ADISCO
ASSOCIAZIONE DONATRICI ITALIANE
SANGUE CORDONE OMBELICALE

Sangue Cordonale: Rifiuto Biologico o Terapia Salva Vita?

… Se l'unità SCO non fosse idonea per il bancaggio a fini trapiantologici, il suo contenuto potrà essere utilizzato per la creazione di emocomponenti, mentre le emazie potranno essere infuse ai prematuri.

CENTRO NAZIONALE SANGUE

BMDR

REGIONE LAZIO

Centro Nazionale Trapianti

SIdEM Società Italiana di Emaferesi e Manipolazione Cellulare

CONVEGNO NAZIONALE ADISCO-OdV

15 novembre 2022

Le Potenzialità delle Cellule Staminali nella rigenerazione di Tessuti e Organi

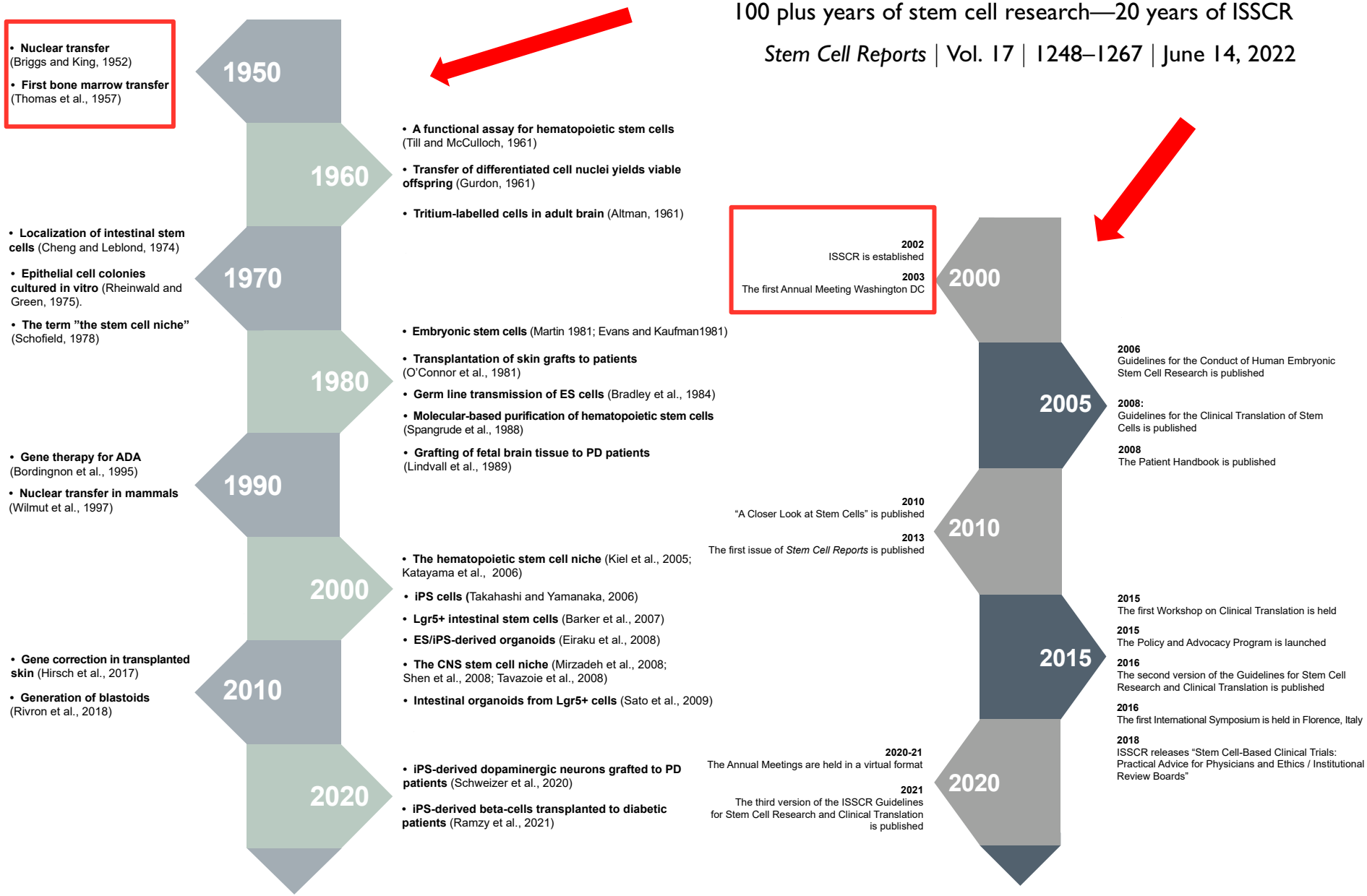
Giorgina Specchia
già Professre Ordinario di Ematologia Università Aldo Moro Bari
Presidente Rete Ematologica Pugliese (REP)
Componente Comitato Scientifico AIL Nazionale

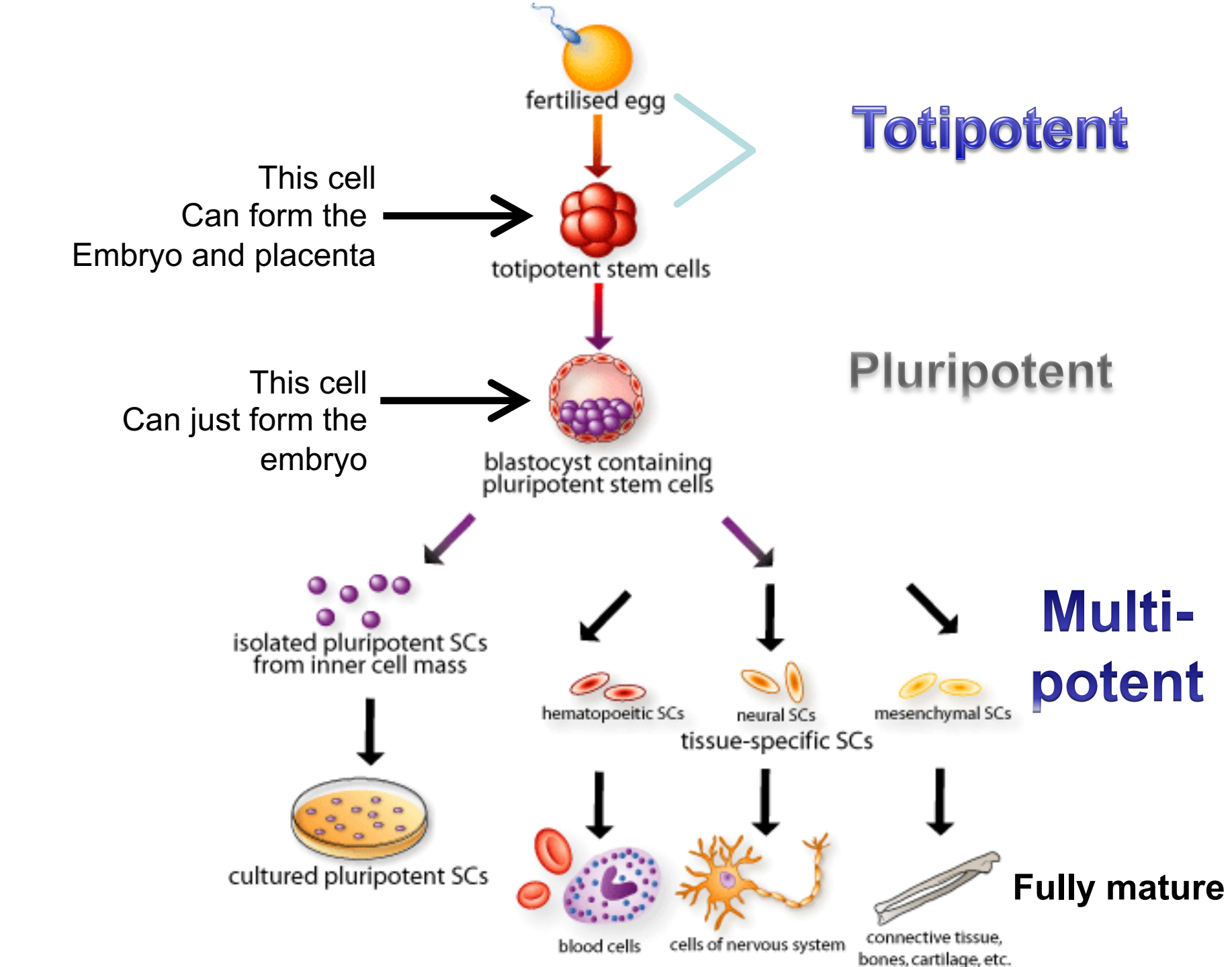
25 major discoveries in stem cell research

Stem Cell Reports
Perspective

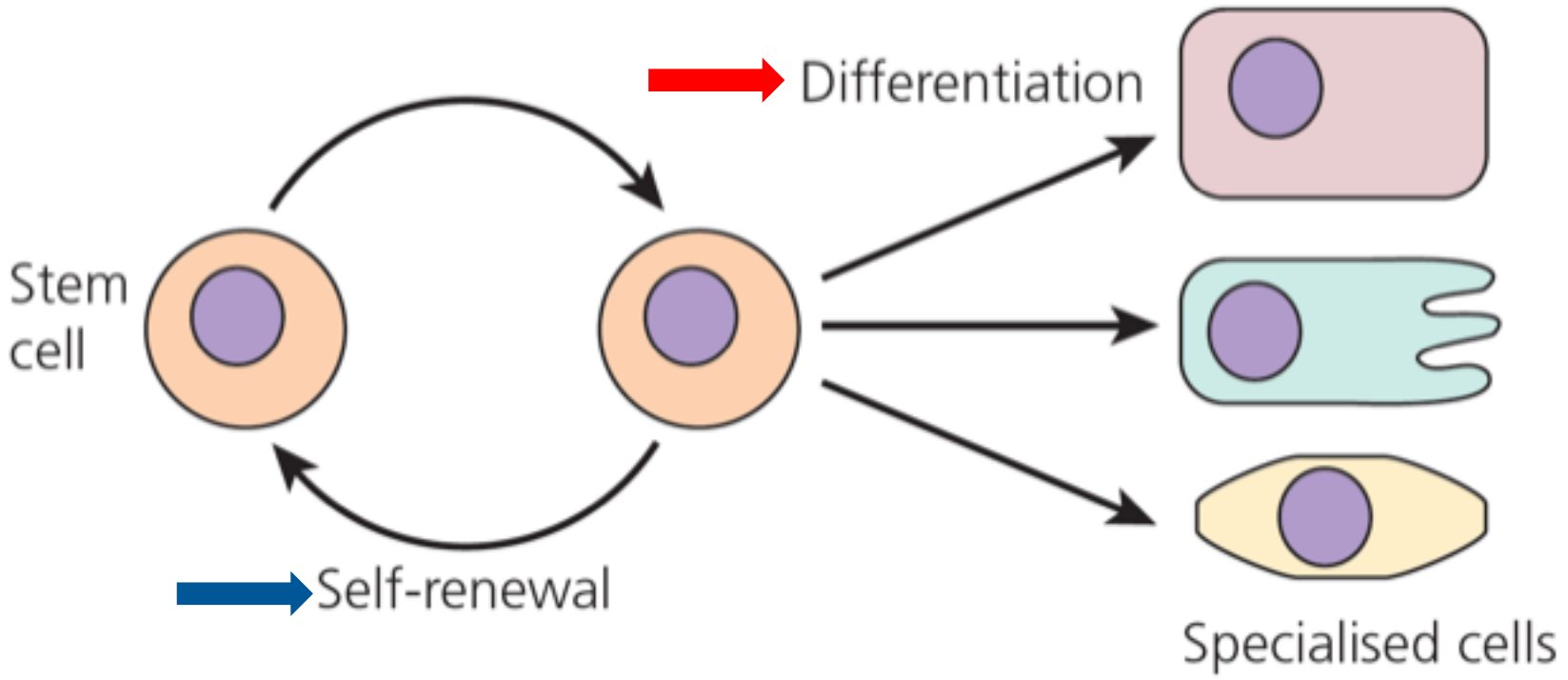
100 plus years of stem cell research—20 years of ISSCR

Stem Cell Reports | Vol. 17 | 1248–1267 | June 14, 2022



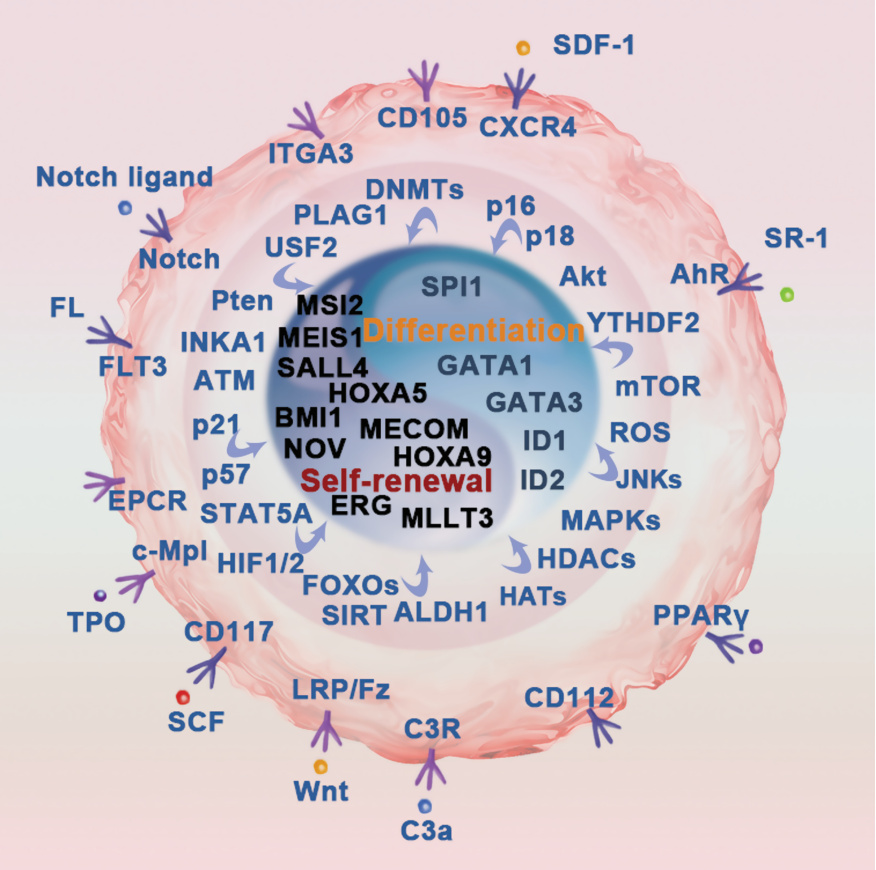

fertilised egg
Totipotent
This cell
Can form the
Embryo and placenta
totipotent stem cells
This cell
Can just form the
embryo
Pluripotent
blastocyst containing
pluripotent stem cells
isolated pluripotent SCs
from inner cell mass
hematopoeitic SCs
neural SCs
mesenchymal SCs
Multi-
potent
tissue-specific SCs
cultured pluripotent SCs
blood cells
cells of nervous system
connective tissue,
bones, cartilage, etc.
Fully mature

Key features of stem cells



Self-renewal: the capacity to proliferate but not differentiate, thus preserving the ability to **generate a stem cell progeny similar to the parent cell**

Stem cell



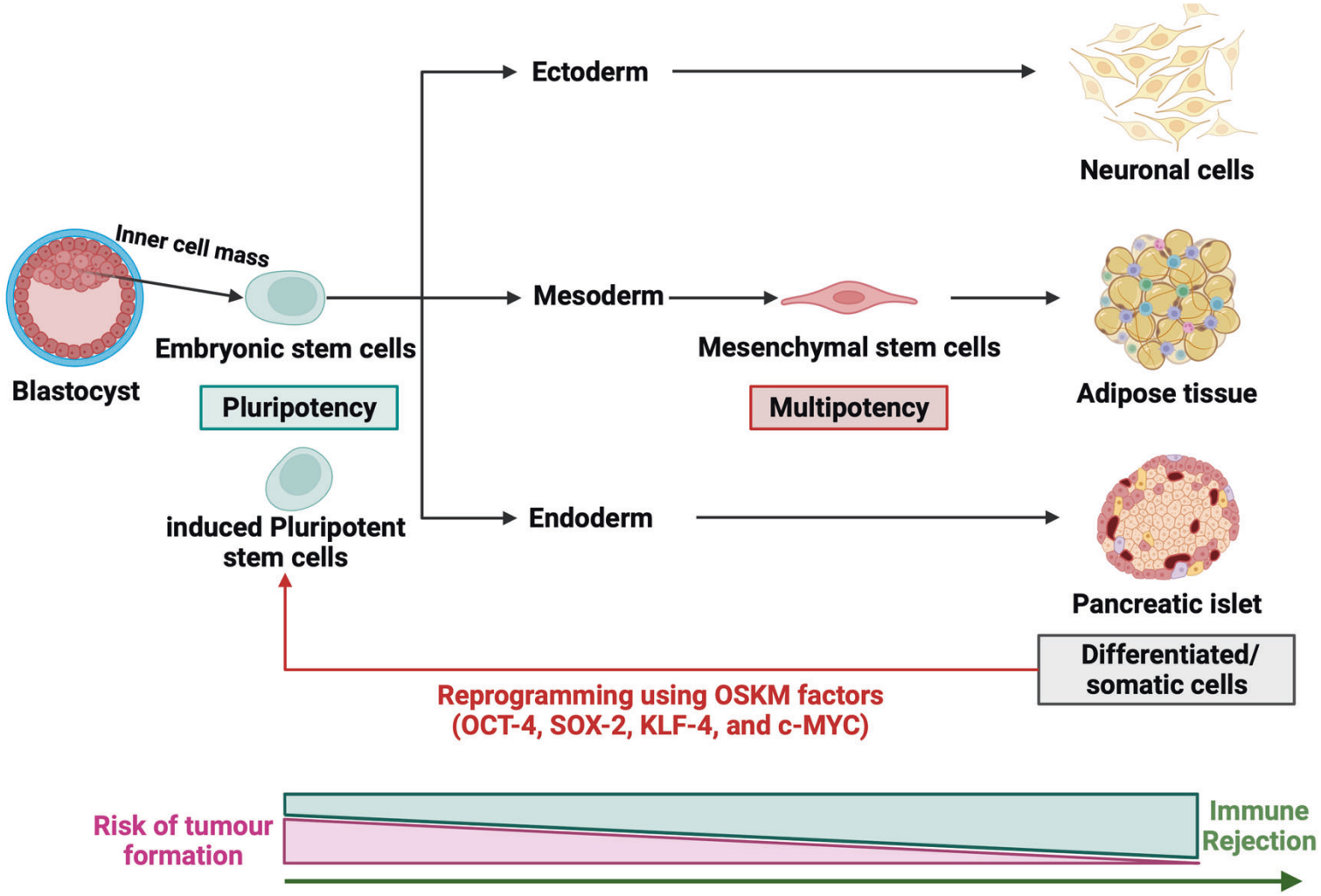
Quali utilizzazioni oggi delle SCs nella rigenerazione di Tessuti e Organi……..

REVIEW ARTICLE

Signal Transduction and Targeted Therapy (2022)7:272

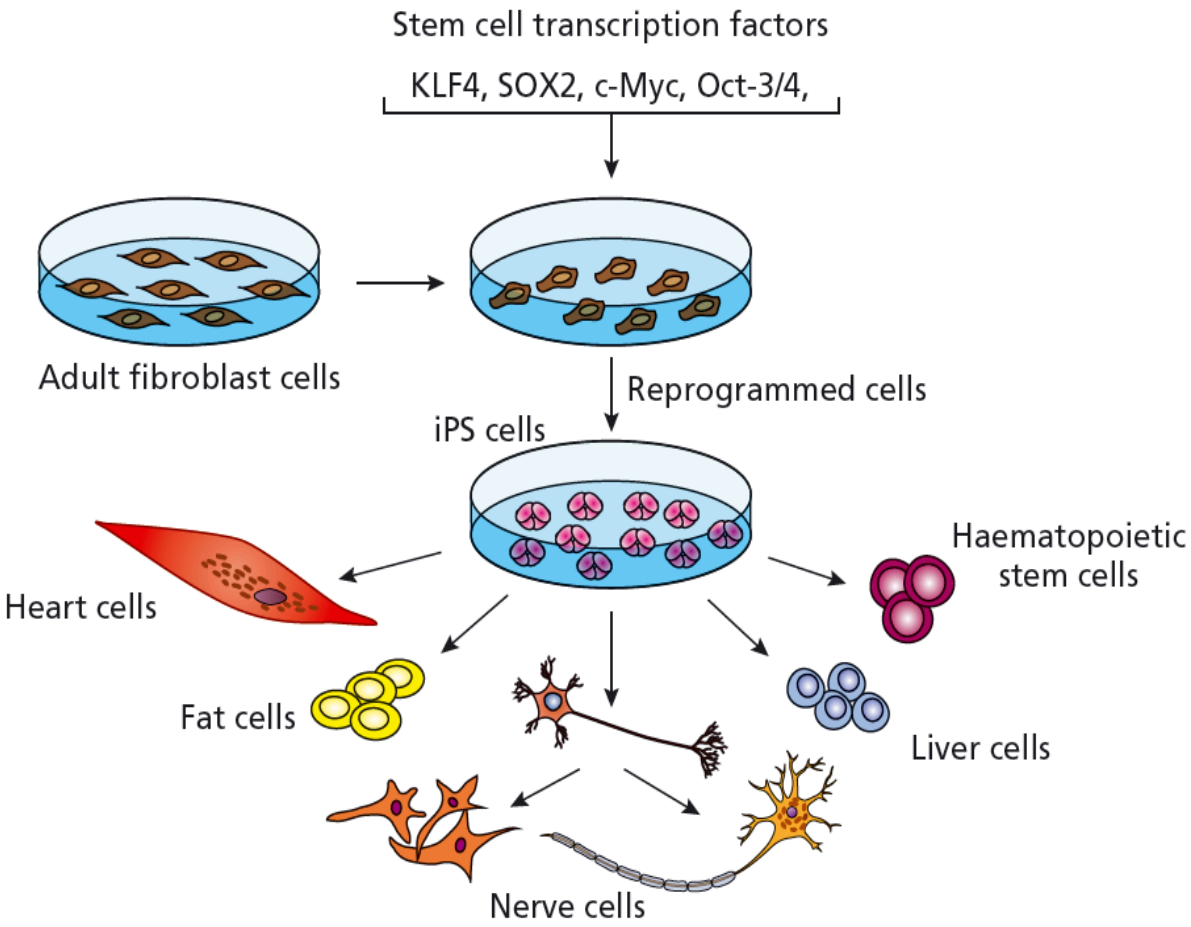
Stem cell-based therapy for human diseases

Duc M. Hoang[1]✉, Phuong T. Pham[2], Trung Q. Bach[1], Anh T. L. Ngo[2], Quyen T. Nguyen[1], Trang T. K. Phan[1], Giang H. Nguyen[1], Phuong T. T. Le[1], Van T. Hoang[1], Nicholas R. Forsyth[3], Michael Heke[4] and Liem Thanh Nguyen[1]

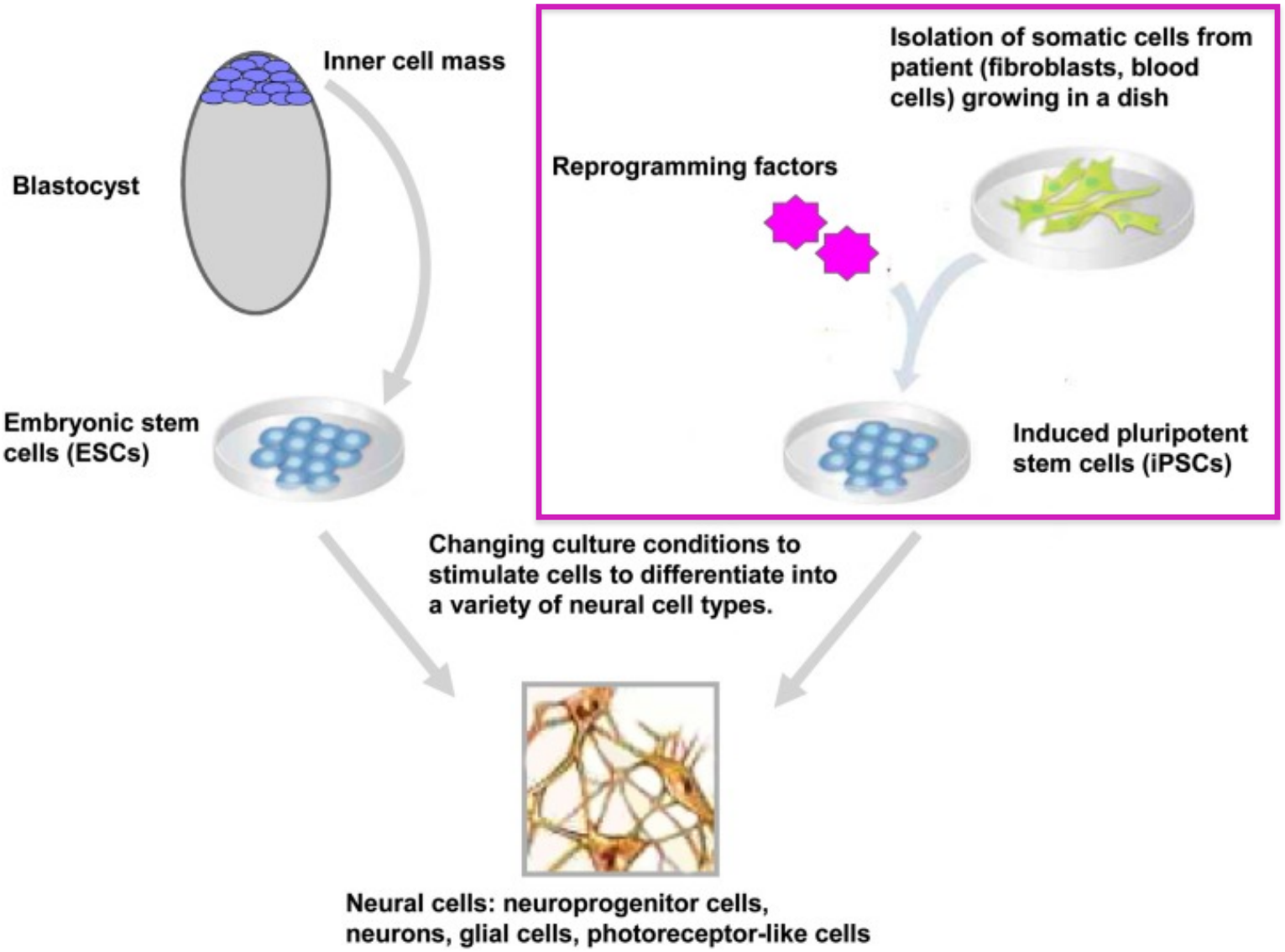


Producing iPS cells

Takahashi and Yamanaka 2006



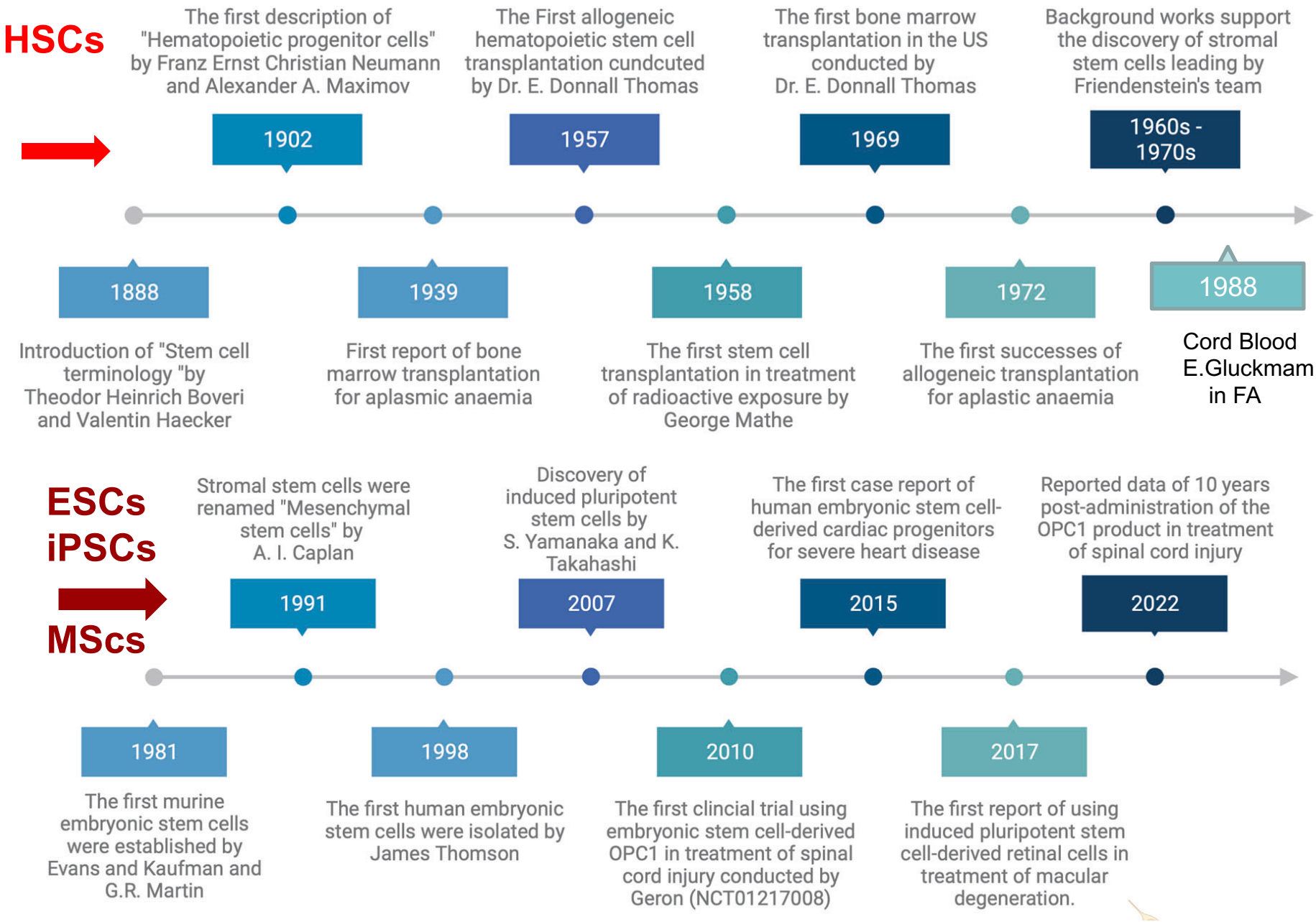
Use of ESCs in Neurological Diseases



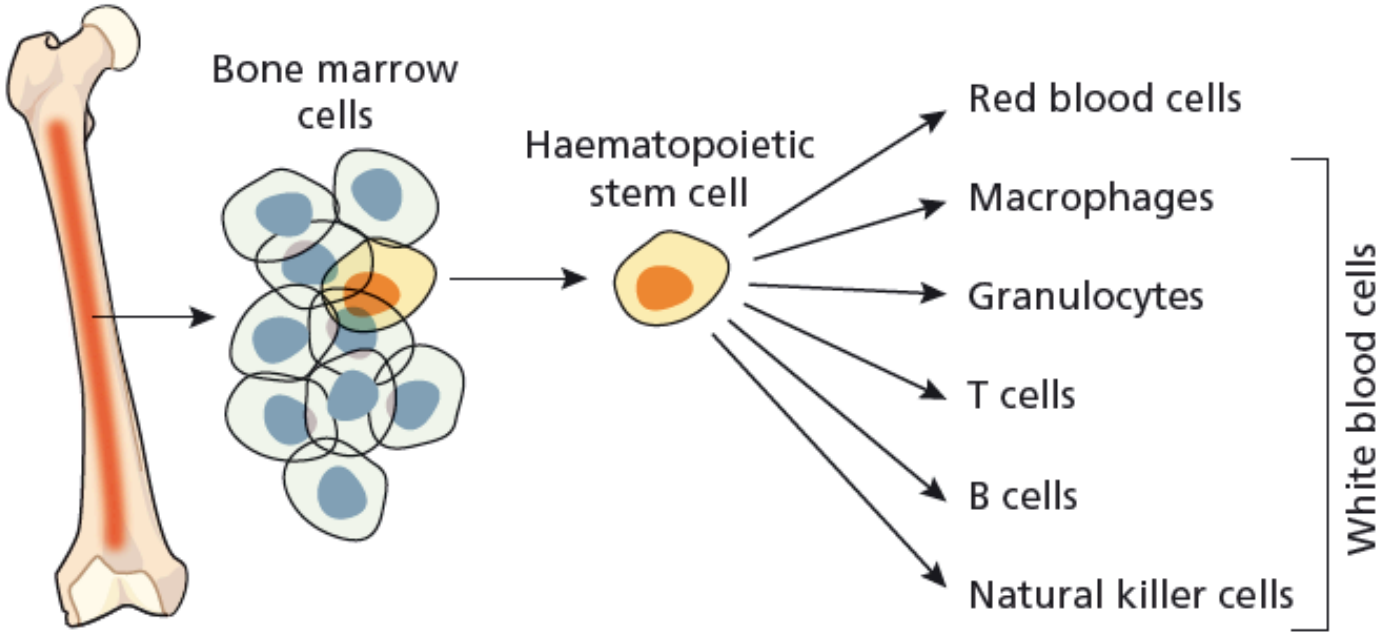
Hibaoui Y et al. Front Physiol. 2012

Use of embryonic stem cells

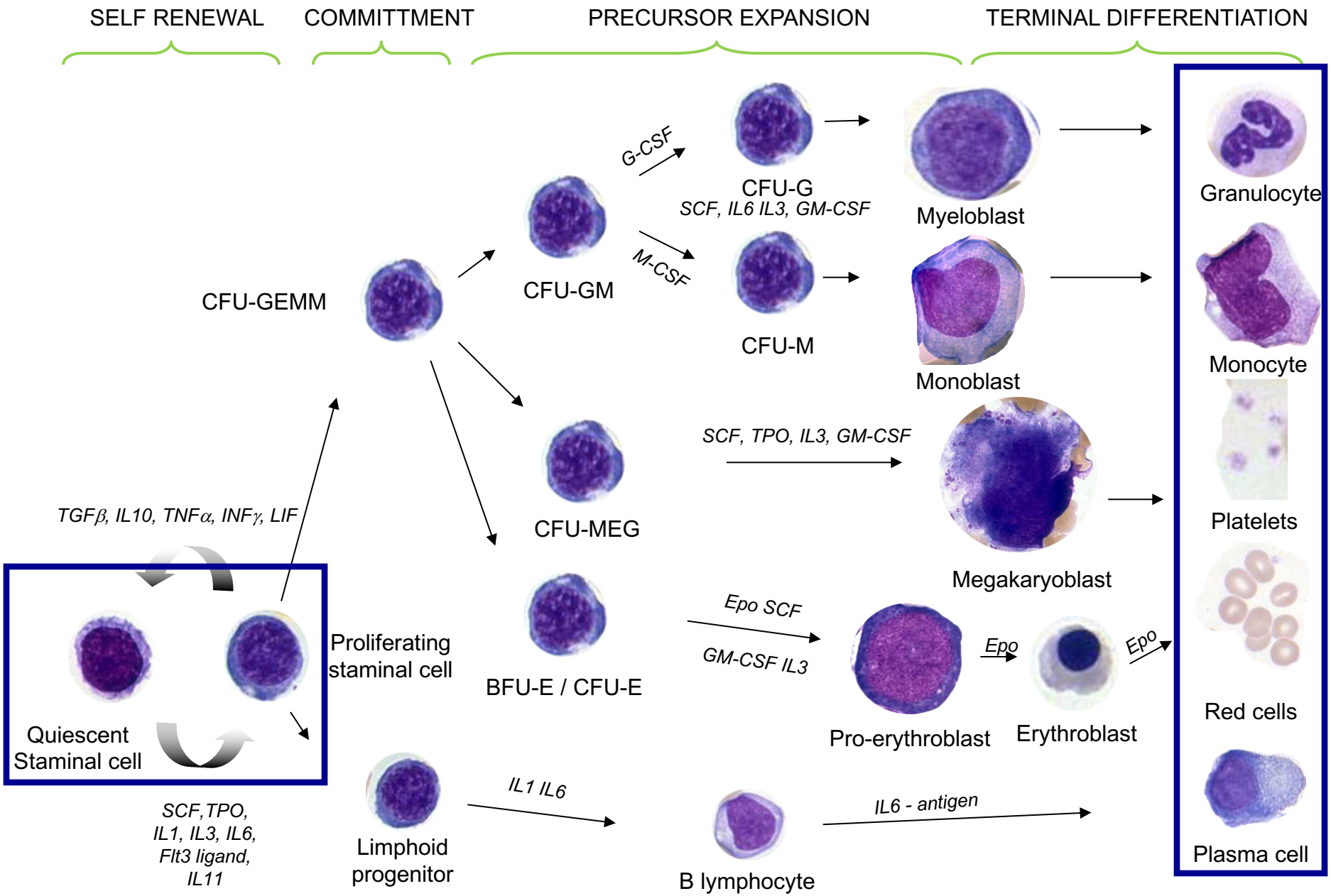
- Embryonic stem cells are **pluripotent**, i.e. can produce any cell in the human body. Consequently, there is the potential to use them in therapy
- They might, for example, be useful in repairing or replacing damaged tissues or organs
- The use of embryonic stem cells raises **ethical issues**, though.
    - Each embryo is capable of producing a human being.
    - Consequently, destroying an embryo prevents the development and birth of a human being
- **The potential risk of immunological rejection,** as hESCs are isolated from pre-implantation blastocysts, which are not autologous in origin
- **In humans, the reprogramming of adult cells iPSCs could trigger the expression of oncogenes**.
- Insertion of genes risks **inserting mutations** into the target cell's genome


HSCs
The first description of "Hematopoietic progenitor cells" by Franz Ernst Christian Neumann and Alexander A. Maximov
1902
The First allogeneic hematopoietic stem cell transplantation cundcuted by Dr. E. Donnall Thomas
1957
The first bone marrow transplantation in the US conducted by Dr. E. Donnall Thomas
1969
Background works support the discovery of stromal stem cells leading by Friendenstein's team
1960s - 1970s
1888
Introduction of "Stem cell terminology "by Theodor Heinrich Boveri and Valentin Haecker
1939
First report of bone marrow transplantation for aplasmic anaemia
1958
The first stem cell transplantation in treatment of radioactive exposure by George Mathe
1972
The first successes of allogeneic transplantation for aplastic anaemia
1988
Cord Blood E.Gluckmam in FA
ESCs
iPSCs
MScs
Stromal stem cells were renamed "Mesenchymal stem cells" by A. I. Caplan
1991
Discovery of induced pluripotent stem cells by S. Yamanaka and K. Takahashi
2007
The first case report of human embryonic stem cell-derived cardiac progenitors for severe heart disease
2015
Reported data of 10 years post-administration of the OPC1 product in treatment of spinal cord injury
2022
1981
The first murine embryonic stem cells were established by Evans and Kaufman and G.R. Martin
1998
The first human embryonic stem cells were isolated by James Thomson
2010
The first clincial trial using embryonic stem cell-derived OPC1 in treatment of spinal cord injury conducted by Geron (NCT01217008)
2017
The first report of using induced pluripotent stem cell-derived retinal cells in treatment of macular degeneration.

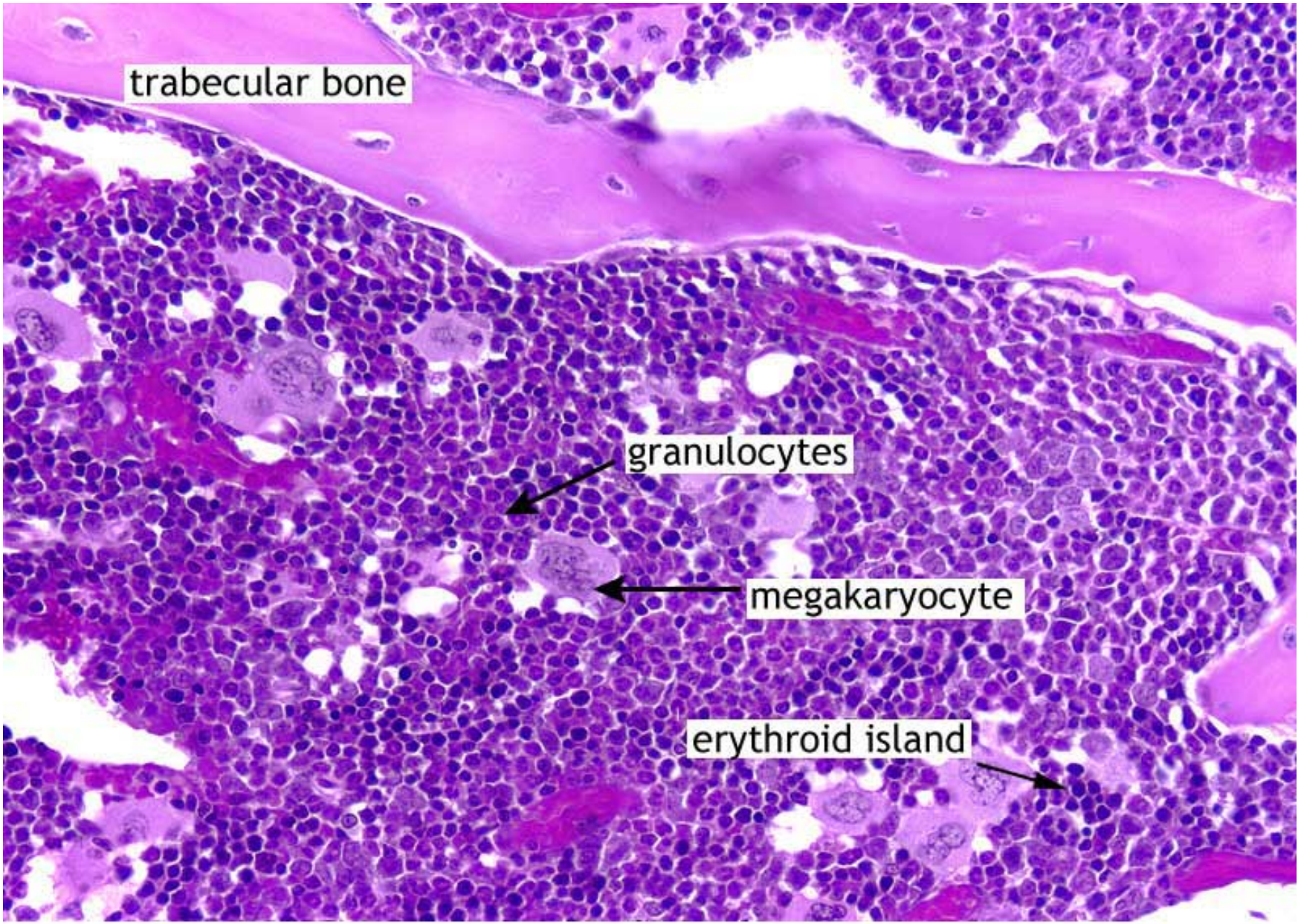
One type of Adult Stem Cell



Ematopoiesi normale



Midollo osseo

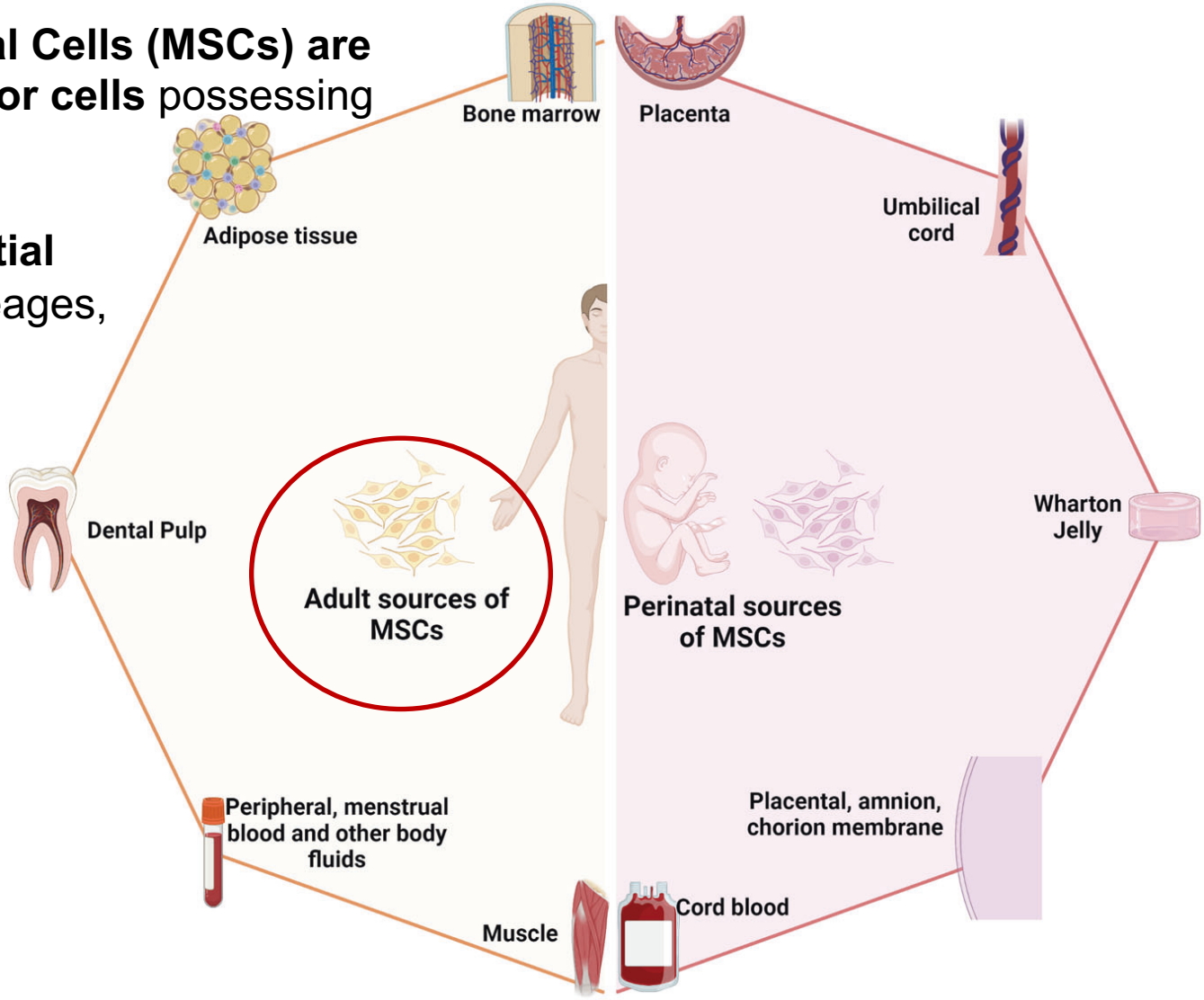


REVIEW ARTICLE *Signal Transduction and Targeted Therapy* (2022)7:272

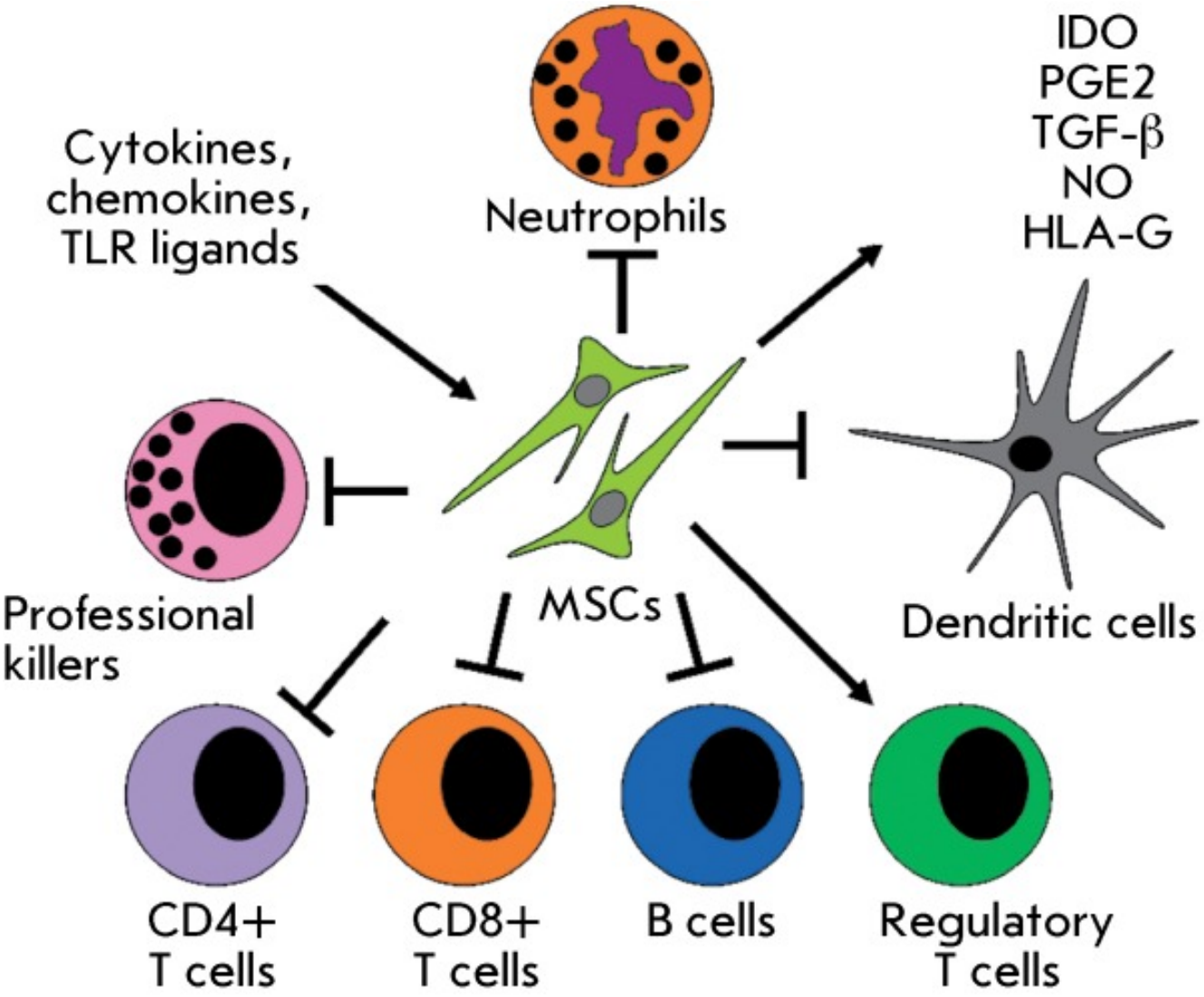
Stem cell-based therapy for human diseases

Duc M. Hoang[1]✉, Phuong T. Pham[2], Trung Q. Bach[1], Anh T. L. Ngo[2], Quyen T. Nguyen[1], Trang T. K. Phan[1], Giang H. Nguyen[1], Phuong T. T. Le[1], Van T. Hoang[1], Nicholas R. Forsyth[3], Michael Heke[4] and Liem Thanh Nguyen[1]

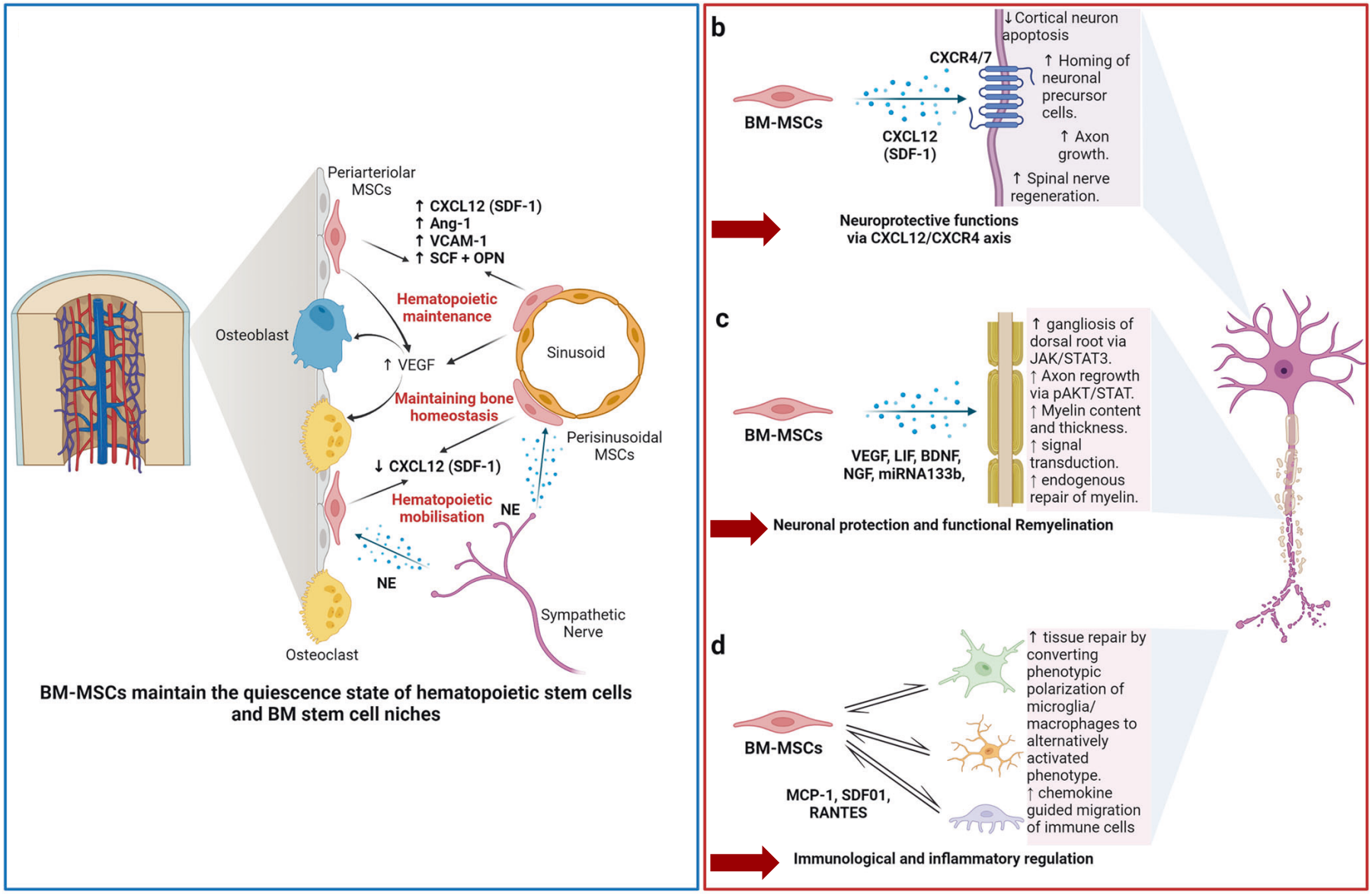
Mesenchimal Stromal Cells (MSCs) are multipotent progenitor cells possessing **self-renewa**l ability (limited in vitro) and **differentiation potential** into mesenchymal lineages, according to the **International Society for Cell and Gene Therapy (ISCT).**

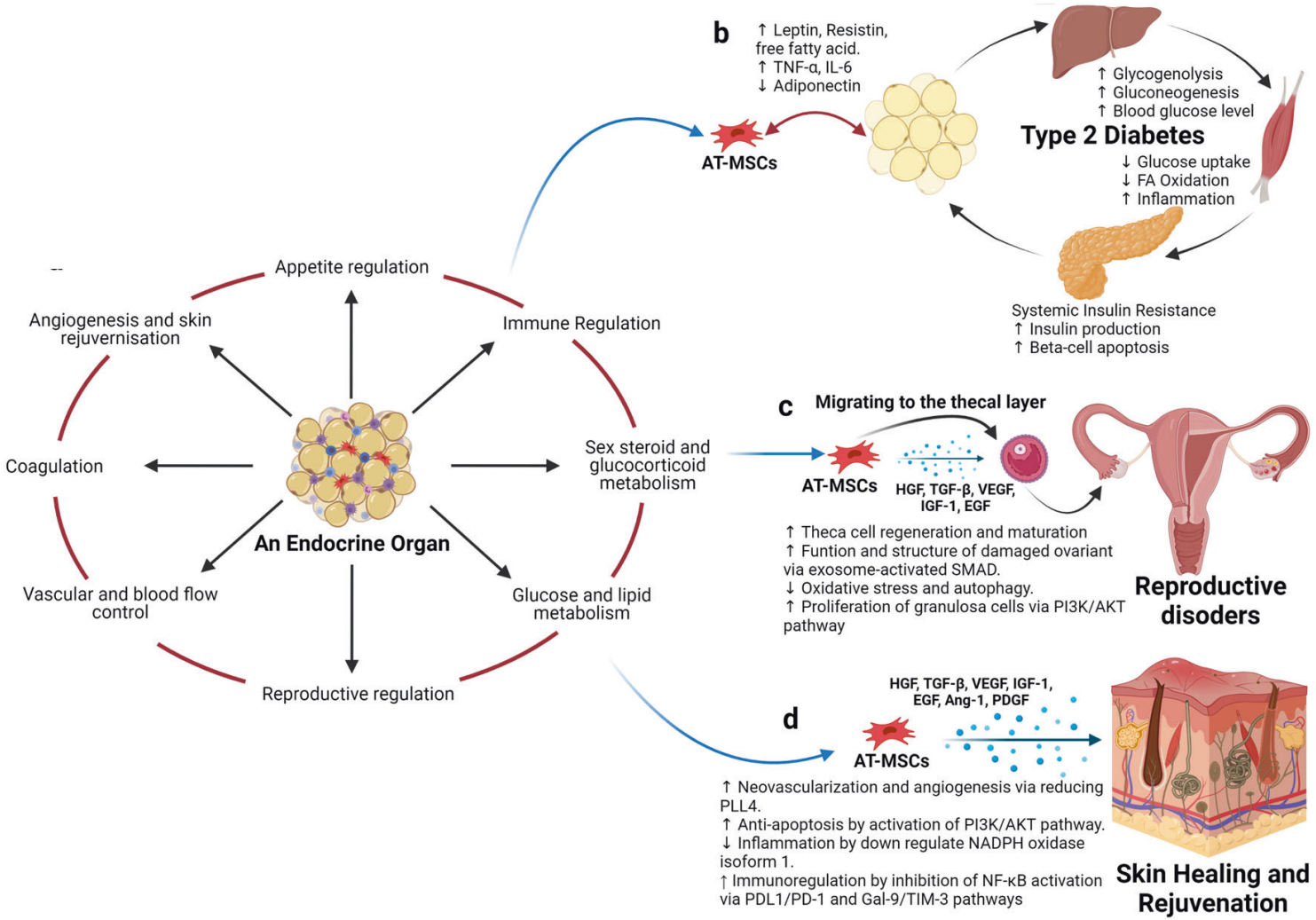


Regulation of Immunity via MSC



Rubtsov YP et al. Acta Nature 2012


Periarteriolar MSCs
↑ CXCL12 (SDF-1)
↑ Ang-1
↑ VCAM-1
↑ SCF + OPN
Hematopoietic maintenance
Osteoblast
↑ VEGF
Sinusoid
Maintaining bone homeostasis
Perisinusoidal MSCs
↓ CXCL12 (SDF-1)
Hematopoietic mobilisation
NE
NE
Sympathetic Nerve
Osteoclast
BM-MSCs maintain the quiescence state of hematopoietic stem cells and BM stem cell niches
b
↓ Cortical neuron apoptosis
CXCR4/7
↑ Homing of neuronal precursor cells.
BM-MSCs
CXCL12 (SDF-1)
↑ Axon growth.
↑ Spinal nerve regeneration.
Neuroprotective functions via CXCL12/CXCR4 axis
c
↑ gangliosis of dorsal root via JAK/STAT3.
↑ Axon regrowth via pAKT/STAT.
↑ Myelin content and thickness.
↑ signal transduction.
↑ endogenous repair of myelin.
BM-MSCs
VEGF, LIF, BDNF, NGF, miRNA133b,
Neuronal protection and functional Remyelination
d
↑ tissue repair by converting phenotypic polarization of microglia/ macrophages to alternatively activated phenotype.
↑ chemokine guided migration of immune cells
BM-MSCs
MCP-1, SDF01, RANTES
Immunological and inflammatory regulation

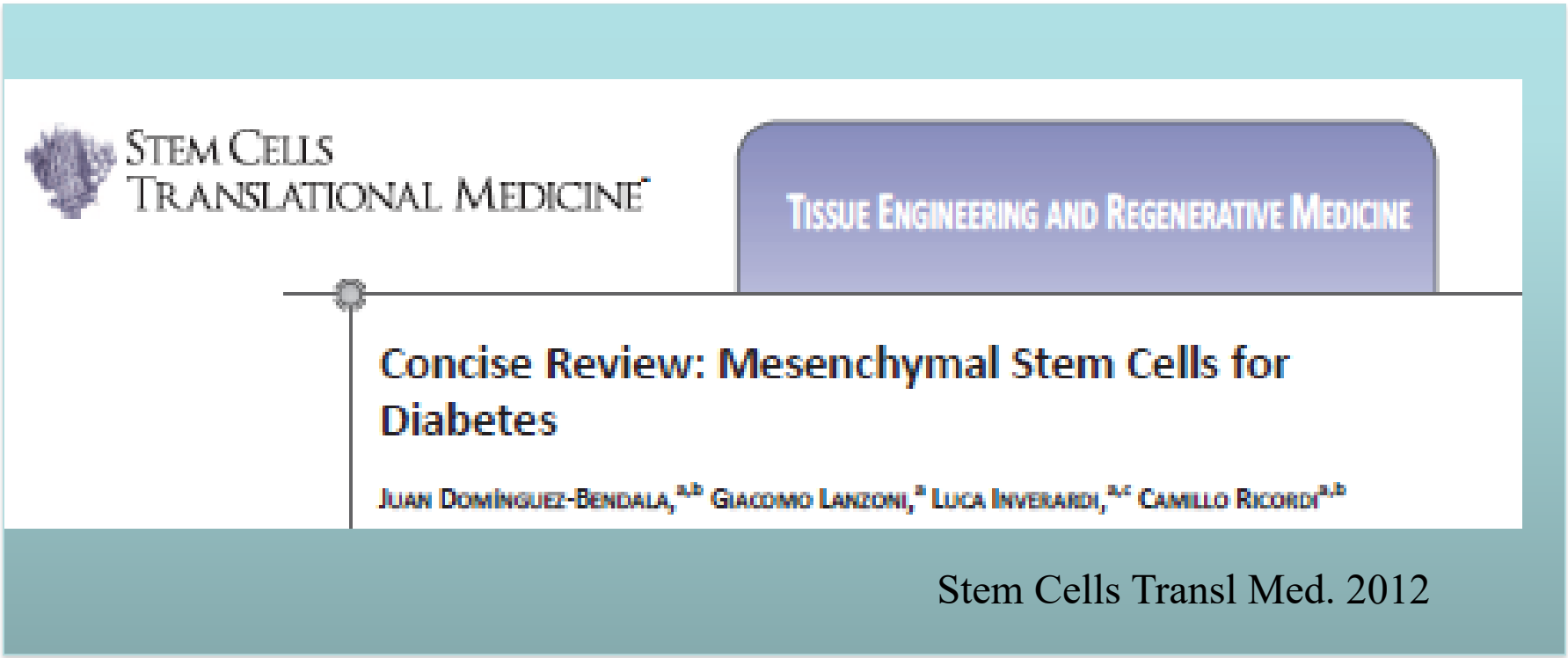


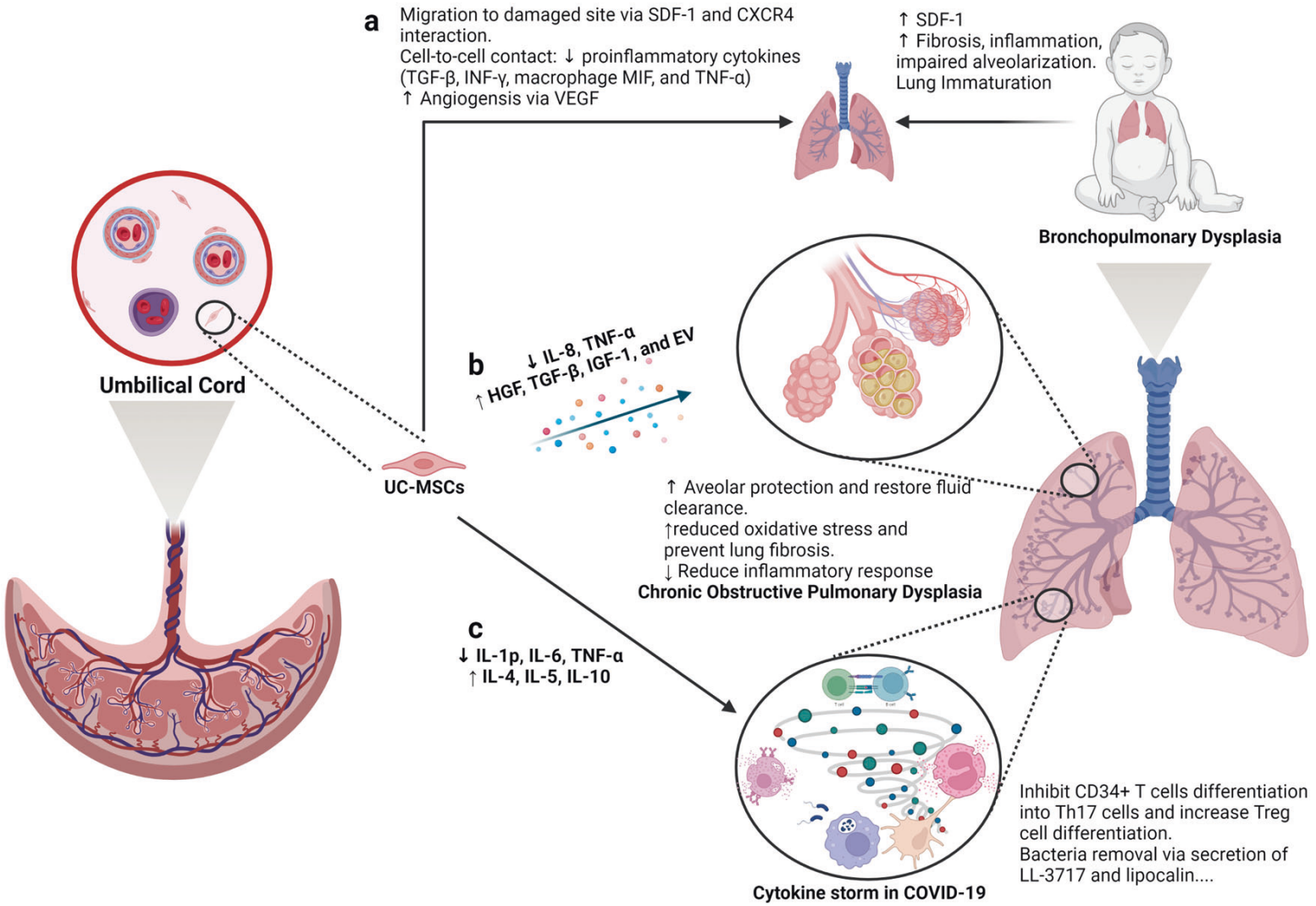
ENDOCRINE DISORDERS, INFERTILITY/REPRODUCTIVE FUNCTION RECOVERY, AND SKIN BURNS: SHOULD WE CONSIDER AT-MSCS AS THE MAIN MSCS BASED ON THEIR ORIGIN

Signal Transduction and Targeted Therapy (2022)7:272

Diabete e cellule staminali

- ricapitolare in vitro lo sviluppo normale delle cellule beta pancreatiche responsive ai livelli di glucosio dopo trapianto a partire dalle ES;





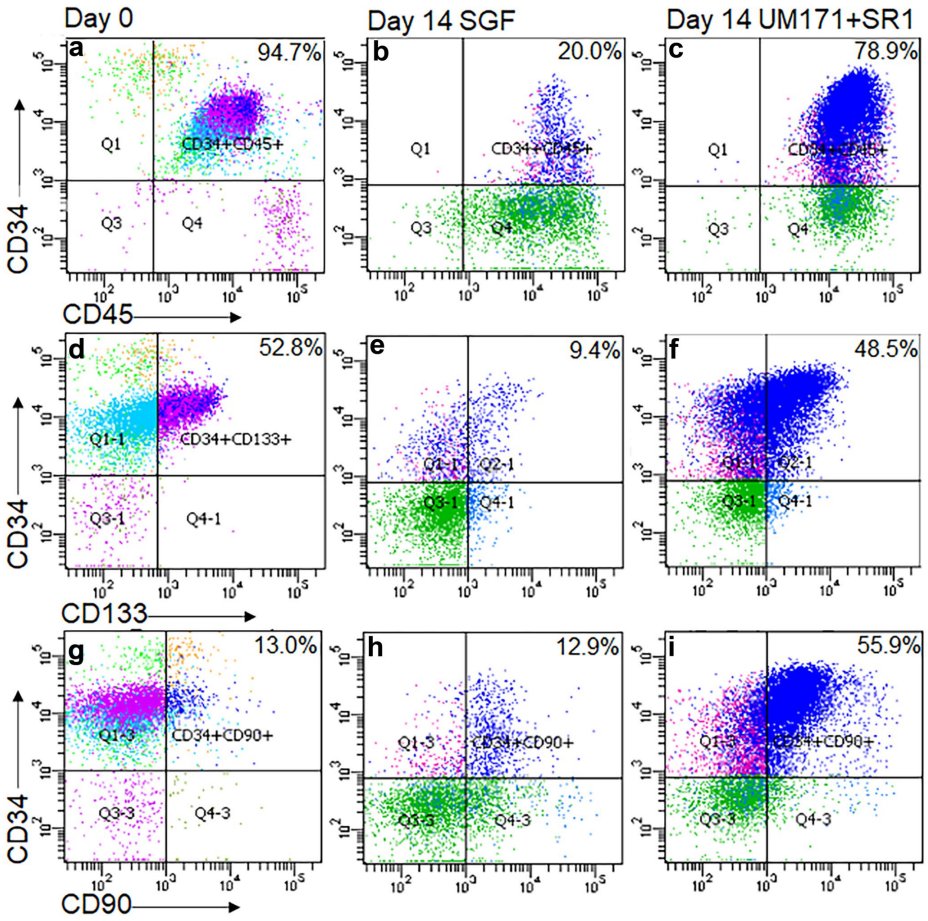
RESPIRATORY DISEASE AND **LUNG FIBROSIS**: CLINICAL DATA SUPPORT **UC** AS A GOOD SOURCE OF MSCS; also in severe COVID disease**

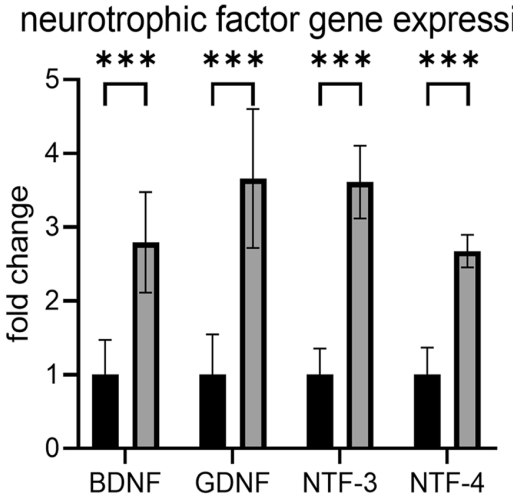
Signal Transduction and Targeted Therapy (2022)7:272

Effect of expansion of human umbilical cord blood CD34 + cells on neurotrophic and angiogenic factor expression and function

Cell and Tissue Research (2022) 388:117–132

Ashalyn P. Watt[1] · Mark Kirkland[2,3] · Lakshmi Nekkanti[1] · Yen Pham[1] · Courtney McDonald[1] · Atul Malhotra[1,4] · Guy Moeneclaey[1,2] · Suzanne L. Miller[1,5] · Graham Jenkin[1,5]





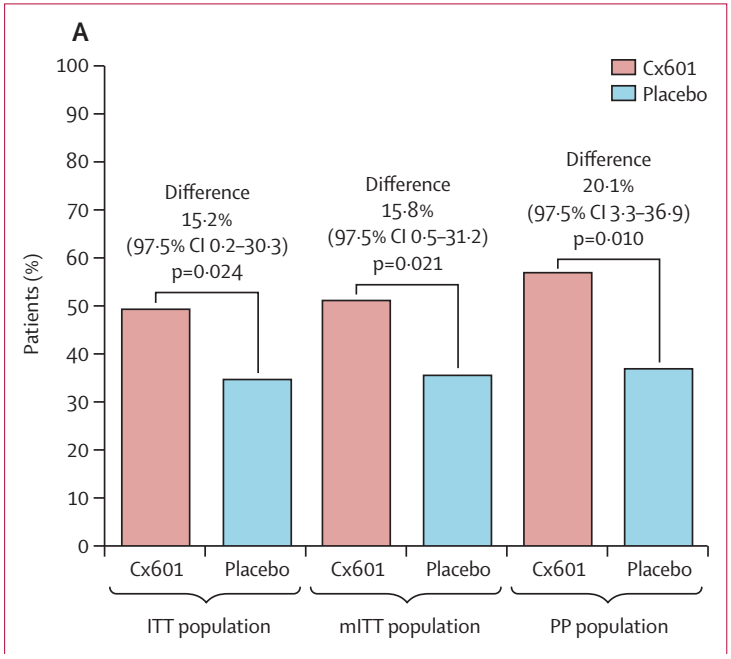
- The expanded cells showed an up-regulation of the **neurotrophic factor genes BDNF, GDNF, NTF-3 and NTF-4, as well as the angiogenic factors VEGF and ANG**

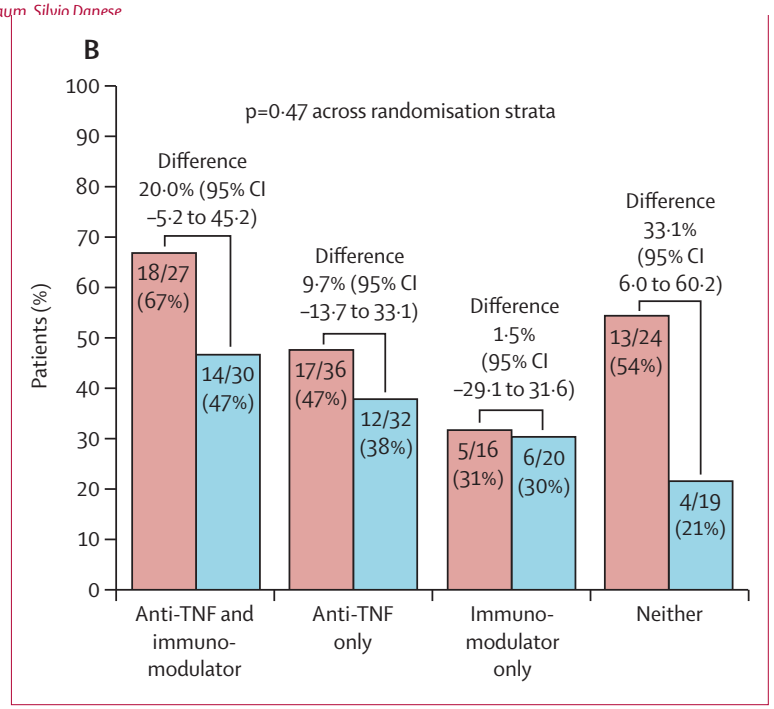
- In vitro functionality testing showed that these expanded cells promoted angiogenesis and, in brain glial cells, promoted cell **proliferation and reduced production of reactive oxygen species (ROS) during oxidative stress**

Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomised, double-blind controlled trial

.thelancet.com Vol 388 September 24, 2016

*Julián Panés, Damián García-Olmo, Gert Van Assche, Jean Frederic Colombel, Walter Reinisch, Daniel C Baumgart, Axel Dignass, Maria Nachury, Marc Ferrante, Lili Kazemi-Shirazi, Jean C Grimaud, Fernando de la Portilla, Eran Goldin, Marie Paule Richard, Anne Leselbaum, Silvio Danese for the ADMIRE CD Study Group Collaborators**





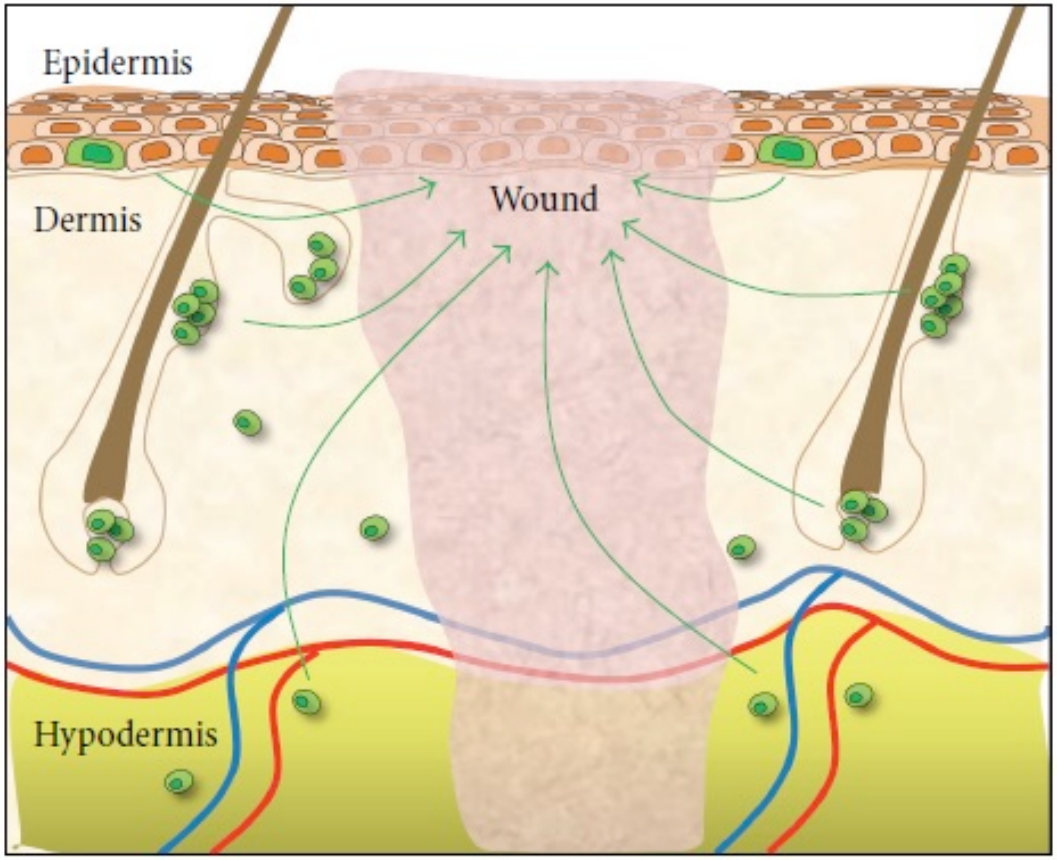
Background Complex perianal fistulas in Crohn's disease are challenging to treat. Allogeneic, expanded, adipose-derived stem cells (Cx601) are a promising new therapeutic approach. We aimed to assess the safety and efficacy of Cx601 for treatment-refractory complex perianal fistulas in patients with Crohn's disease.

Interpretation Cx601 is an effective and safe treatment for complex perianal fistulas in patients with Crohn's disease who did not respond to conventional or biological treatments, or both.

Review Article

Stem Cell Niches for Skin Regeneration

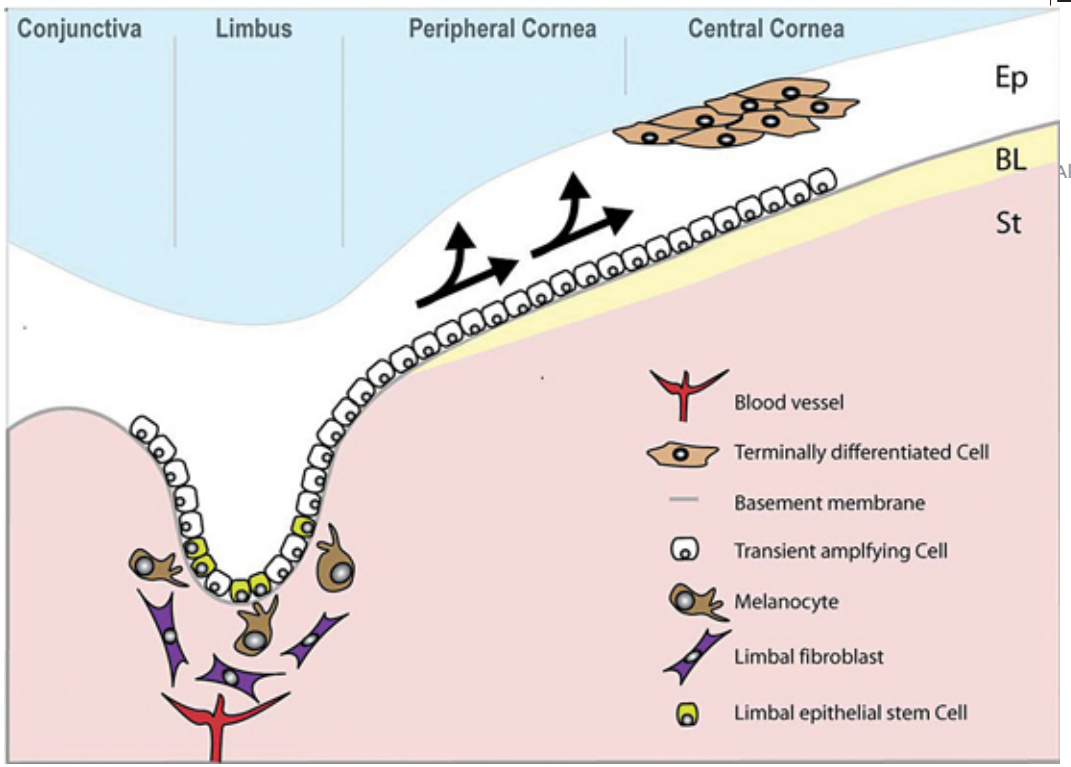
Victor W. Wong,[1,2] Benjamin Levi,[3] Jayakumar Rajadas,[4] Michael T. Longaker,[2] and Geoffrey C. Gurtner[2]



: Locally derived skin stem cells may harbor the potential to regenerate skin. Stem cells populations have been identified in various niches throughout the skin, including the epidermal stem cell in the hair follicle bulge, sebaceous glands, and interfollicular epidermis. Dermal stem cells may exist in the dermal papilla or dermal extracellular matrix. Adipose-derived stem cells appear to be intimately associated with the perivascular space.

Hindawi Publishing Corporation
International Journal of Biomaterials
Volume 2012, Article ID 926059, 8 pages
doi:10.1155/2012/926059

Cornea



Long-term restoration of damaged corneal surfaces with autologous cultivated corneal epithelium

G.Pellegrini, M. De Luca

THE LANCET

1997

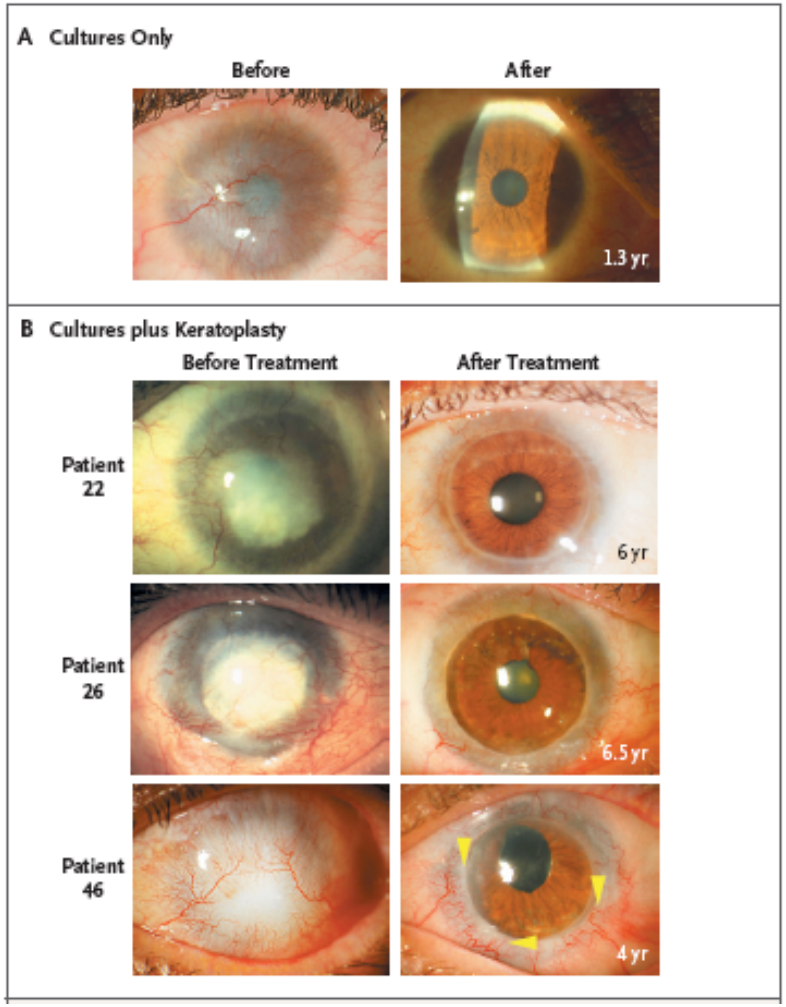
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

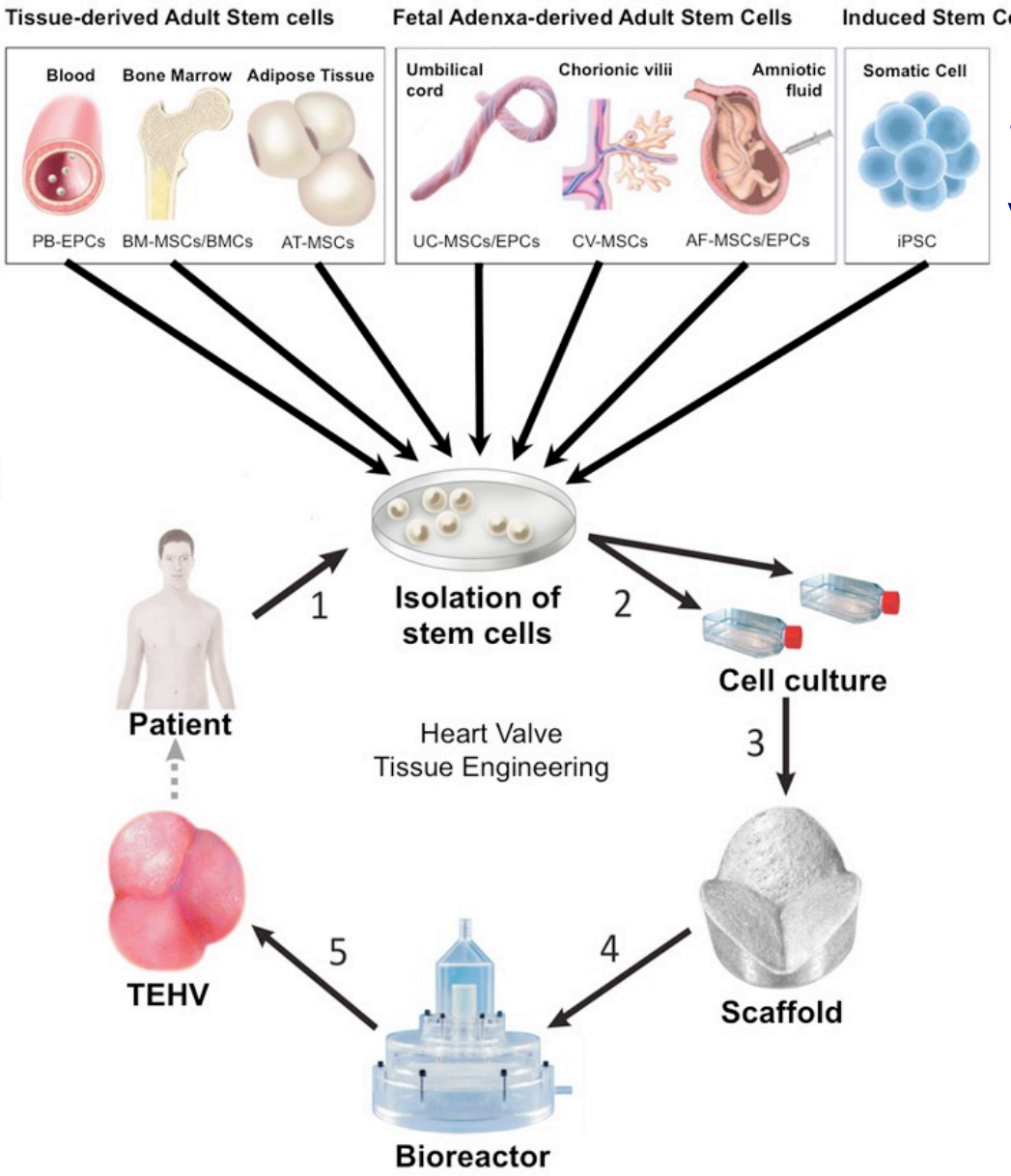
Limbal Stem-Cell Therapy and Long-Term Corneal Regeneration

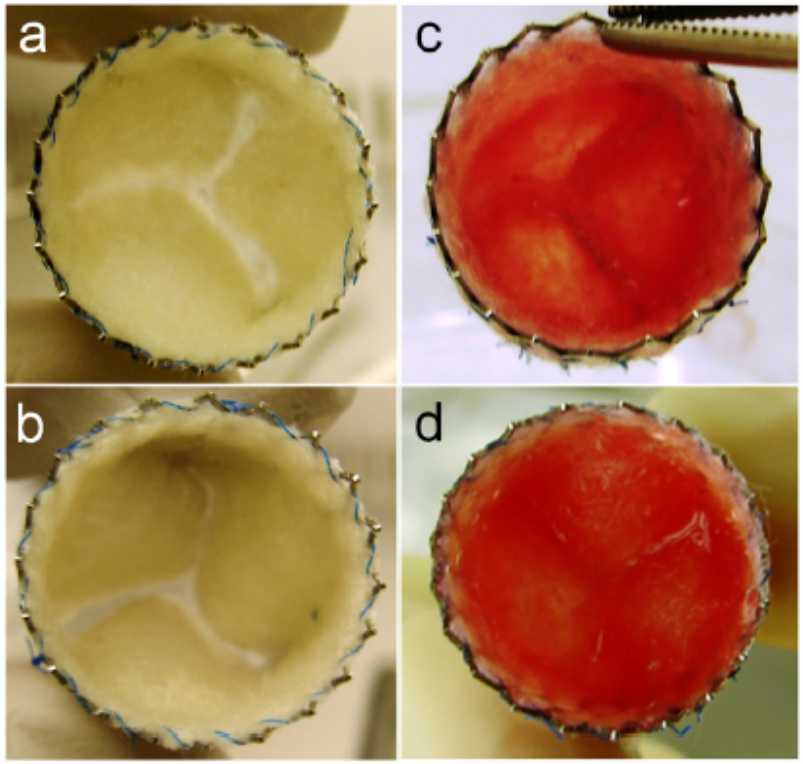
Paolo Rama, M.D., Stanislav Matuska, M.D., Giorgio Paganoni, M.D., Alessandra Spinelli, M.D., Michele De Luca, M.D., and Graziella Pellegrini, Ph.D.

2010



Stem cells for heart valve regeneration





Weber B et al. Swiss Med Wkly.Eur Heart J. 2012

Autologous Umbilical Cord Blood–Derived Mononuclear Cell Therapy Promotes Cardiac Proliferation and Adaptation in a Porcine Model of Right Ventricle Pressure Overload

Cell Transplantation 2022

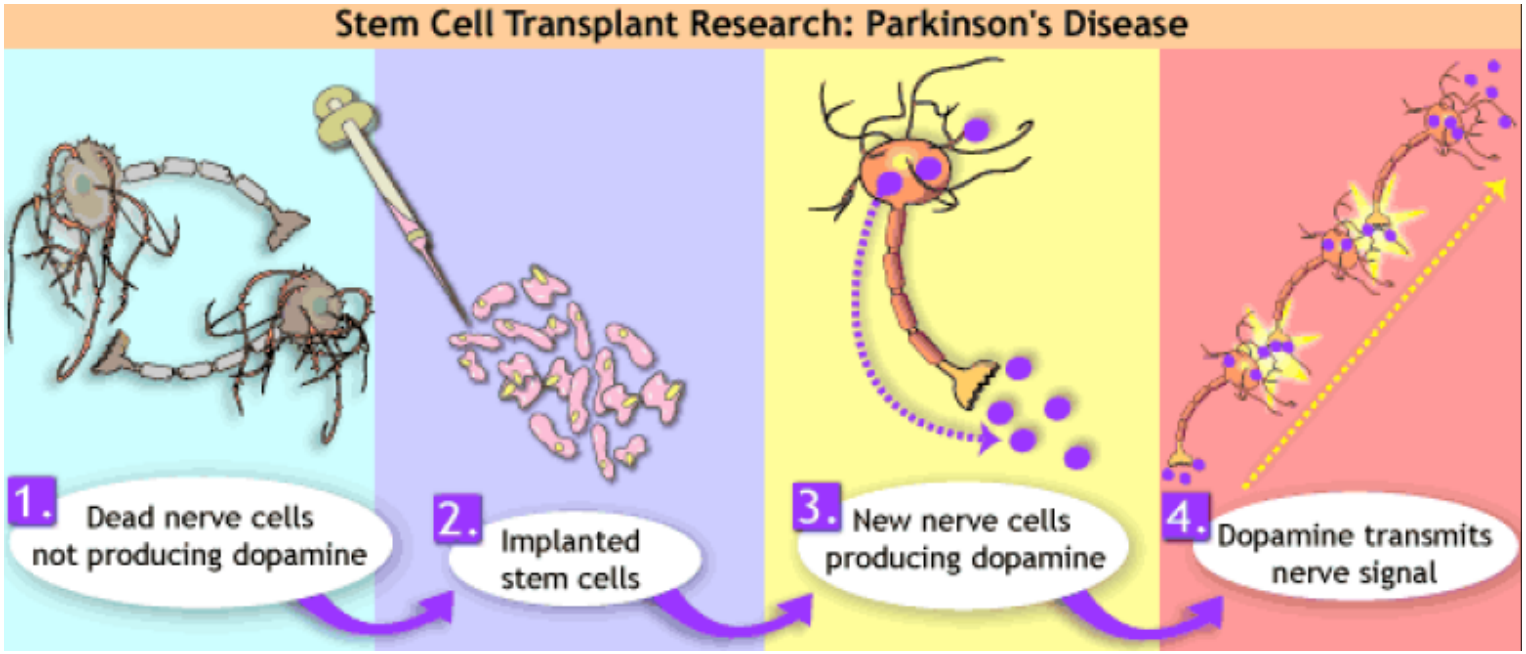
Saji Oommen[1*], Susana Cantero Peral[1*], Muhammad Y. Qureshi[2]
Kimberly A. Holst[3], Harold M. Burkhart[4], Matthew A. Hathcock[5],
Walter K. Kremers[5], Emma B. Brandt[1], Brandon T. Larsen[6],
Joseph A. Dearani[3], Brooks S. Edwards[7], Joseph J. Maleszewski[8],
Timothy J. Nelson[1], and Wanek Program Pre-Clinical Pipeline[†]

UCB-Derived MNCs Promote a Dose-Dependent Increase of Proliferating Cardiomyocytes

Myocardial Remodeling is Associated with Enhanced Cardiomyocyte Proliferation, Angiogenesis, and Regulation of Cardiac Specific Gene expression

This randomized, double-blinded, placebo-controlled pre-clinical trial establishes the safety of **UCB-MNCs** delivered via **intramyocardial injections** in a dysfunctional right ventricle and validates the induction of **cardiac proliferation and angiogenesis as transient paracrine mechanisms** that may be important to optimize long-term outcomes for surgically repaired congenital heart diseases.

Patologie degenerative del SNC



Probabilmente la malattia candidata al trapianto di staminali è il Parkinson.Diverse staminali sono state proposte, a partire dalle **mesenchimali o dalle cordonali**, ma le evidenze disponibili in ambito preclinico a questo proposito sono ancora troppo limitate e il meccanismo non completamente chiaro

Expert Review of Neurotherapeutics

2011

Cell-based therapies for Parkinson's disease

Dyson SC, Barker RA

PROGRESS IN BRAIN RESEARCH

2010

Neural grafting in Parkinson's disease Problems and possibilities

Brundin P, Barker RA, Parmar M

-Neural transplantation has emerged as a possible therapy for Parkinson's disease (PD).

-Future possibilities offered by stem cells as potential sources of dopamine neurons that can be used for transplantation in PD.

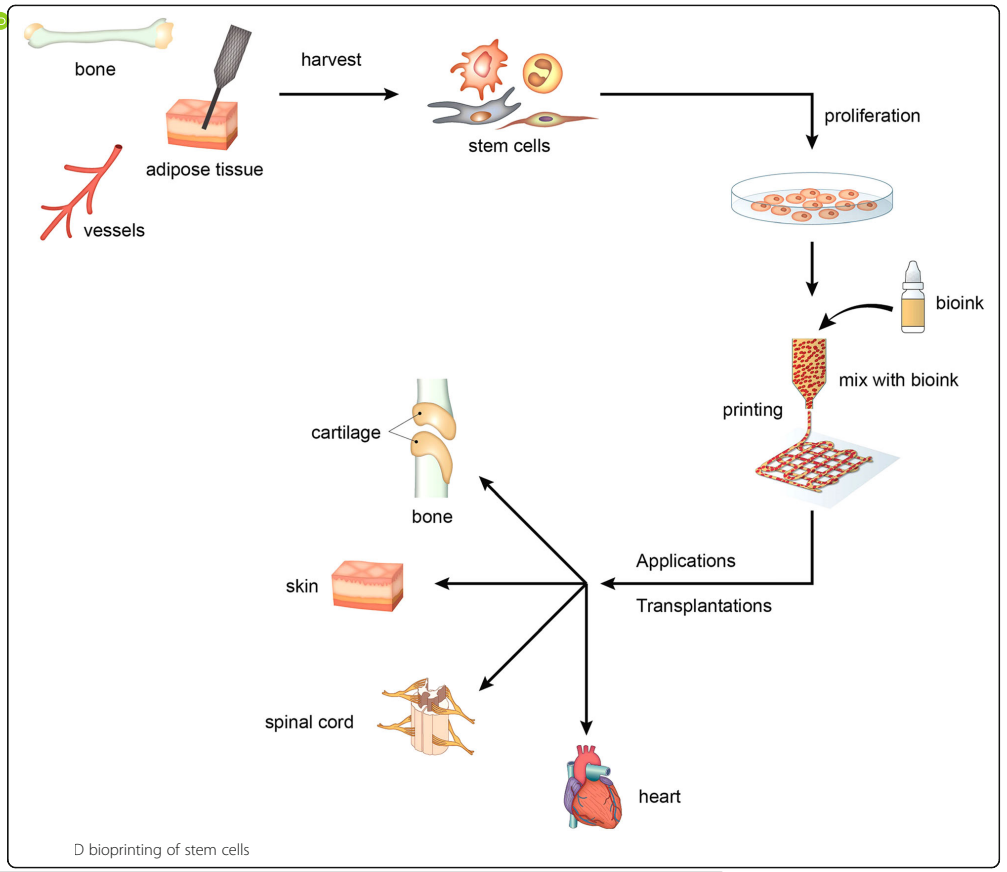
REVIEW Open Access

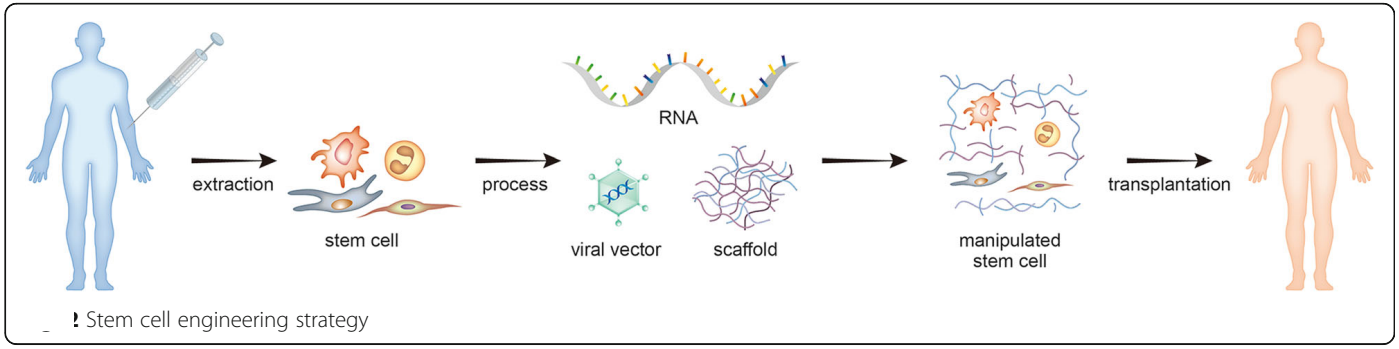
Recent advances in stem cell therapeutics and tissue engineering strategies

Biomaterials Research (2018) 22:36

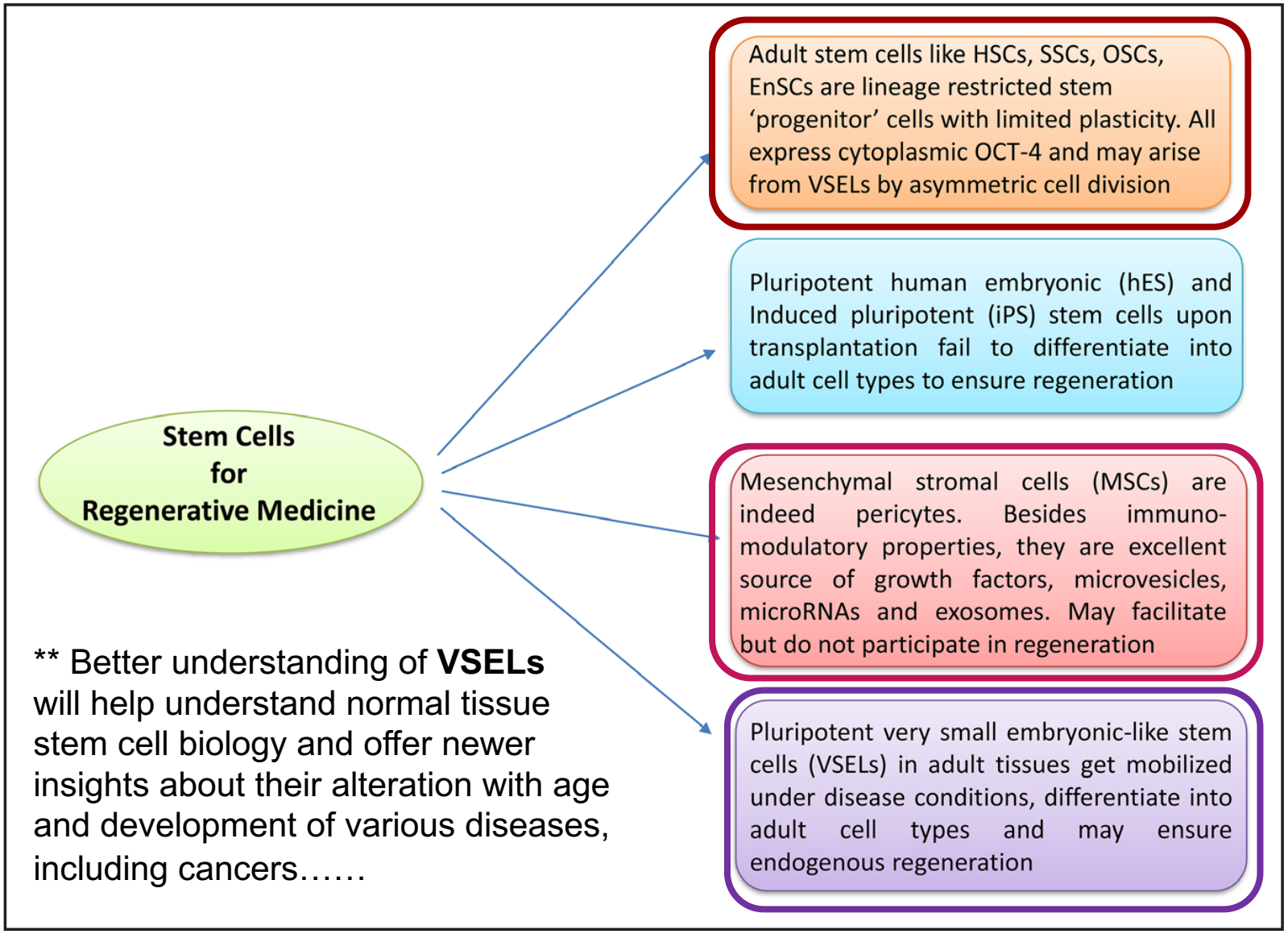
Seong Gyu Kwon[1], Yang Woo Kwon[1], Tae Wook Lee[1], Gyu Tae Park[1] and Jae Ho Kim[1,2*]

The combination of **SCs** and **Tissue engineering techniques** overcomes the limitations of stem cells in therapy of human diseases, and presents a new path toward regeneration of injured tissues





Potenzialità delle SCs oggi e domani



** Better understanding of **VSELs** will help understand normal tissue stem cell biology and offer newer insights about their alteration with age and development of various diseases, including cancers……

Clinical Translation of Stem Cells for Regenerative Medicine
A Comprehensive Analysis

Deepa Bhartiya

(*Circ Res*. 2019;124:840-842.

Take home messages

- Le terapie cellulari e la medicina rigenerativa, sempre più basate sui progressi della biologia delle cellule staminali, **hanno iniziato da molti anni a porre le basi della Medicina Rigenerativa**

- Le sfide, ancora aperte al fine di ottimizzare le potenzialità delle cellule staminali, sono tuttavia molteplici e **richiedono un approccio multidisciplinare integrato……**

- L'utilità clinica delle staminali potrà essere certa solo se in grado di fornire al paziente strategie sicure a lungo termine e **sostanzialmente più efficaci di qualsiasi altro trattamento disponibile……**