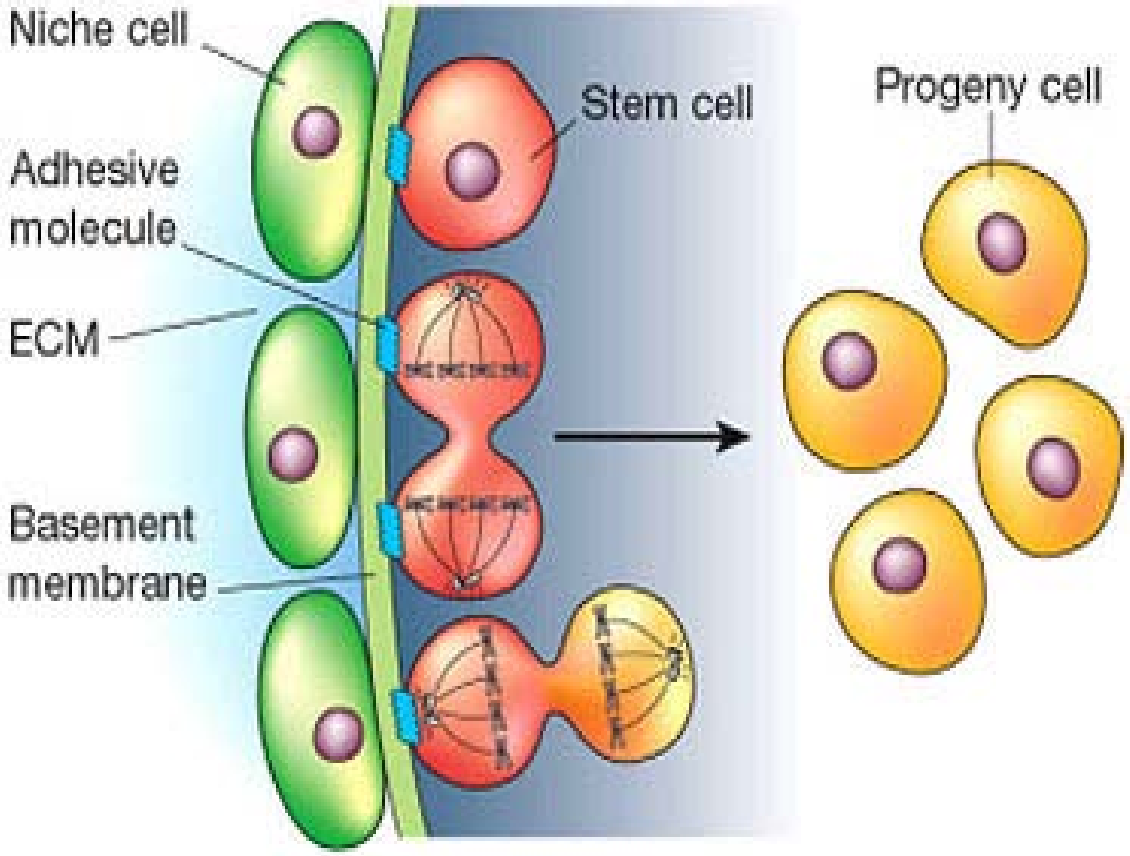
Células Madre Adultas

- Capacidad de autorenovarse
- Se encuentran en áreas específicas en la mayoría de órganos y tejidos de mamíferos adultos
- Multipotentes
  - Dentro de su tejido de orígen participan activamente en los procesos de mantenimiento



Células Madre Adultas

El Nicho celular, proporciona el microambiente necesario para mantener su estado quiescente y multipotente



Células Madre Adultas

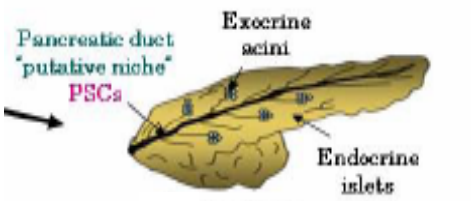
Origen Endodérmico

Células Madre Epiteliales Pulmonares

Células Madre del Tracto Gastrointestinal

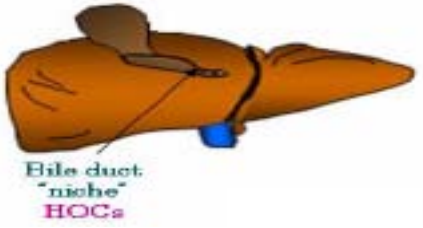
Células Madre Pancreáticas

PANCREAS



Células Ovales Hepáticas

HIGADO

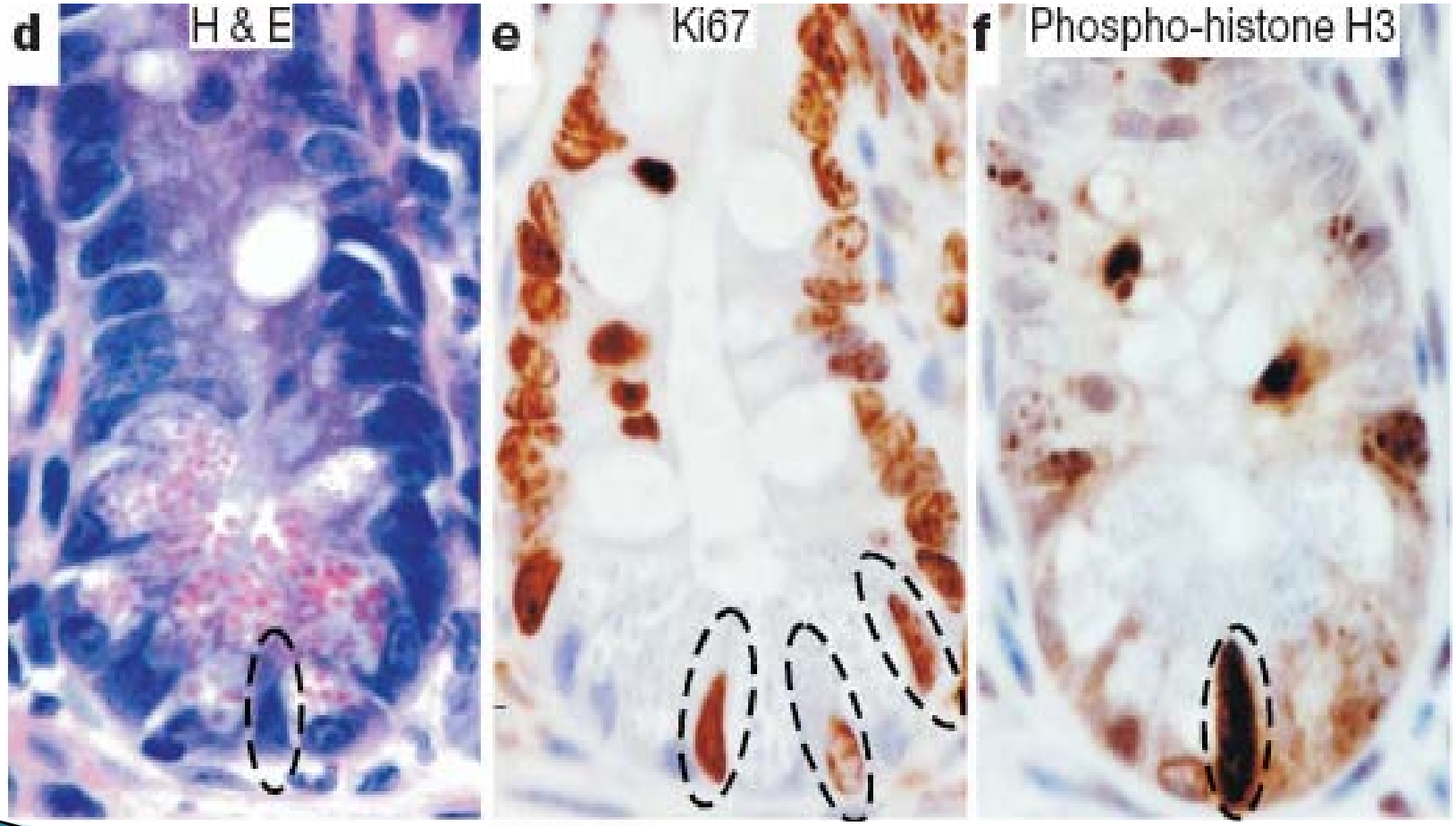


Células Madre Urogenitales

- Células Madre de Glándula Mamaria y Prostática
- Células Madre Ováricas y Testiculares

Células Madre Adultas

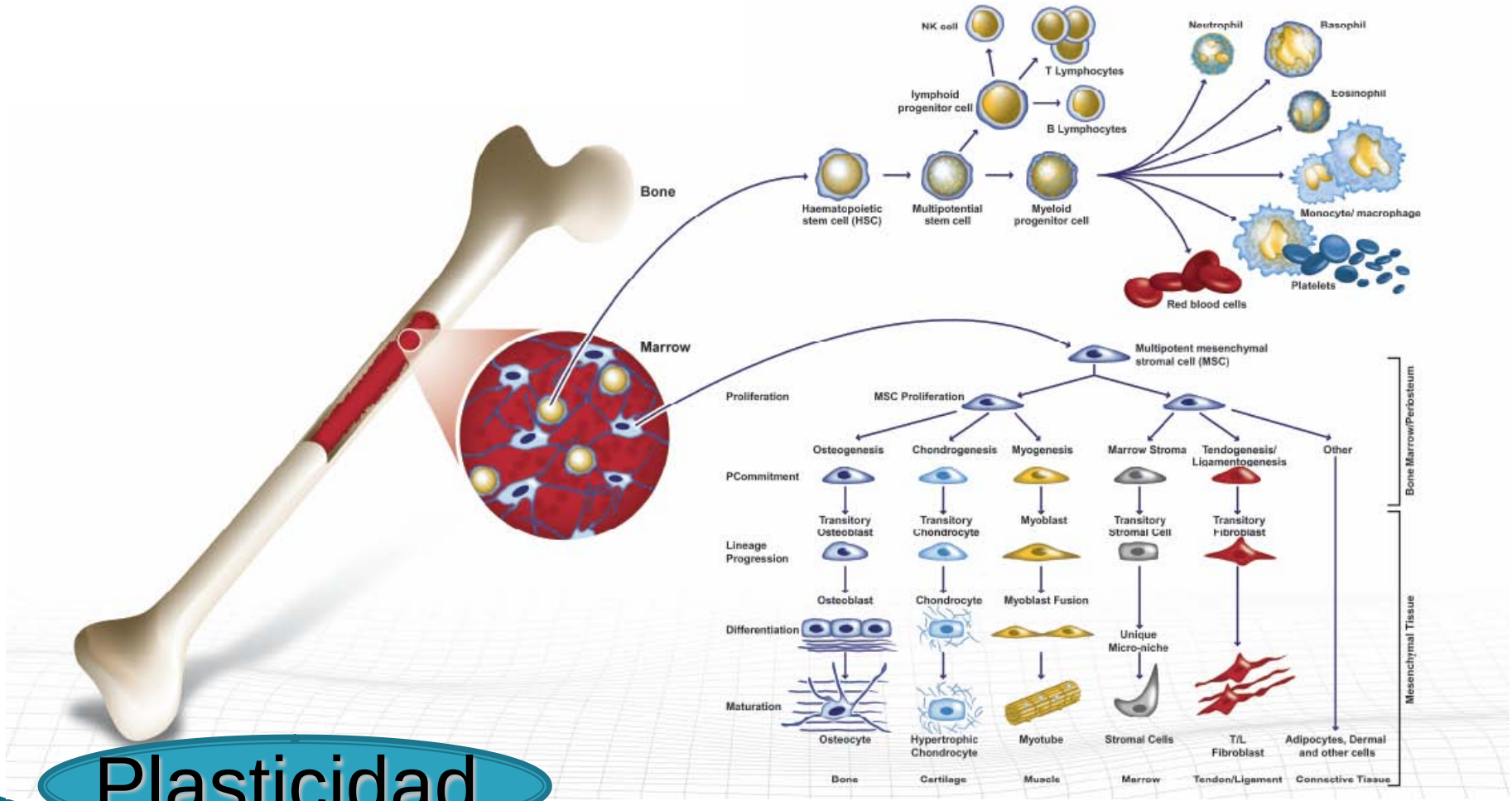
Origen Endodérmico: criptas intestinales



(He et al., 2004)

Células Madre Adultas

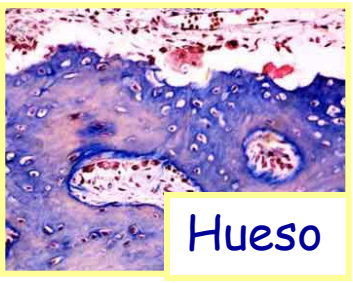
Origen Mesodérmico: Médula ósea

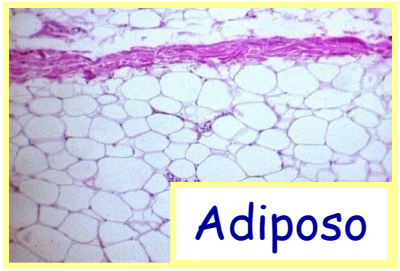


Plasticidad

Células Madre Adultas

Origen Mesodérmico





Signaling LRP-5/Wnt
Cbfa-1

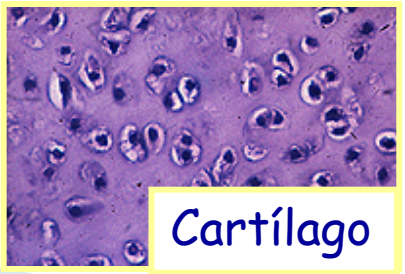
Signaling Wnt

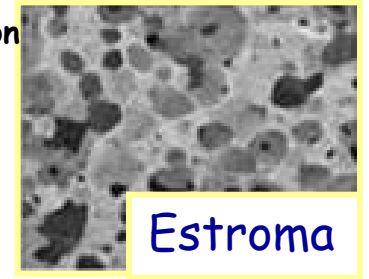
Célula madre mesenquimal

Citoquines (IL-1,IL-6)

Signaling bHLH

Signaling SMAD, MAPK
Extracellular matrix interaction

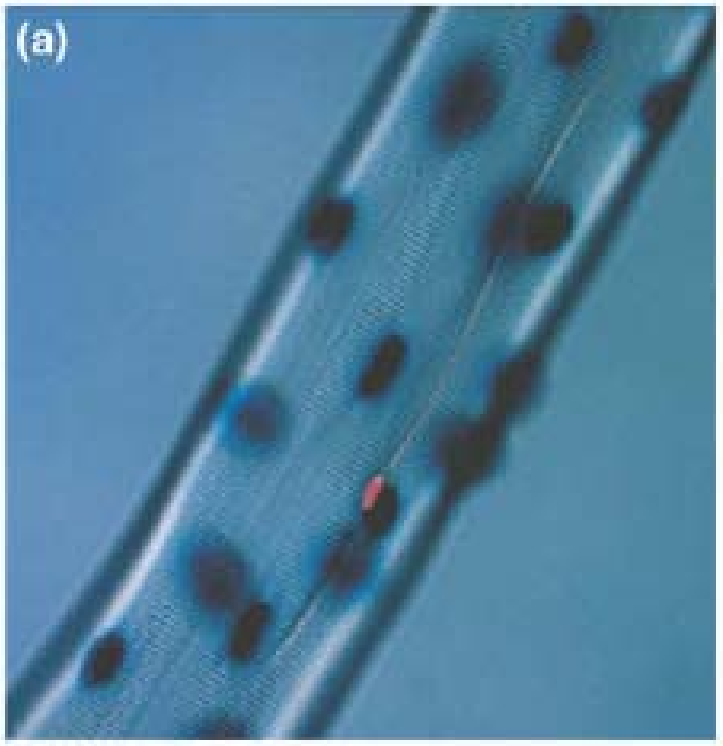


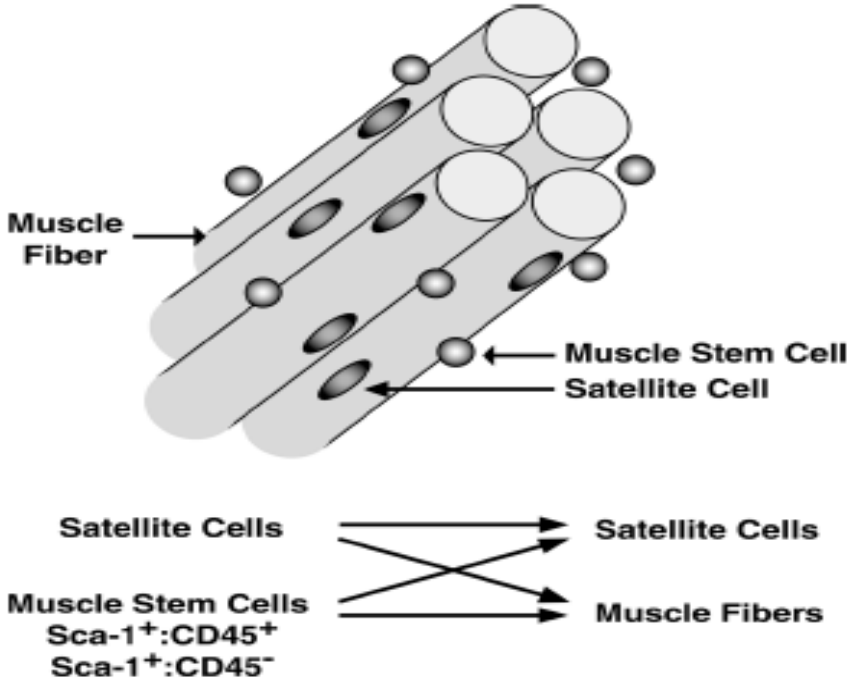


(Tuan *et al*., 2002)

Células Madre Adultas

Origen Mesodérmico: Músculo



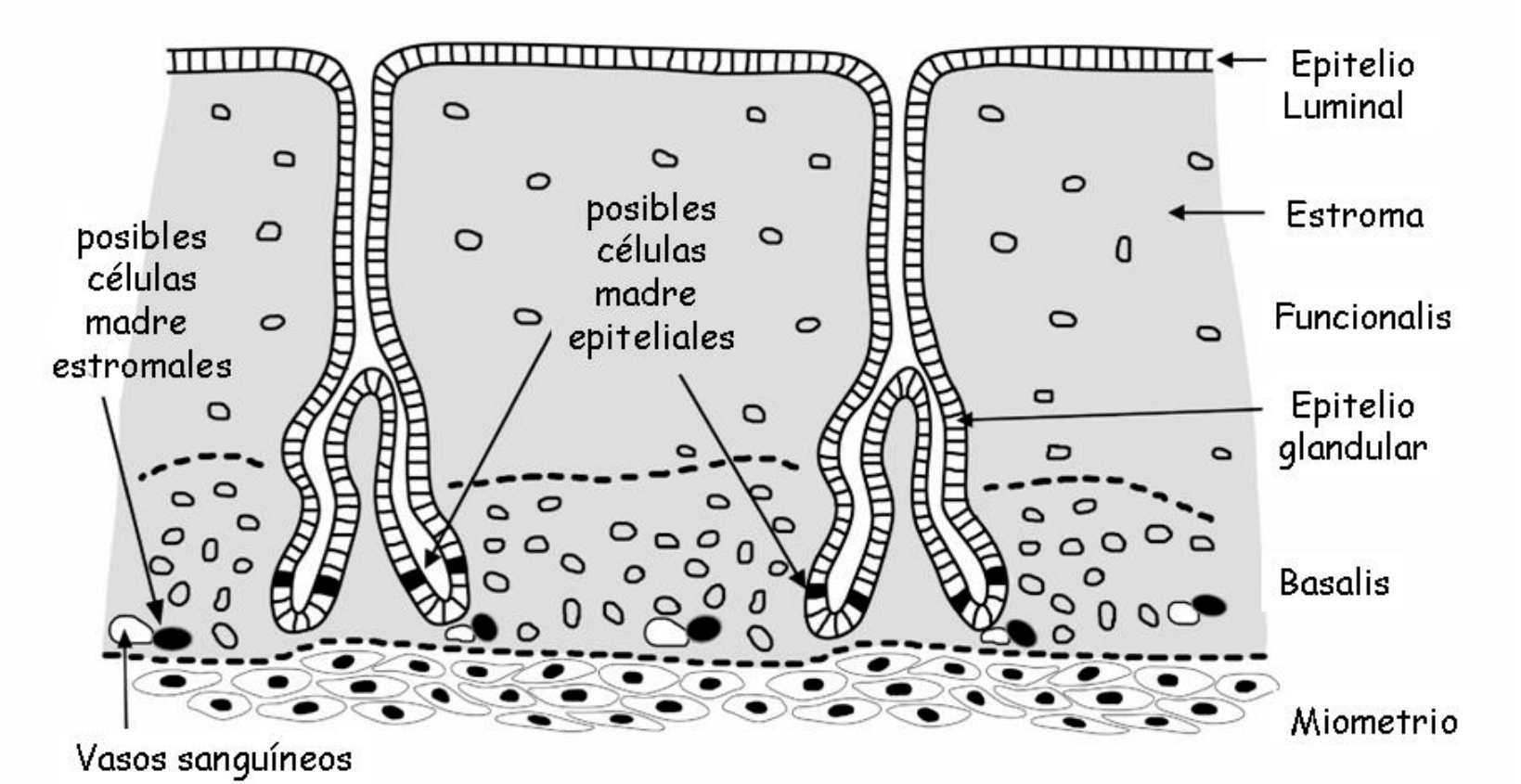


Las células madre musculares residen junto a la lámina basal del músculo esquelético y permanecen quiescentes hasta que se reactivan ante un proceso de regeneración o crecimiento muscular.

(Beauchamp et al., 2000)

Células Madre Adultas

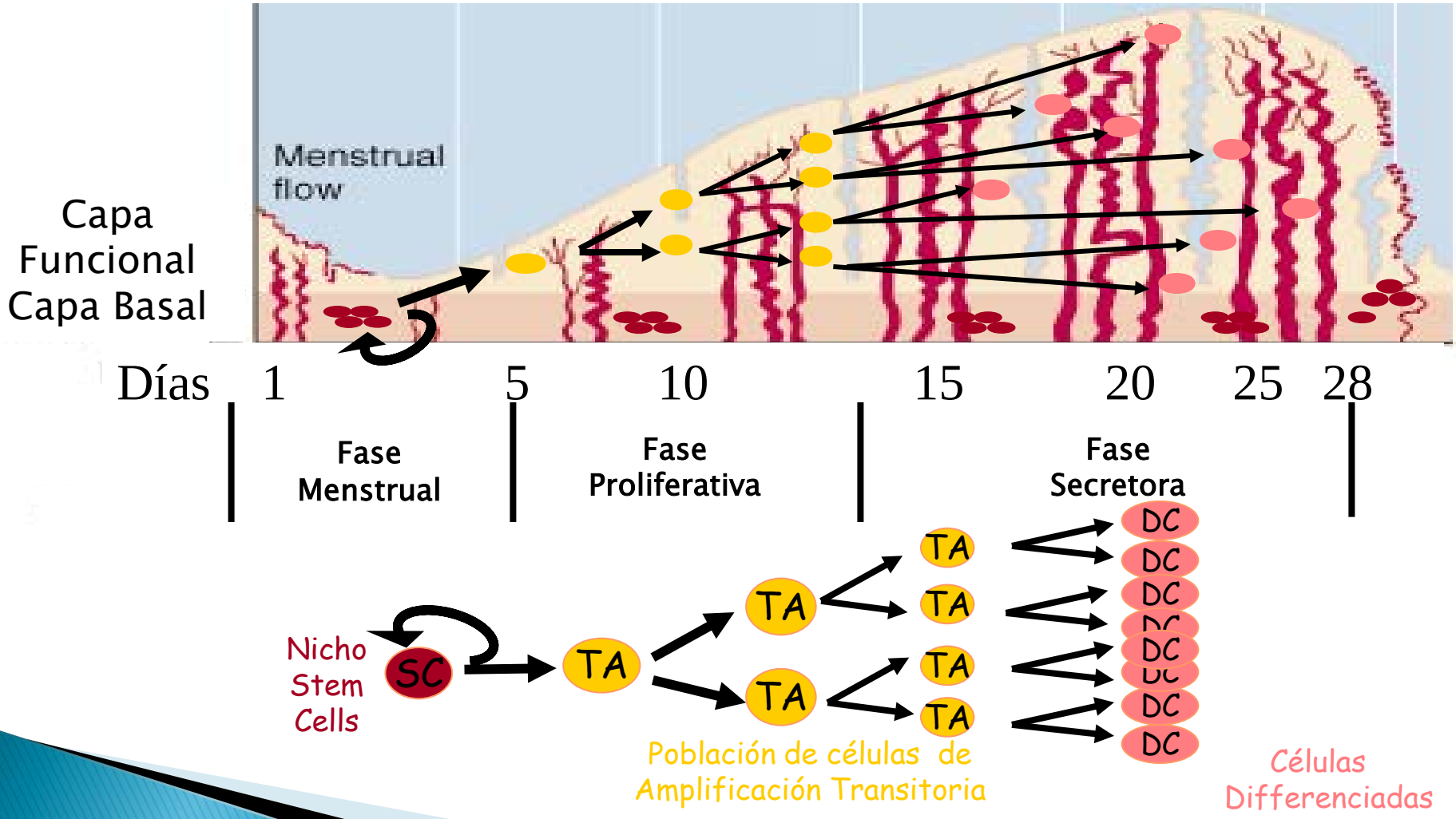
Origen Mesodérmico: Endometrio



Gargett y cols. Stem Cells, 2006
Cervelló I/Simón C. Hum Reprod, 2007

Células Madre Adultas

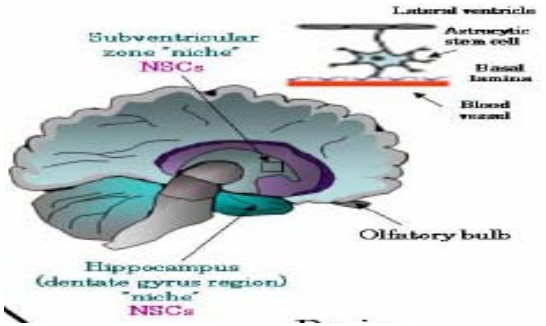
Origen Mesodérmico: Endometrio



Células Madre Adultas

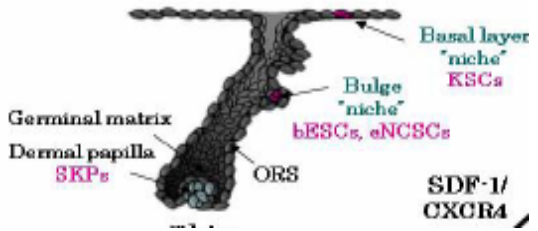
Origen Ectodérmico

Células Madre Neurales



CEREBRO

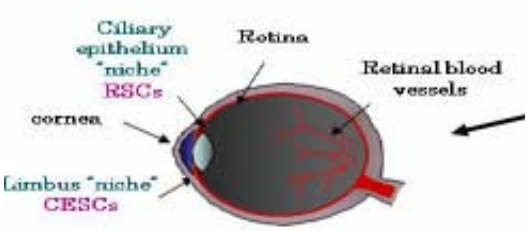
Células Madre de Piel



PIEL

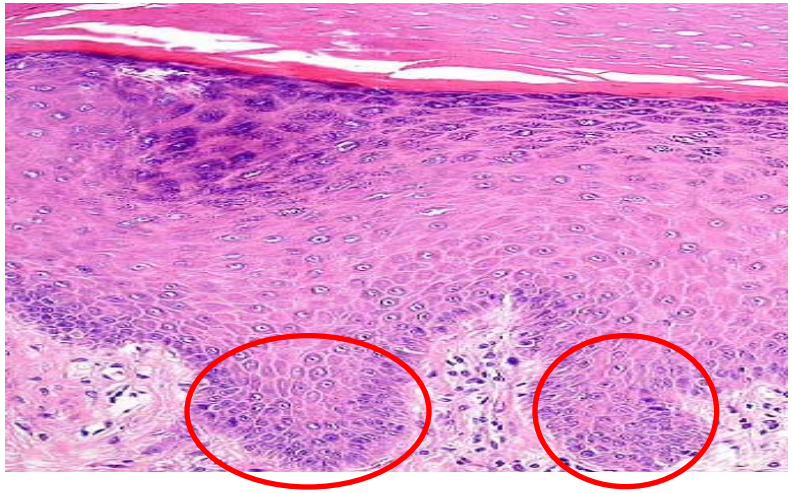
OJO

Células Madre Oculares



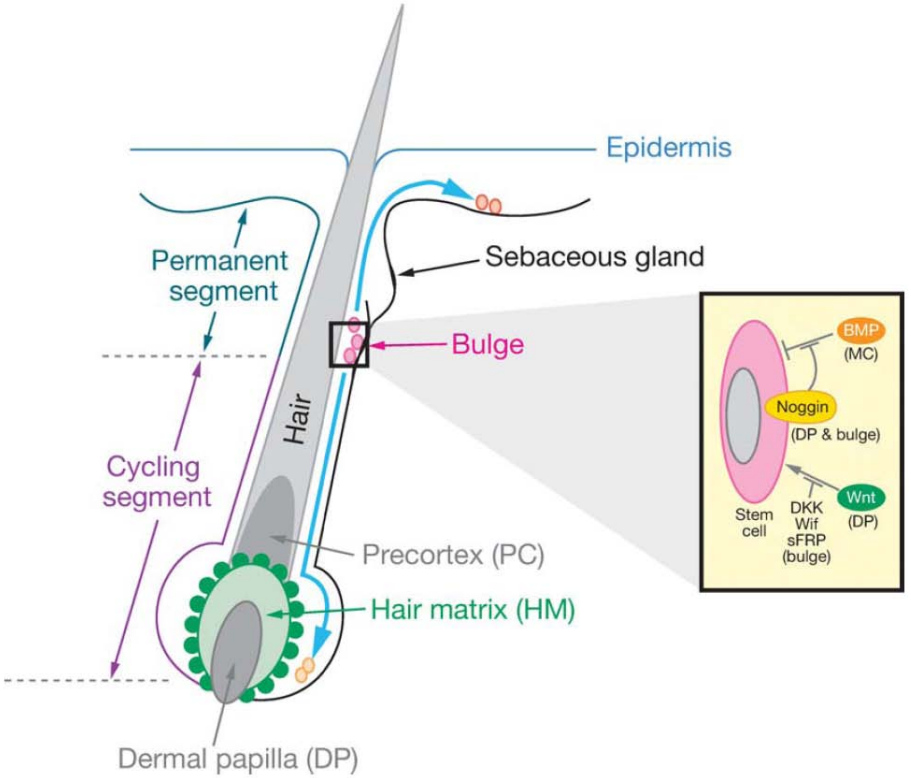
Células Madre Adultas

Origen Ectodérmico: epidermis



Primer transplante autólogo de células epiteliales cultivadas *in vitro.*

Reparación epidérmica



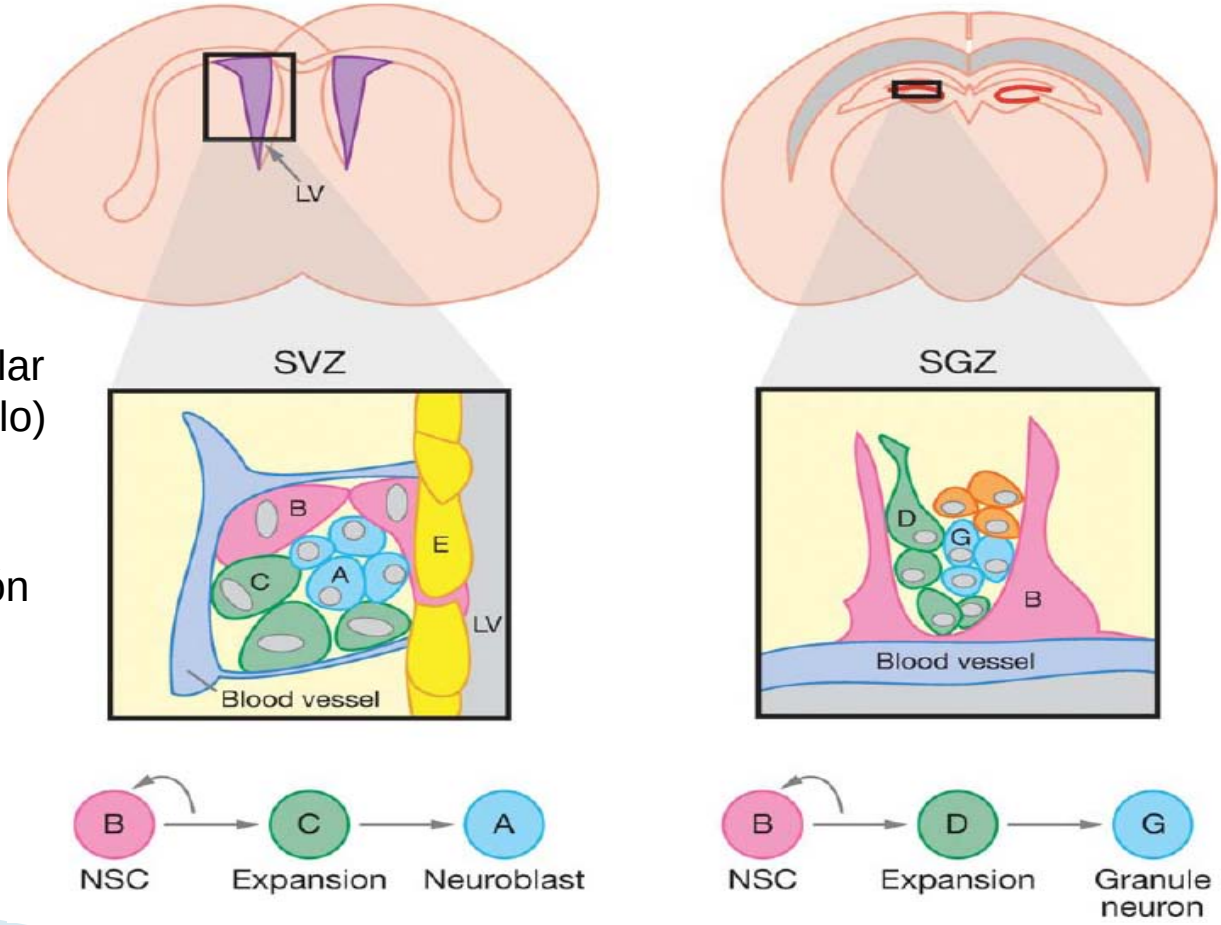
O'Connor et al., 1981

Células Madre Adultas

Origen Ectodérmico: Sist. nervioso

Zona subventricular (3º Ventrículo)

Regeneración del bulbo olfatorio.



Zona subgranular (Hipocampo)

Auto-regeneración tras ataques epilépticos.

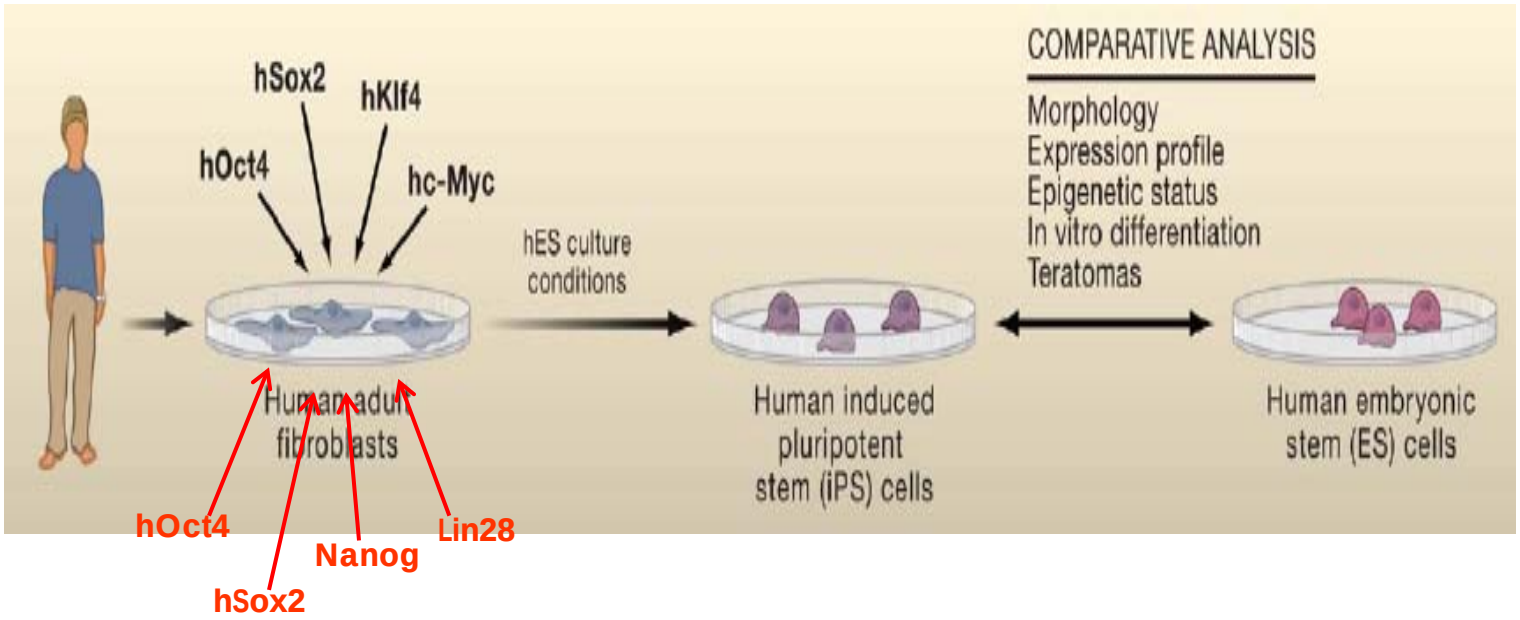
(Doetsch, 2003)

Reprogramación celular

Reprogramación celular *in vitro*

Reprogramación de células somáticas a un estado pluripotente

Takahashi K *et al*. Cell 2007;131:1



Yu J *et al*. Science 2007;318:1917

Células Madres Fetales

- Son multipotentes
- No forman teratomas in vivo
- Alta plasticidad
- Potencial migratorio

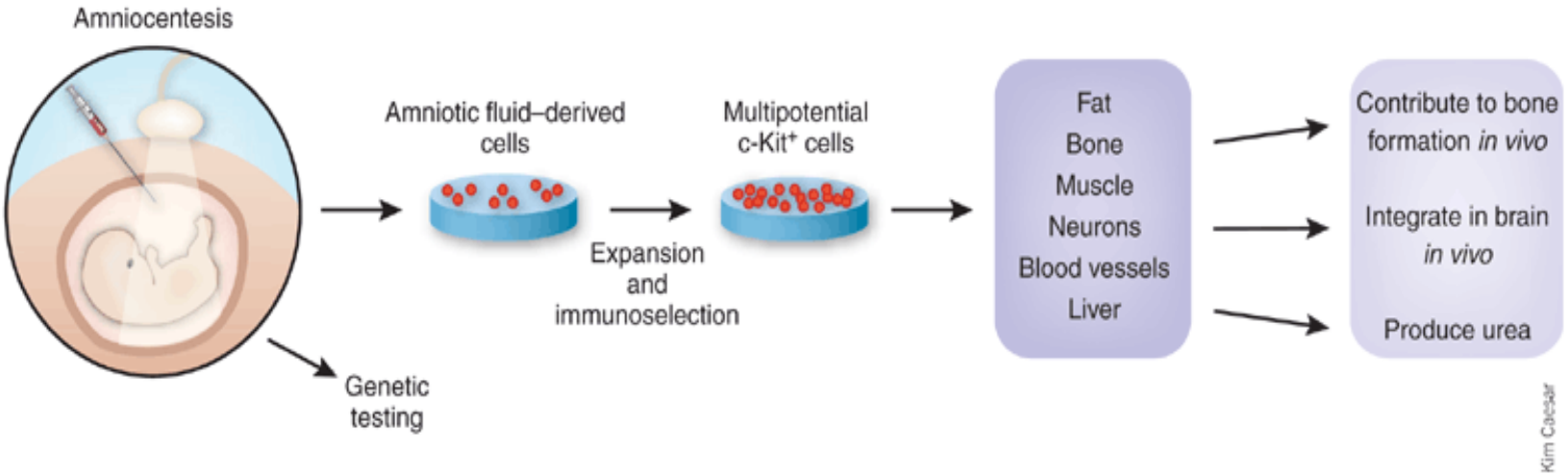
Fuentes de Células Multipotentes

Células Madre de Cordón Umbilical

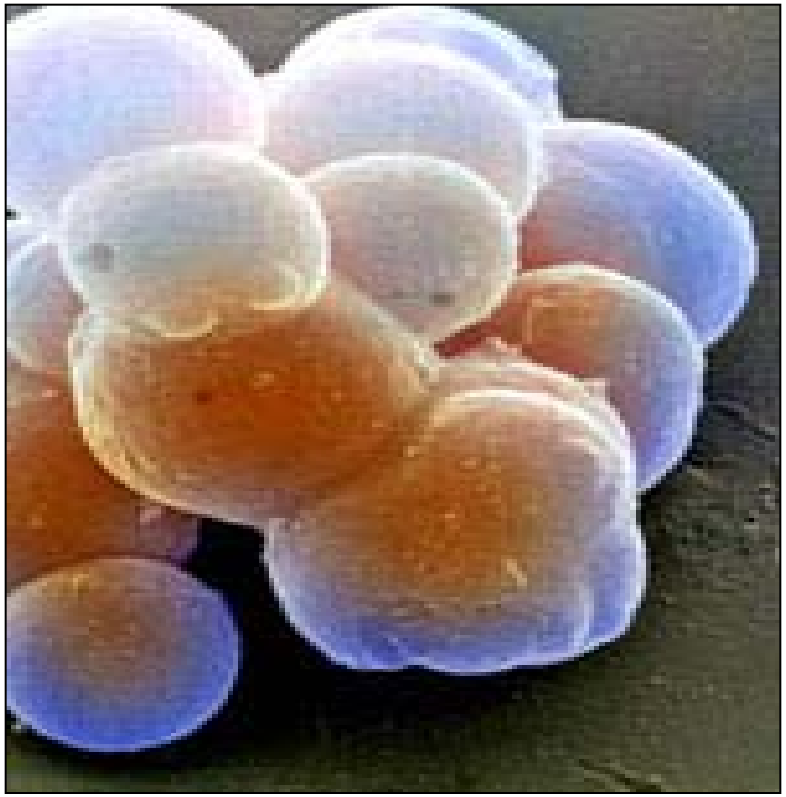
- Fuentes SCs: epitelio (UCE) y sangre (UCB)
- UCB: Alta capacidad de expansión hematopoyética
- Son multipotentes
- *in vitro* se diferencian a:
  - Células Hematopoyéticas
  - Células Dendríticas
  - Células progenitoras neuronales
  - Endotelio
- Contiene una subpoblacion de células madre mesenquimales

Fuentes de Células Multipotentes

Células Madre de Líquido Amniótico



Del Laboratorio a la clínica



Aspectos a considerar:

- Inmunogenicidad
- Formación de Tumores
- Selección de Lineaje y Purificación
- Métodos de Producción a gran escala
- Condiciones de Producción “Xeno-free”

Terapias basadas en Células Madre

ClinicalTrials.gov
A service of the U.S. National Institutes of Health
Developed by the National Library of Medicine

Home | Search | Listings | Resources | Help | What's New | About

ClinicalTrials.gov provides regularly updated information about federally and privately supported clinical research in human volunteers. ClinicalTrials.gov gives you information about a trial's purpose, who may participate, locations, and phone numbers for more details. The information provided on ClinicalTrials.gov should be used in conjunction with advice from health care professionals. Before searching, you may want to learn more about clinical trials.

INVESTIGATOR NOTE: Investigators wishing to register trials should refer to http://prsinfo.clinicaltrials.gov.

Search Clinical Trials

Example: heart attack, Los Angeles

STEM CELL THERAPY [Search] Tips

Search within Specific Fields

Focused Search - search by disease, location, treatment, sponsor...

Resource Information

Understanding Clinical Trials - information explaining and describing clinical trials
What's New - studies in the news
Glossary - terms related to clinical trials
MedlinePlus - authoritative consumer health information
Genetics Home Reference - consumer information about genes and genetic conditions
NIH Health Information - research supported by the National Institutes of Health

Trial Listings

List by Condition - studies listed by disease or condition
List by Sponsor - studies listed by funding organization
List by Status - studies listed by recruitment status

www.clinicaltrials.gov

2056 Ensayos clínicos

1023 Completados

1033 En marcha

Terapias basadas en Células Madre

Aspectos a considerar

DERIVACIÓN

Células Madre Humanas Indiferenciadas
(Embrionarias, Adultas o Germinales)

↓

DIFERENCIACIÓN

Células Pre ó Diferenciadas

↓

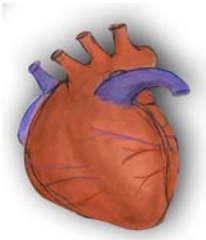
APLICACIÓN MÉDICA

↙ Terapia Tisular "*in situ*"

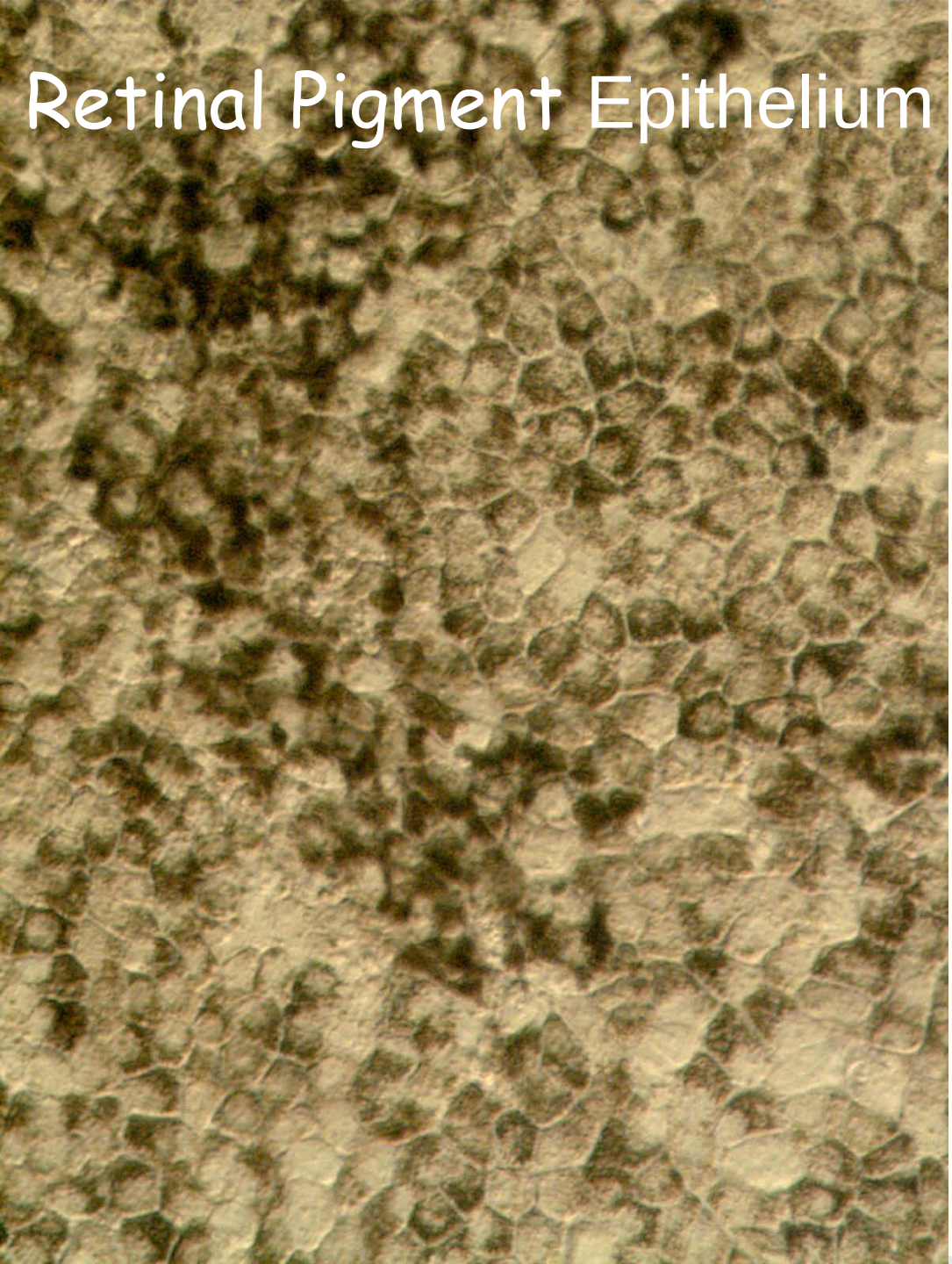
↘ Ingeniería Tisular
Órganos Artificiales Híbridos

Próximos ensayos clínicos

- En los Estados Unidos se programaron tres ensayos clínicos con células madre embrionarias que comenzarían en 2008 para tratar:
  - **Lesiones de médula espina**
  - **Infarto de miocardio**
  - **Degeneración macular**


- Ensayos adicionales fueron programados para el año siguiente para reemplazar:
  - **Células productoras de insulina en diabetes**
  - **Neuronas dopaminérgicas en Parkinson**

RPE functions

Photoreceptor “life support”:
-- metabolism of vitamin A
-- phagocytosis of shed rod fragments
-- absorption of stray light
--barrier

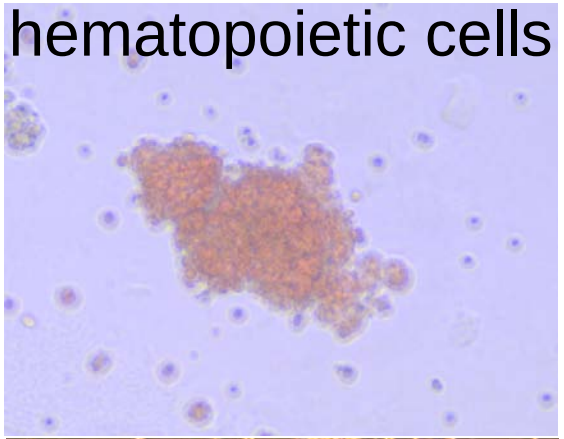
RPE malfunction:

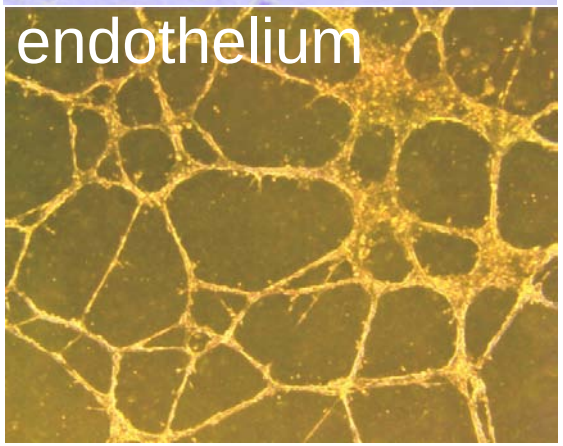
Macular degeneration
Rhetinitis pigmentosa
Retinal dystrophies
Stargard’s disease

Hemangioblast and its derivatives – a road to “universal blood”?

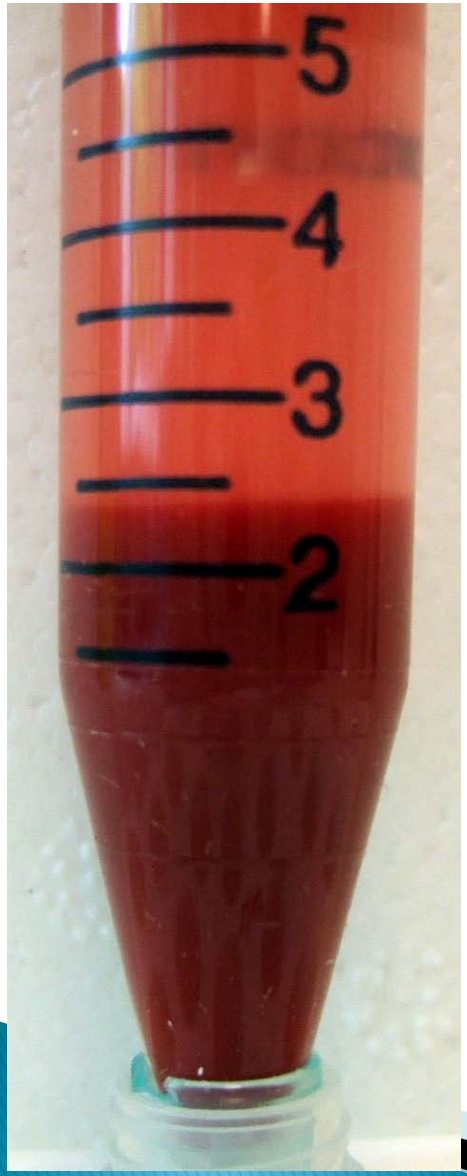
Hemangiobast – a common progenitor of hematopoietic cells and endothelium.

Derived form hES cells and can differentiate *in vivo* and *in vitro*





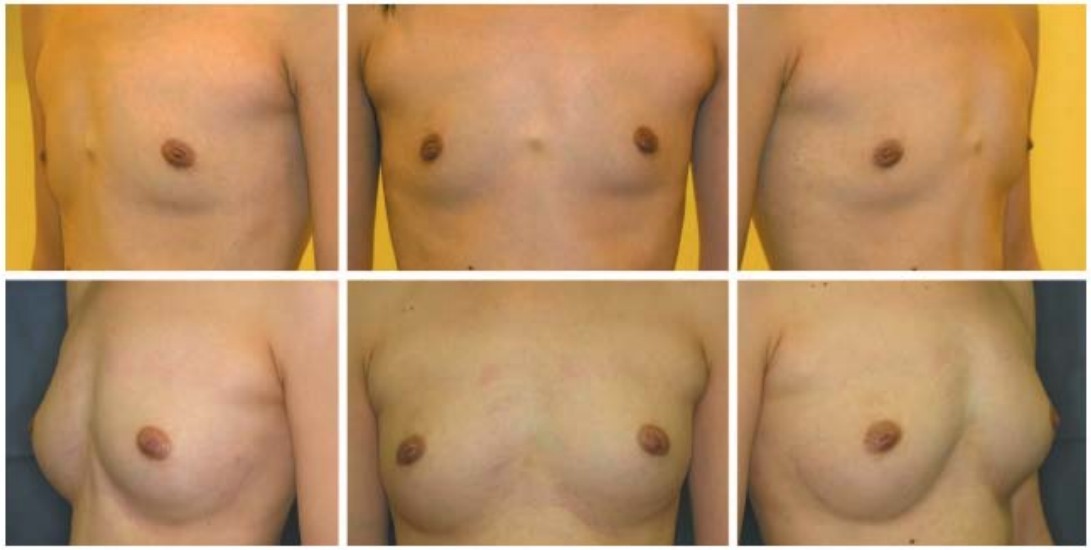
Hemangioblast derivative -- erythrocytes



Can be generated from hES cells of group 0/ Rhesus negative Such erythrocytes would be suitable for any person –
“universal blood”

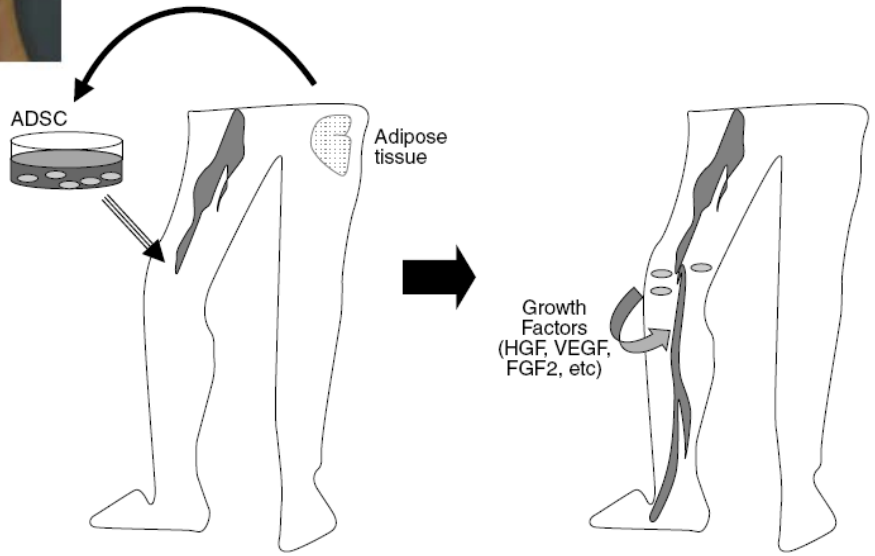
Terapias basadas en Células Madre

Células Madre Adultas



ADSC pueden ser usadas en cirujía recosntructiva mamaria *(Yoshimura, 2006).*

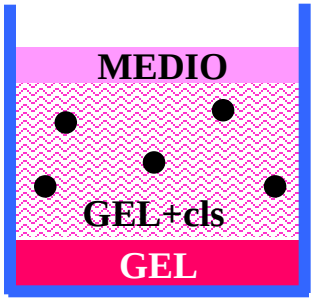
Los transplantes de ADSC secretan factores de crecimiento que promueven la angiogénesis en areas isquémicas *(Nakagami et al., 2006).*

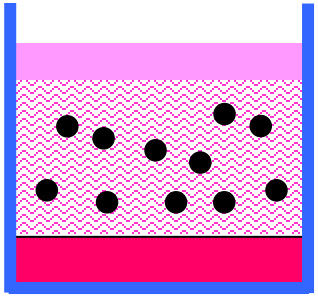


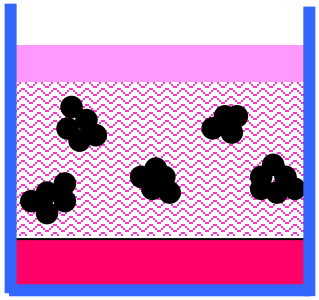
Terapias basadas en Células Madre

Células Madre Adultas

Método de Capacitación Osteogénica (MCO)







SELECCIÓN
0.5% FBS + TGF-β1
10 días

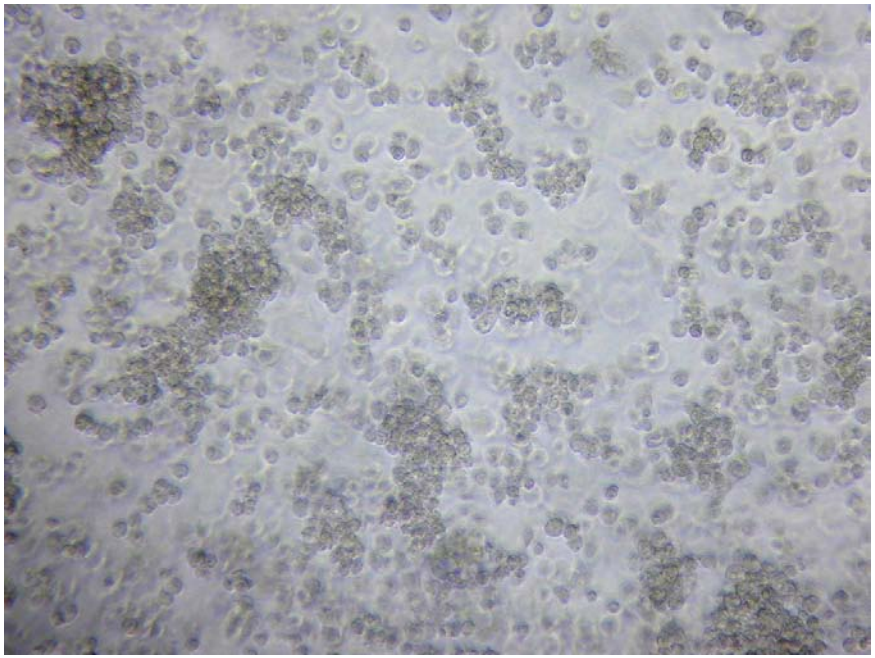
AMPLIFICACIÓN
10% FBS + TGF-β1
4 días

DIFERENCIACIÓN
10% FBS + Dex + β-GP
2 días

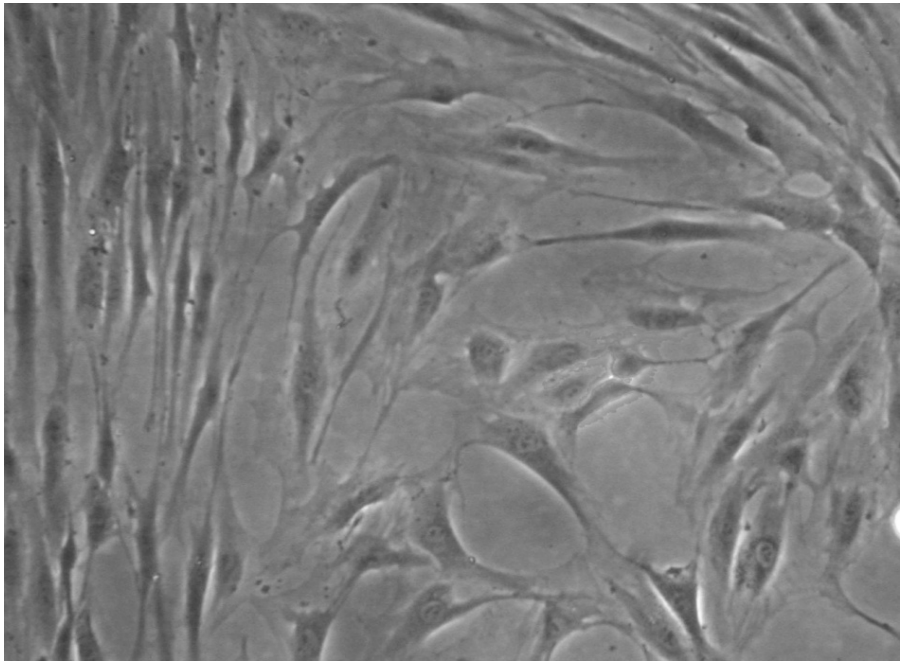
Dr. Jose Becerra. Universidad de Malaga
Dr. Enrique Guerado Hospital Costa del Sol. Marbella

Terapias basadas en Células Madre

Células Madre Adultas



Cultivo 3D
(MCO)



Cultivo 2D
(ADH)

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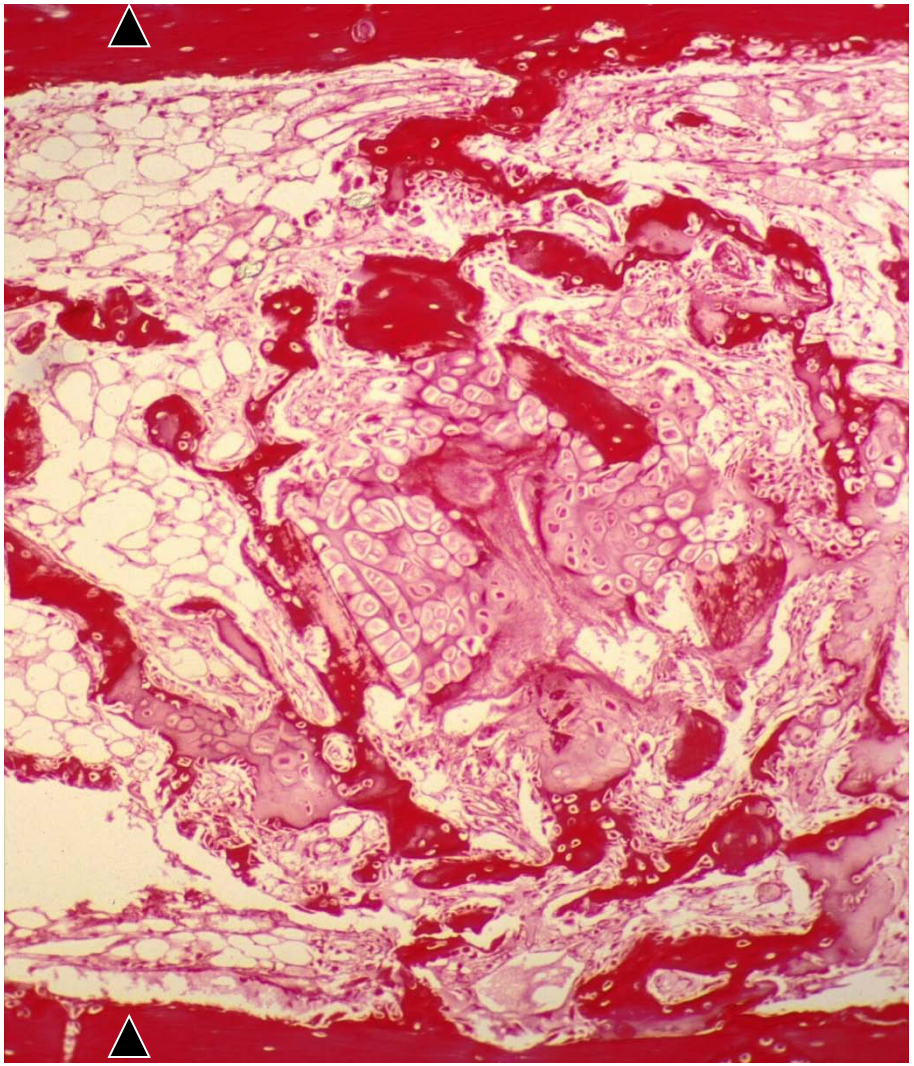
Dr. Enrique Guerado Hospital Costa del Sol. Marbella

Terapias basadas en Células Madre

Células Madre Adultas

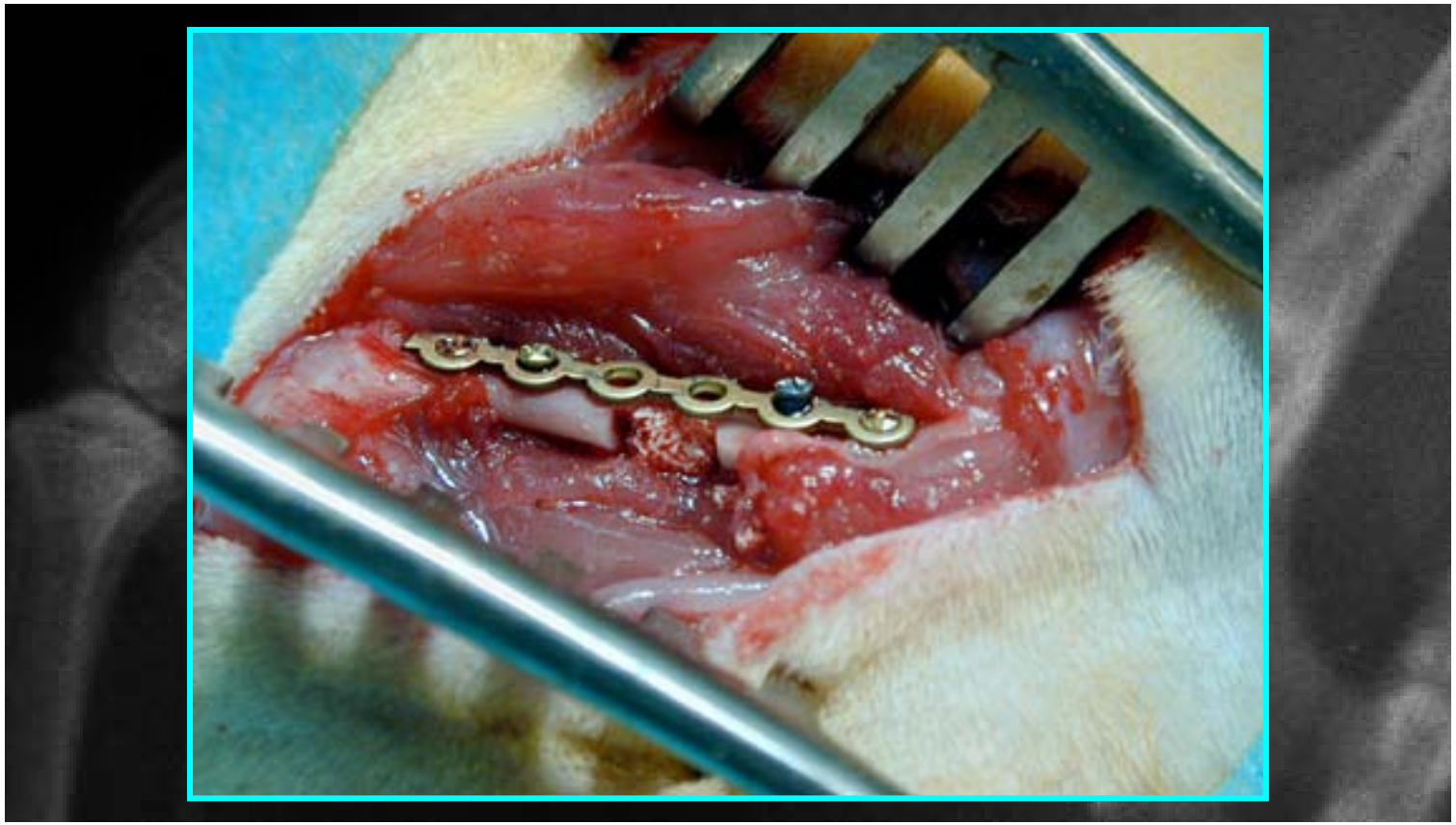
DBM Chambers



FORMACIÓN OSEA ECTOPICA

Terapias basadas en Células Madre

Células Madre Adultas



RESECCIONES SEGMENTARIAS

Uncertainties

-Zoonosis.

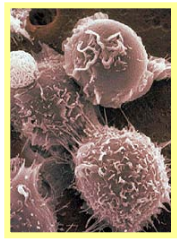
Most of existing human ES lines have been exposed to products and cells of animal origin.

(NIH & FDA criteria,zoonosis)

-Differentiation ineficient.

They could generate tumors if they are transplanted to humans.

-Immune Rejection.
hESC express antigens of histocompatibility MHC-I they are able to induce the rejection process (Drukker et al., 2002)



The dark side

Company	Source of cells	Treatment	Price	Others
Institute for Regenerative Medicine (Barbados)	Embryonic stem cell obtained from donors (not compensated)	Cancer, coronary heart disease, diabetes, liver disease, ageing problems...	US$25.000 per session	No factual scientific evidence
Medra Inc. (Dominican Republic)	Human fetal stem cell obtained from Soviet republic Georgia	Cancer, brain damage, anemia, spinal cord injury...and there are promises of rejuvenation and longevity	US$25.000 per session, each follow up session is cheaper: only US$8.500	Painless procedure which takes place in 1h, no negative side effects
Ramirez del Río (Mexico)	Cells from cord blood (??)	Dental work and cosmetic surgery	US$ 6.500 per injection	No websites, no information about procedures or source of stem cells

PRINCIPE FELIPE

CENTRO DE INVESTIGACION

BANCO DE LÍNEAS CELULARES