Reprogrammation cellulaire et transfusion

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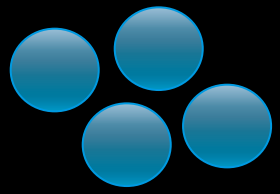
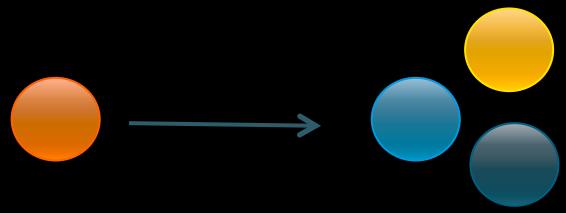
- Cellules différenciées

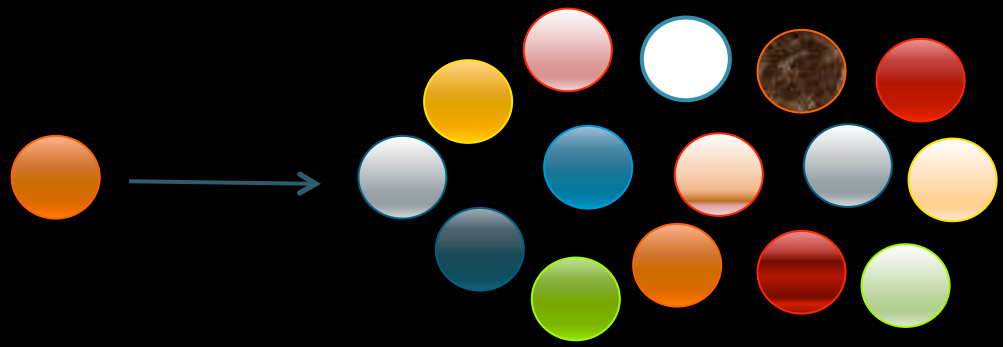


- CS Unipotentes

- CS Multipotentes



- CS Pluripotentes



CELLULES SOUCHES MULTIPOTENTES

- Cellules souches
  - hématopoïétiques
  - neurales
  - mésenchymateuses
  - etc.

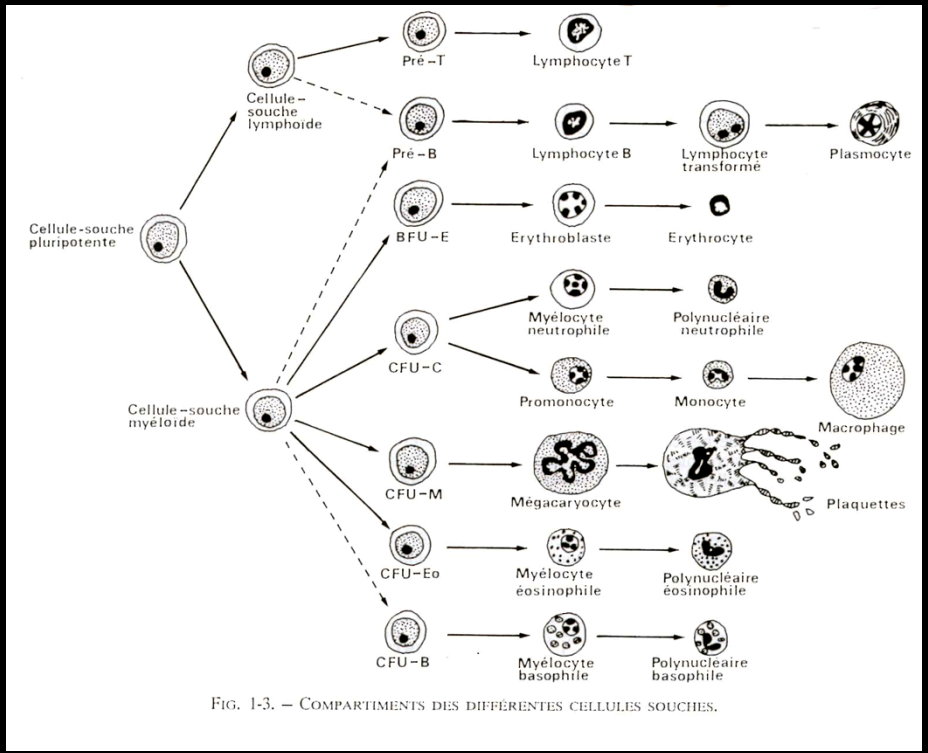
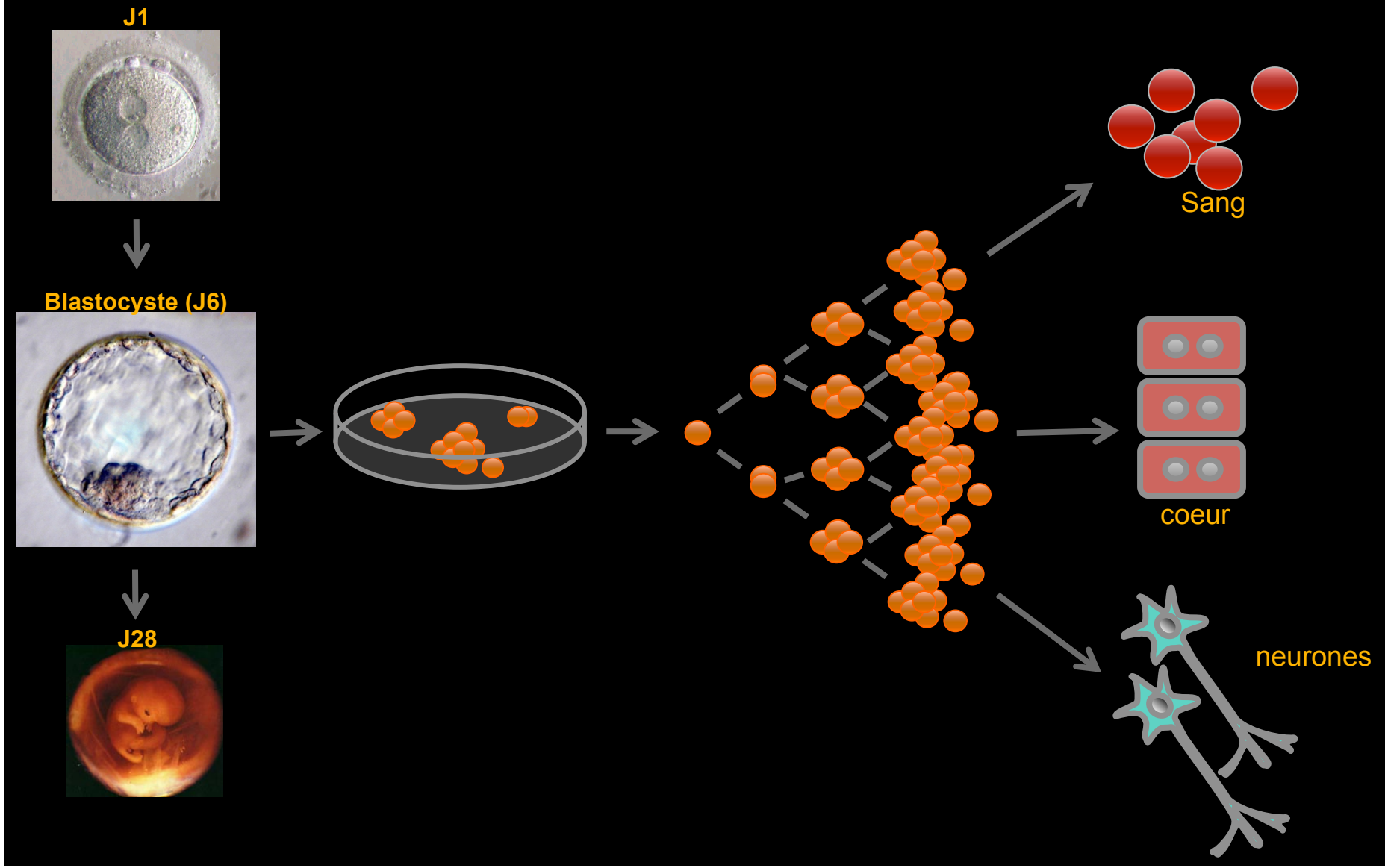
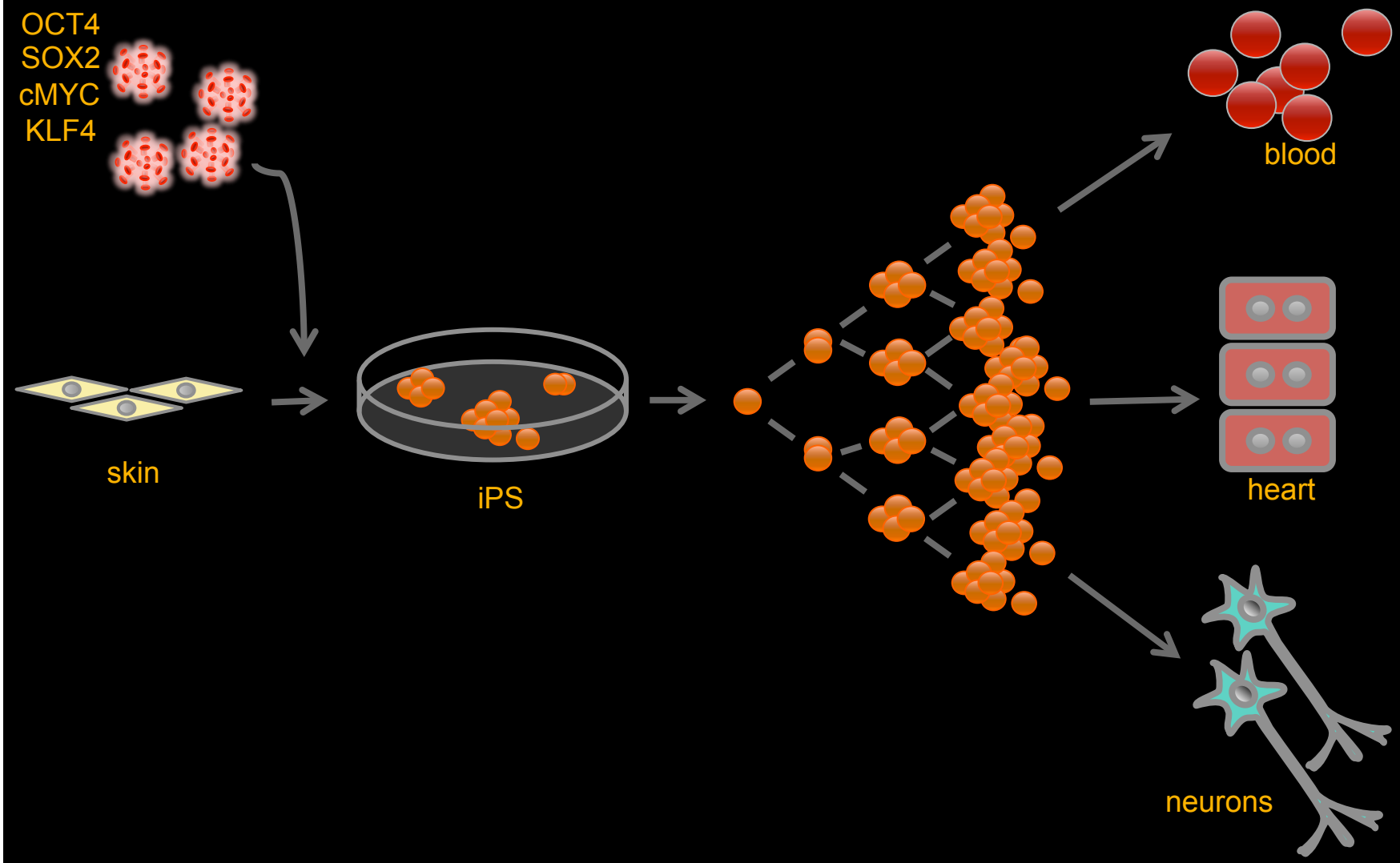


FIG. 1-3. – COMPARTIMENTS DES DIFFÉRENTES CELLULES SOUCHES.

Cellules souches embryonnaires

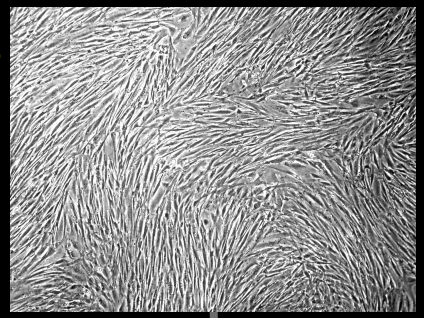


Induced pluripotent stem cells (iPS)

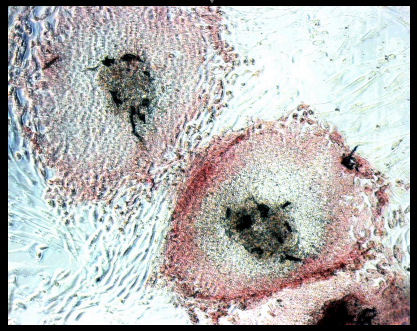


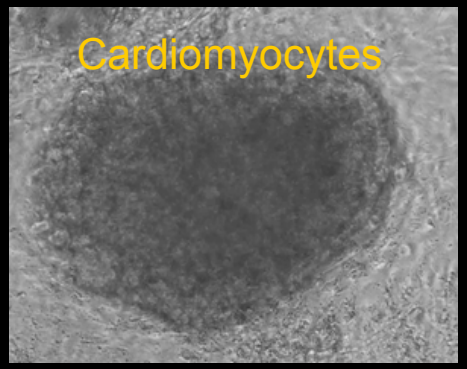
Résulats reproductibles

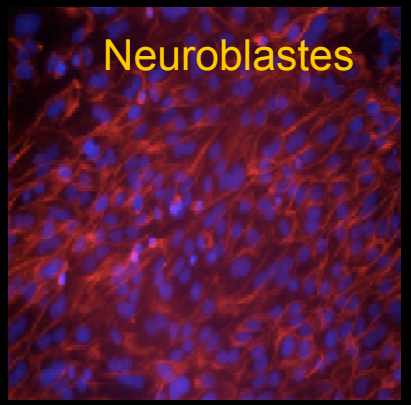
Fibroblastes cutanés

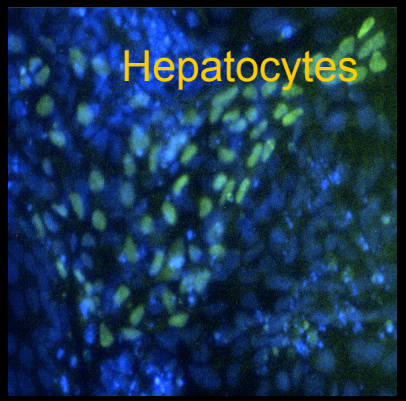


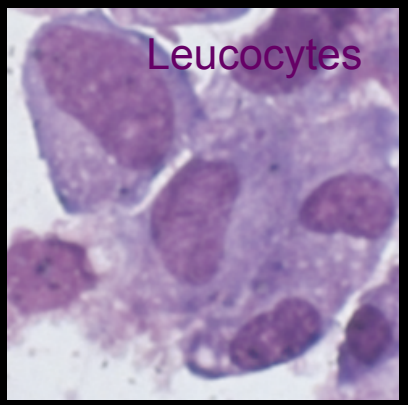
iPS











PEAU → COEUR

J Wright – The alchimist, In Search of the Philosophers' Stone

Substituts de sang

REVIEW

Hemoglobin-based blood substitutes: oxygen carriers, pressor agents, or oxidants?

Abdu I. Alayash

Laboratory of Plasma Derivatives, Center for Biologics Evaluation and Research, Food and Drug Administration, NIH campus, Building 29, Room 112, 8800 Rockville Pike, Bethesda MD 20892 (Alayash@cber.fda.gov).

Nat Biotech 1999, 17:545

Brief Report

TRANSFUSIONS OF POLYMERIZED BOVINE HEMOGLOBIN IN A PATIENT WITH SEVERE AUTOIMMUNE HEMOLYTIC ANEMIA

JOHN MULLON, M.D., GEORGE GIACOPPE, M.D., CYNTHIA CLAGETT, M.D., DAVID MCCUNE, M.D., AND THOMAS DILLARD, M.D.

NEJM, 2000, 342:1638

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Nat Biotech 1999, 17:545

Brief Report

Transfusions of Polymerized Bovine Hemoglobin in a Patient with Severe Autoimmune Hemolytic Anemia

John Mullon, M.D., George Giacoppe, M.D., Cynthia Clagett, M.D., David McCune, M.D., and Thomas Dillard, M.D.

NEJM, 2000, 342:1638

Setbacks for blood substitute companies

Alliance Pharmaceuticals (La Jolla, CA) announced on August 28 that it is pulling out of PFC Therapeutics, its joint venture with Baxter Healthcare (Deerfield, IL) to develop Oxygent, an artificial oxygen carrier. Alliance, which is rapidly running out of money, has fired 55 of its 135 employees and said it will look for a new partner to finance phase 3 clinical trials of Oxygent in Europe, after a funding dispute with Baxter. Alliance is just one of several companies trying to develop oxygen-carrying blood substitutes that have run into difficulties. Many analysts say that troubled financing, poor decision making in clinical trials, and a general reluctance by physicians to use a product unless it's as safe and as cheap as donated blood means that such products are unlikely to succeed in the commercial market for the next several years.

Oxygent, an emulsion consisting of perfluorochemicals, water, salts, and a surfactant, performed well in a phase 2 clinical

Analysts say oxygen-carrying blood substitutes are unlike to succeed for the next several years—not in the commercial market, at least.

Hemopure for use in orthopedic surgery.

Nat Biotech 2002, 20: 962

Cellule souche hématopoïétique ➔ GR

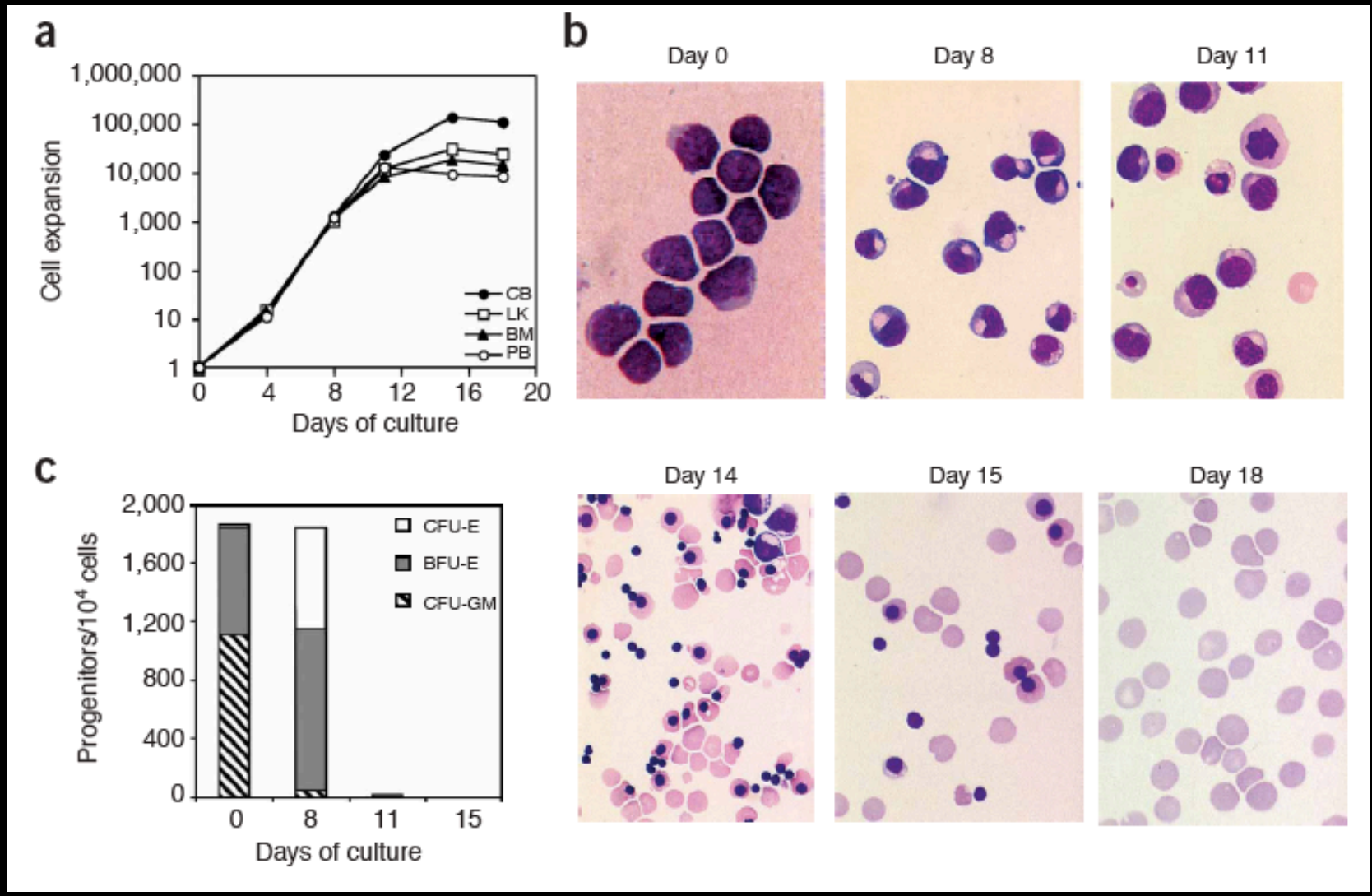
Ex vivo generation of fully mature human red blood cells from hematopoietic stem cells

Marie-Catherine Giarratana[1], Ladan Kobari[1], Hélène Lapillonne[1,2], David Chalmers[1,3], Laurent Kiger[4], Thérèse Cynober[5], Michael C Marden[4], Henri Wajcman[6] & Luc Douay[1,2]

We describe here the large-scale *ex vivo* production of mature human red blood cells (RBCs) from hematopoietic stem cells of diverse origins. By mimicking the marrow microenvironment through the application of cytokines and coculture on stromal cells, we coupled substantial amplification of $CD34^+$ stem cells (up to 1.95×10^6-fold) with 100% terminal differentiation into fully mature, functional RBCs. These cells survived in nonobese diabetic/severe combined immunodeficient mice, as do native RBCs. Our system for producing 'cultured RBCs' lends itself to a fundamental analysis of erythropoiesis and provides a simple *in vitro* model for studying important human viral or parasitic infections that target erythroid cells. Further development of large-scale production of cultured RBCs will have implications for gene therapy, blood transfusion and tropical medicine.

Nature Biotech 2005 vol. 23: 69

Cellule souche hématopoïétique ➔ GR



Nature Biotech 2005 vol. 23: 69

Cellule souche hématopoïétique ➔ GR

Proof of principle for transfusion of in vitro–generated red blood cells

*Marie-Catherine Giarratana,[1,2] *Hélène Rouard,[3,4] Agnès Dumont,[5] Laurent Kiger,[6] Innocent Safeukui,[7] Pierre-Yves Le Pennec,[8] Sabine François,[1,2,9] Germain Trugnan,[10] Thierry Peyrard,[8] Tiffany Marie,[1-3] Séverine Jolly,[1-3] Nicolas Hebert,[1-3] Christelle Mazurier,[1-3] Nathalie Mario,[11] Laurence Harmand,[1-3] Hélène Lapillonne,[1,2,12] Jean-Yves Devaux,[5] and Luc Douay[1-3,13]

[1]UPMC Paris 06, UMR_S938 CDR Saint-Antoine, Prolifération et Différenciation des Cellules Souches, Paris, France; [2]Inserm, UMR_S938, Prolifération et Différenciation des Cellules Souches, Paris, France; [3]EFS Ile de France, Unité d'Ingénierie et de Thérapie Cellulaire, Créteil, France; [4]UPEC, Université Paris Est Créteil, France; [5]AP-HP Hôpital St Antoine, Service de Médecine Nucléaire, Paris, France; [6]Inserm U473, Hôpital du Kremlin-Bicêtre, Kremlin-Bicêtre, France; [7]CNRS URA 2581, Institut Pasteur, Molecular Immunology of Parasites Unit, Paris, France; [8]CNRGS, INTS, Paris, France; [9]IRSN, BP 17, Fontenay-aux-Roses, France; [10]UPMC Université Paris 06; ERL Inserm U1057/UMR7203; FMPMC, Paris, France; [11]AP-HP, Hôpital Saint-Antoine, Service de Biochimie A, Paris, France; [12]AP-HP, Hôpital Trousseau, Service d'Hématologie Biologique, Paris, France; and [13]AP-HP, Hôpital St Antoine, Service d'Hématologie et Immunologie Biologiques, Paris, France

In vitro RBC production from stem cells could represent an alternative to classic transfusion products. Until now the clinical feasibility of this concept has not been demonstrated. We addressed the question of the capacity of cultured RBCs (cRBCs) to survive in humans. By using a culture protocol permitting erythroid differentiation from peripheral $CD34^+$ HSC, we generated a homogeneous population of cRBC functional in terms of their deformability, enzyme content, capacity of their hemoglobin to fix/release oxygen, and expression of blood group antigens. We then demonstrated in the nonobese diabetes/severe combined immunodeficiency mouse that cRBC encountered in vivo the conditions necessary for their complete maturation. These data provided the rationale for injecting into one human a homogeneous sample of 10^{10} cRBCs generated under good manufacturing practice conditions and labeled with ^{51}Cr. The level of these cells in the circulation 26 days after injection was between 41% and 63%, which compares favorably with the reported half-life of 28 ± 2 days for native RBCs. Their survival in vivo testifies globally to their quality and functionality. These data establish the proof of principle for transfusion of in vitro–generated RBCs and path the way toward new developments in transfusion medicine. This study is registered at http://www.clinicaltrials.gov as NCT0929266. (*Blood*. 2011;118(19):5071-5079)

Blood 2011 Nov 10;118(19):5071

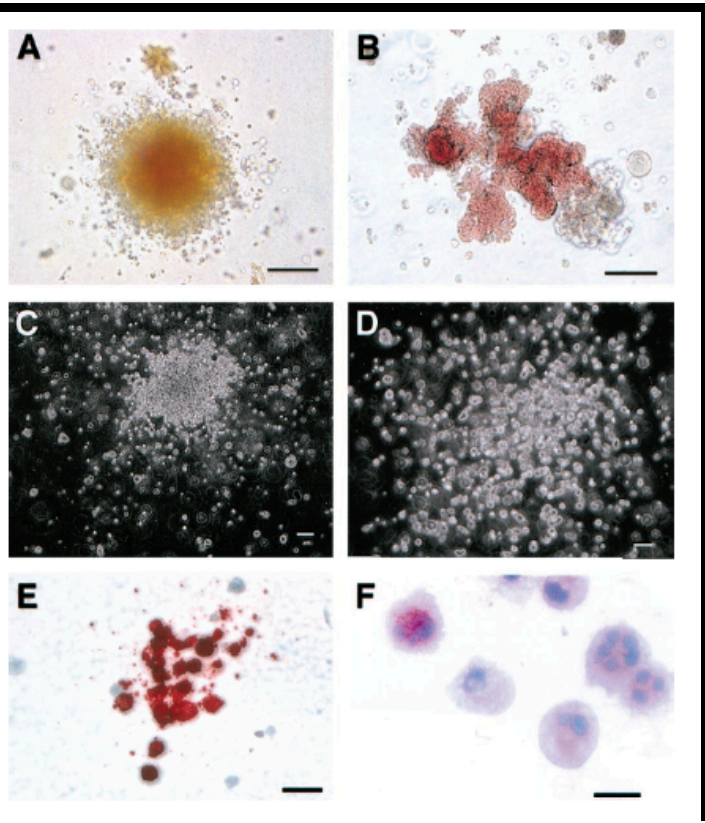
Cellules souches pluripotentes ➔ GR

Hematopoietic colony-forming cells derived from human embryonic stem cells

Dan S. Kaufman*, Eric T. Hanson†, Rachel L. Lewis†, Robert Auerbach‡, and James A. Thomson†§¶

*Section of Hematology, Department of Internal Medicine, University of Wisconsin Hospital and Clinics, 600 Highland Avenue, Madison, WI 53792; †Wisconsin Regional Primate Research Center, University of Wisconsin, 1220 Capitol Court, Madison, WI 53715; ‡Laboratory of Developmental Biology, University of Wisconsin, 1117 West Johnson Street, Madison, WI 53706; and §Department of Anatomy, School of Medicine, University of Wisconsin, 1300 University Avenue, Madison, WI 53706

PNAS 2001 vol. 98: 10716



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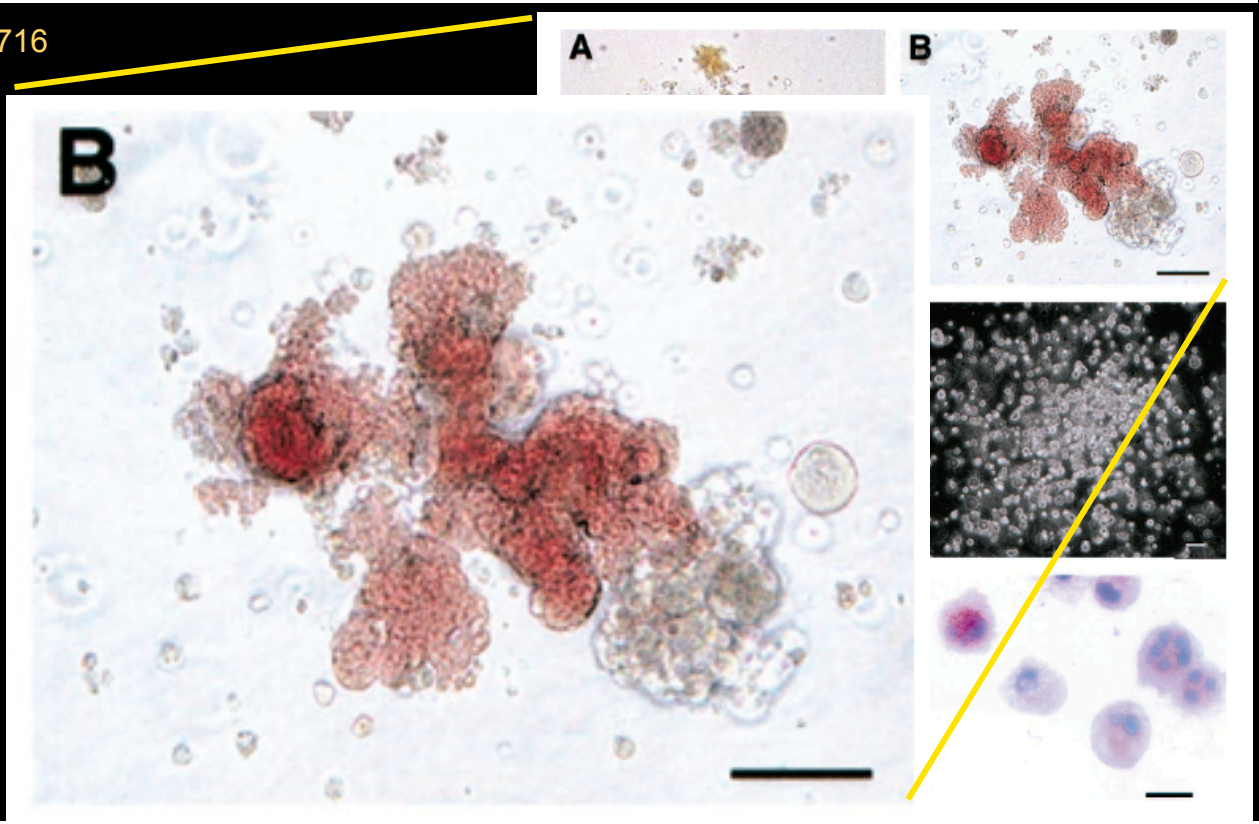

Cellules souches pluripotentes ➔ GR

Biologic properties and enucleation of red blood cells from human embryonic stem cells

*Shi-Jiang Lu,[1] *Qiang Feng,[1] *Jennifer S. Park,[1] Loyda Vida,[2] Bao-Shiang Lee,[3] Michael Strausbauch,[4] Peter J. Wettstein,[4] George R. Honig,[2] and Robert Lanza[1]

[1]Advanced Cell Technology, Worcester, MA; [2]Department of Pediatrics, University of Illinois at Chicago; [3]Protein Research Laboratory, Research Resources Center, University of Illinois at Chicago; and [4]Departments of Surgery and Immunology, Mayo Clinic, Rochester, MN

Human erythropoiesis is a complex multistep process that involves the differentiation of early erythroid progenitors to mature erythrocytes. Here we show that it is feasible to differentiate and mature human embryonic stem cells (hESCs) into functional oxygen-carrying erythrocytes on a large scale (10^{10}-10^{11} cells/6-well plate hESCs). We also show for the first time that the oxygen equilibrium curves of the hESC-derived cells are comparable with normal red blood cells and respond to changes in pH and 2,3-diphosphoglyerate. Although these cells mainly expressed fetal and embryonic globins, they also possessed the capacity to express the adult β-globin chain on further maturation in vitro. Polymerase chain reaction and globin chain specific immunofluorescent analysis showed that the cells increased expression of β-globin (from 0% to > 16%) after in vitro culture. Importantly, the cells underwent multiple maturation events, including a progressive decrease in size, increase in glycophorin A expression, and chromatin and nuclear condensation. This process resulted in extrusion of the pycnotic nuclei in up to more than 60% of the cells generating red blood cells with a diameter of approximately 6 to 8 μm. The results show that it is feasible to differentiate and mature hESCs into functional oxygen-carrying erythrocytes on a large scale. (Blood. 2008;112:4475-4484)

Blood 2008 vol. 112: 4475

Cellules souches pluripotentes ➔ GR

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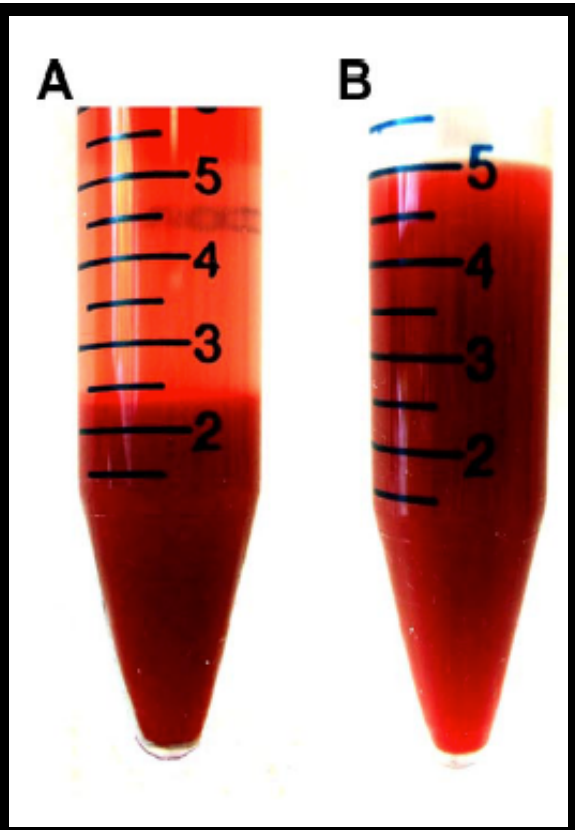
Blood 2008 vol. 112: 4475



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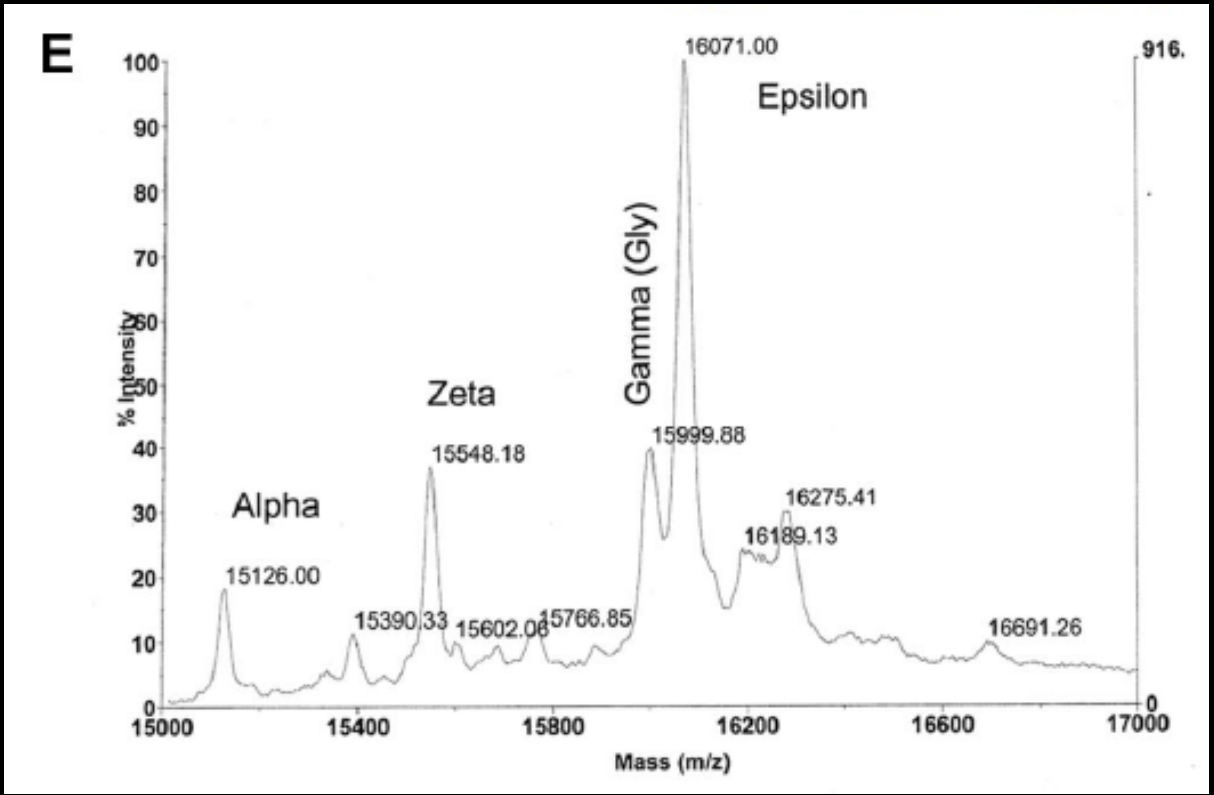


Cellules souches pluripotentes ➔ GR

Original Articles

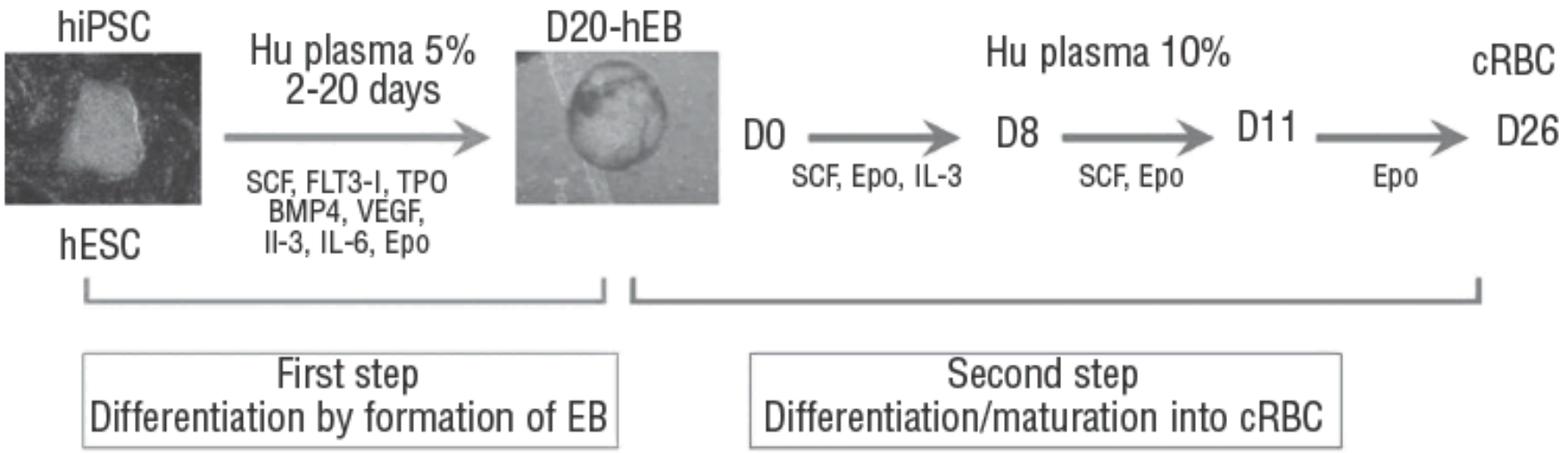
Red blood cell generation from human induced pluripotent stem cells: perspectives for transfusion medicine

Hélène Lapillonne,[1,2,3*] Ladan Kobari,[1,2] Christelle Mazurier,[1,4] Philippe Tropel,[5,6] Marie-Catherine Giarratana,[1,2] Isabelle Zanella-Cleon,[7] Laurent Kiger,[8*] Marie Wattenhofer-Donzé,[9] Hélène Puccio,[9] Nicolas Hebert,[1,2] Alain Francina,[10] Georges Andreu,[11] Stéphane Viville,[5] and Luc Douay[1,2,3,4]

[1]INSERM, UMR_S938, Proliferation and Differentiation of Stem Cells, Paris, France; [2]UPMC Univ Paris 06, UMR_S938, Proliferation and Differentiation of Stem Cells, Paris, France; [3]AP-HP, Hôpital Armand Trousseau, Service d'Hématologie biologique, Paris, France; [4]Etablissement Français du Sang Ile de France, Ivry-sur-Seine, France; [5]IGBMC, Department of Cell Biology and Development, Illkirch Cedex, France; [6]INSERM/UEVE UMR-861, I-STEM, AFM, Institute for Stem Cell Therapy and Exploration of Monogenic Diseases, 5 rue Henri Desbruères, 91030 Evry cedex, France; [7]Institut de Biologie et de Biochimie des Protéines, CNRS UMR 5086, IFR 128, Université Claude Bernard-Lyon I, Lyon, France; [8]INSERM U473, Hôpital de Bicêtre, Le Kremlin Bicêtre, France; [9]IGBMC, Department of Neurobiology and Genetics, Illkirch Cedex, France; [10]Unité de Pathologie Moléculaire du Globule Rouge, Fédération de Biochimie et de Biologie Spécialisée, Hôpital Edouard Herriot, Lyon, France, and [11]Institut National de la Transfusion Sanguine (INTS), Paris, France

Haematologica 2010 vol. 95: 1651

Cellules souches pluripotentes ➔ GR



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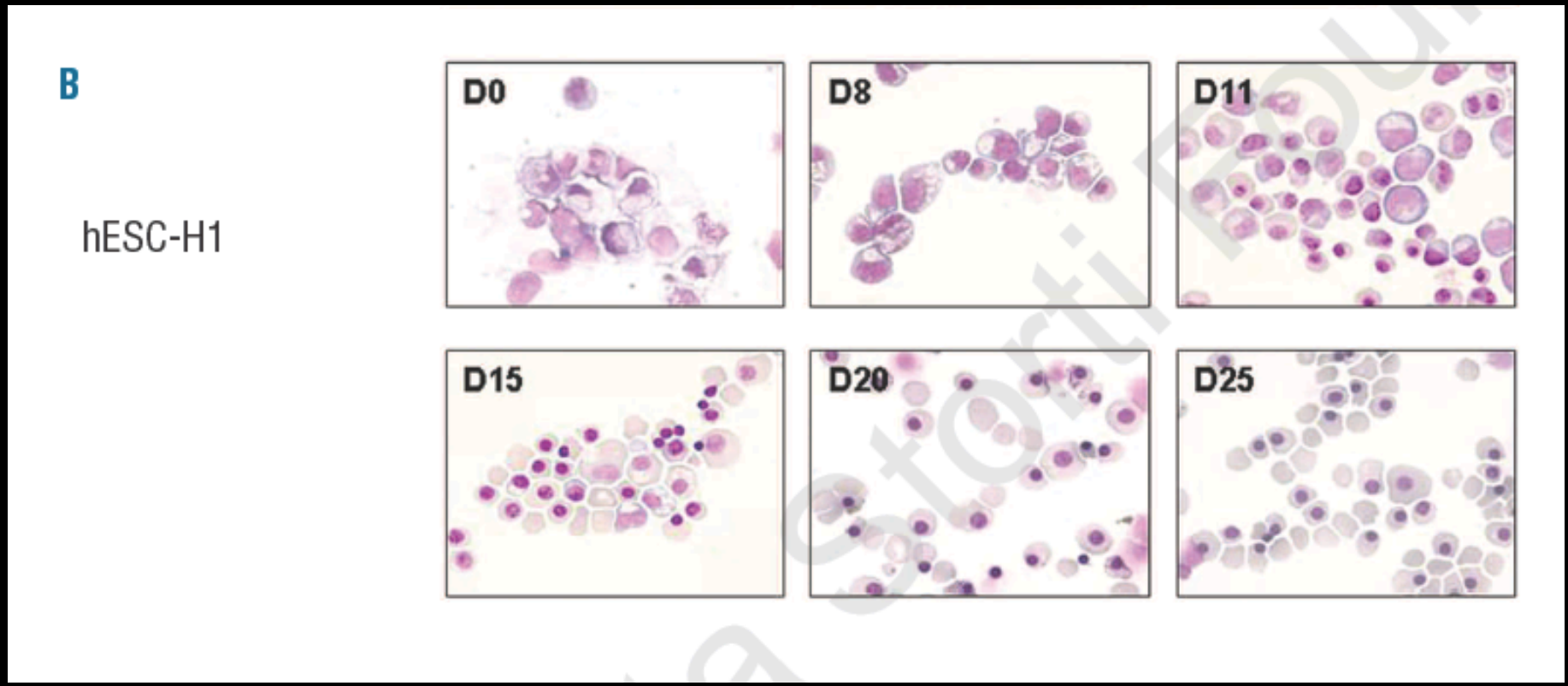

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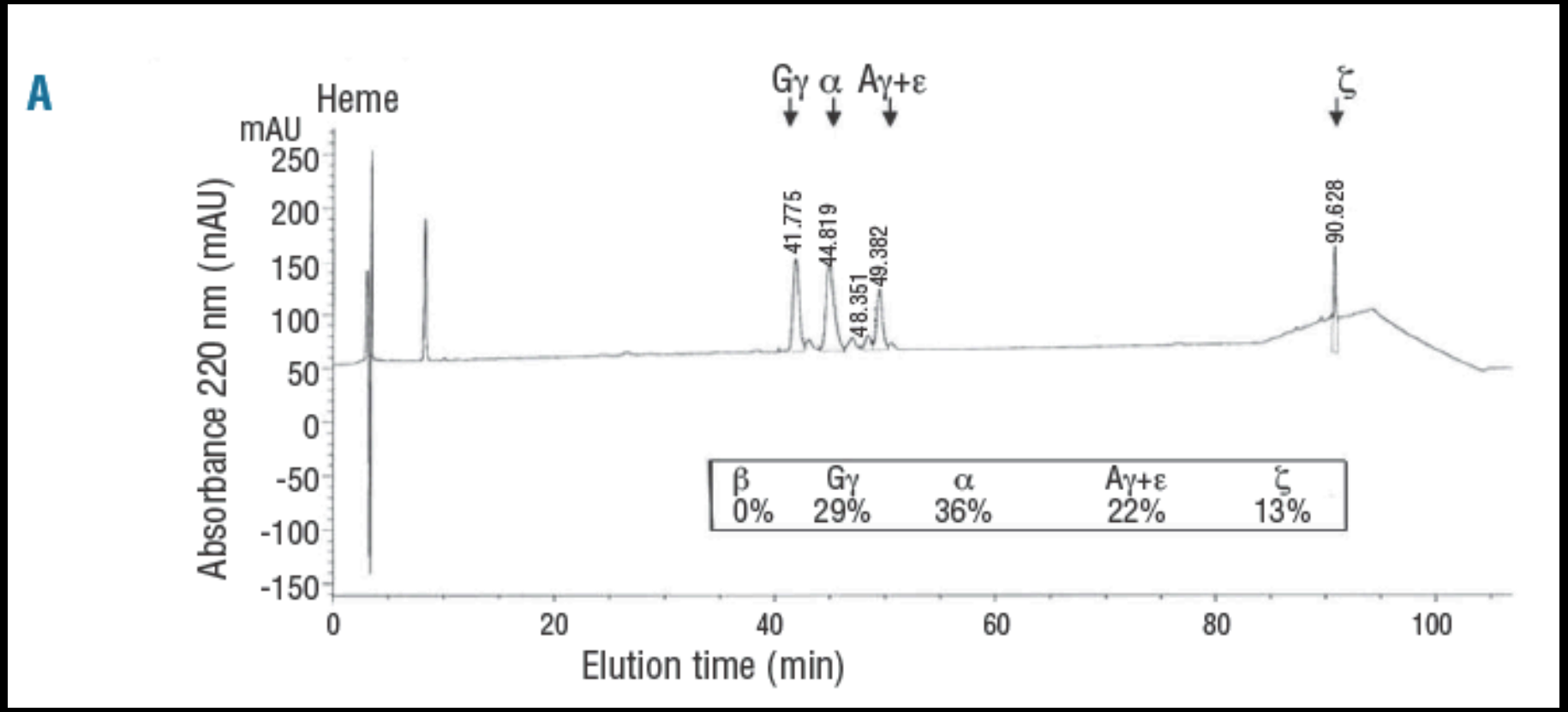

Haematologica 2010 vol. 95: 1651

* Equipe « Instabilité génétique des cellules souches pluripotentes »

- Instabilité génétique
- Pluripotence

Qiang BAI
Jean-Marie RAMIREZ
Fabienne BECKER
John DE VOS

* Plateforme de reprogrammation cellulaire SAFE-iPS

Responsables : J DE VOS et JM LEMAÎTRE

Demande de labellisation Infrastructure nationale Biologie Santé

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