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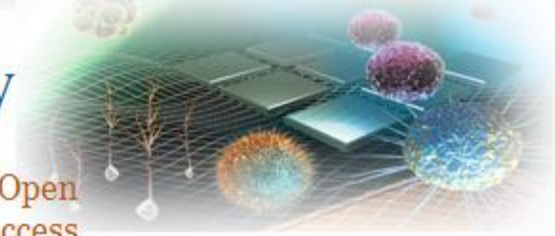
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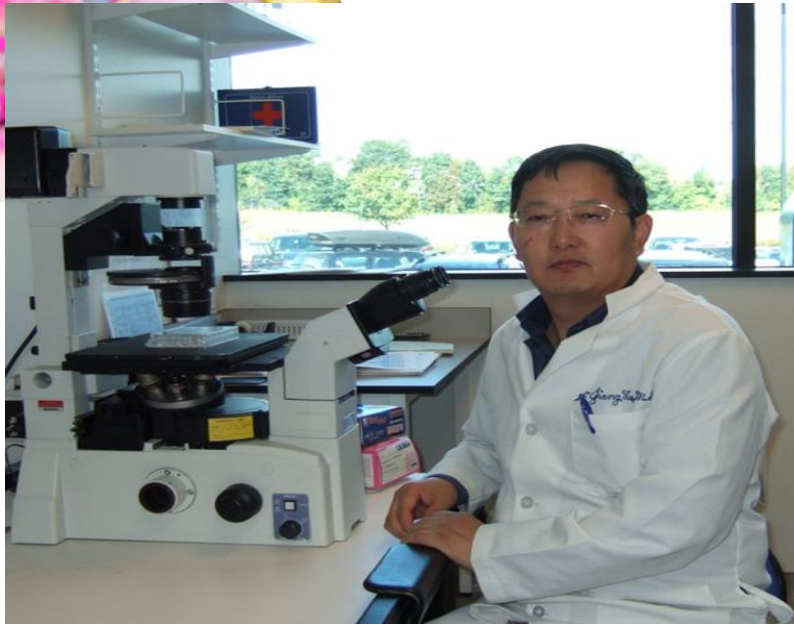
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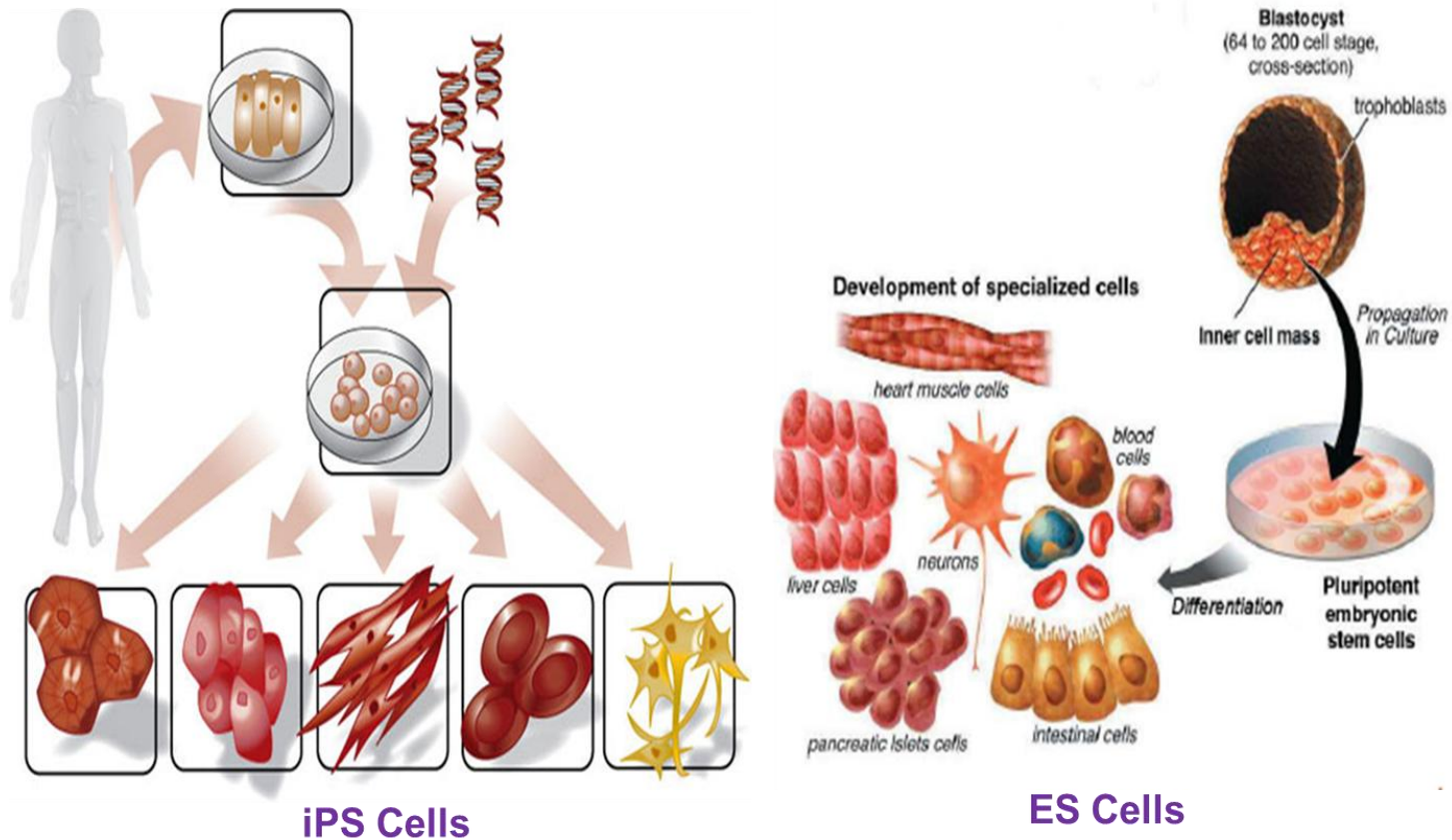


Shi-Jiang (John) Lu, PhD, MPH

Senior Director for Research
Advanced Cell Technology Inc.
33 Locke Drive
Marlborough, MA 01752, USA



Human Pluripotent Stem Cells and Therapy ----From Bench to Clinic



Stem Cell Therapy Products: The Challenges

The Challenges:

TUMORIGENICITY & IMPURITY: Inappropriate differentiation, Not 100% of target cells and/or Undifferentiated stem cells

COMPLEXITY: Inadequate markers predictive of cell state and cell fate;
Poor understanding of how cells interact with their microenvironment

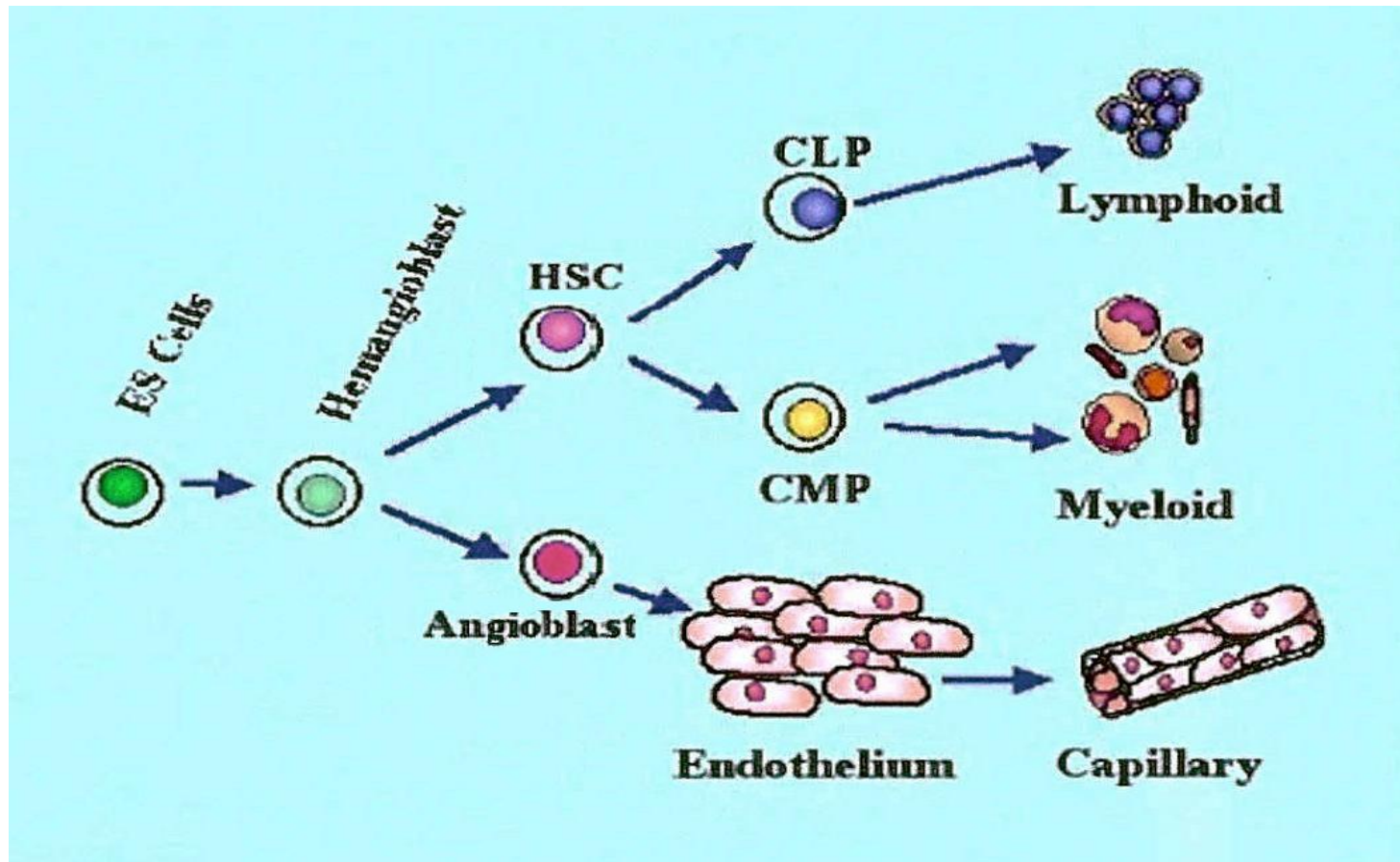
MISDIFFERENTIATION & CELL DEATH: Poor understanding of cell fate and survival post transplantation, Migration and ectopic tissue formation

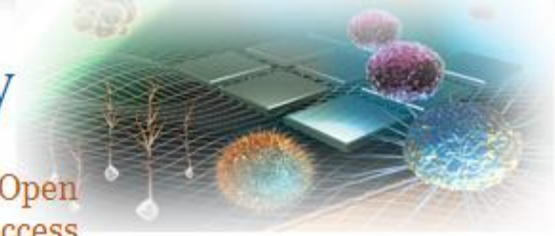
IMMUNOGENICITY: Host rejection

Stem Cell Therapy Products: The Strategy

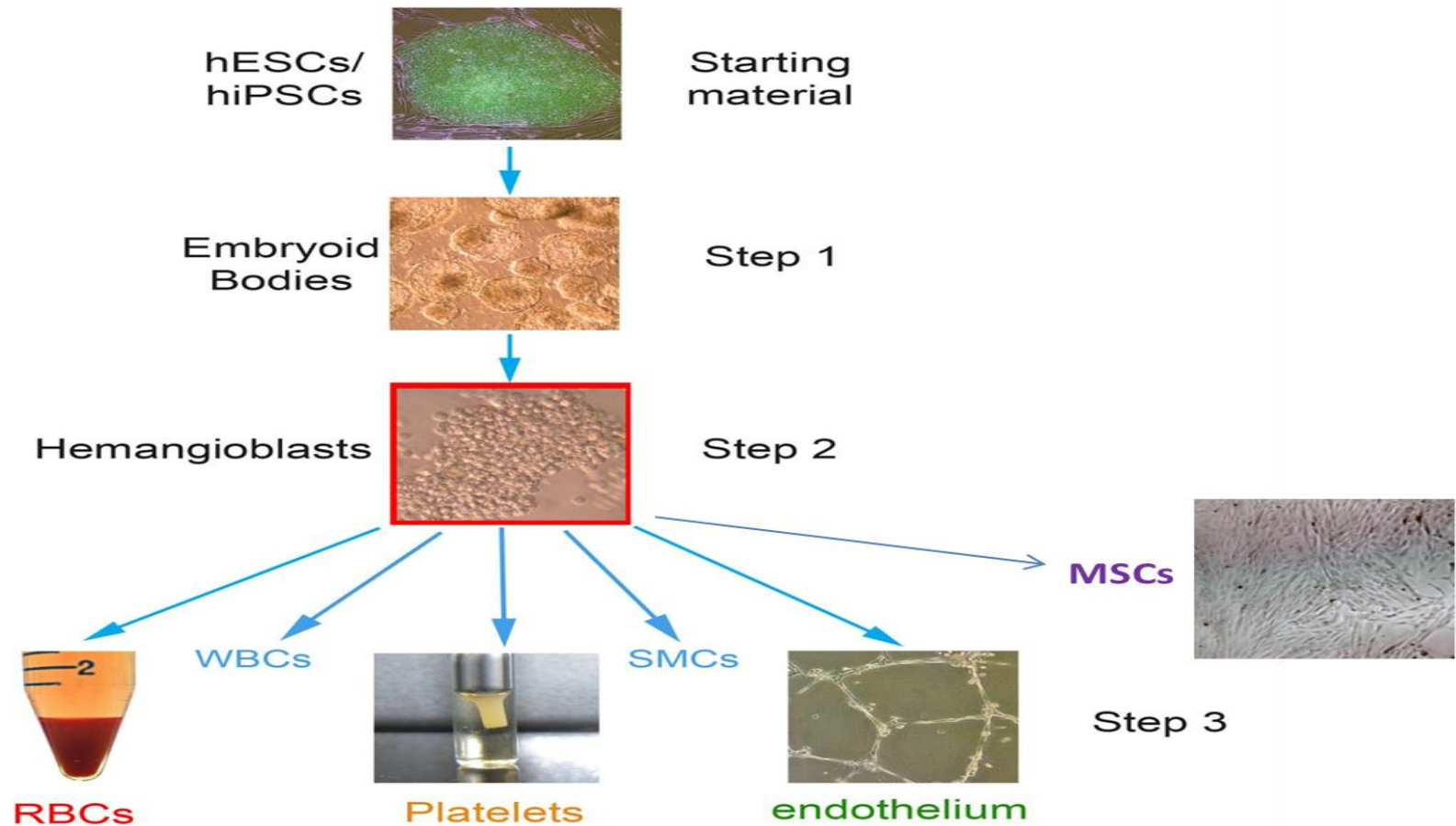
- **Research Goal**
 - Simple, most predictive tests for characterization of cell-based products
 - A disease treatable locally by cells with an obvious endpoint
- **Outcome**
 - Efficient product development
 - Minimize testing costs
 - Safe, effective products to market
 - Minimum immune rejection

Hemangioblast



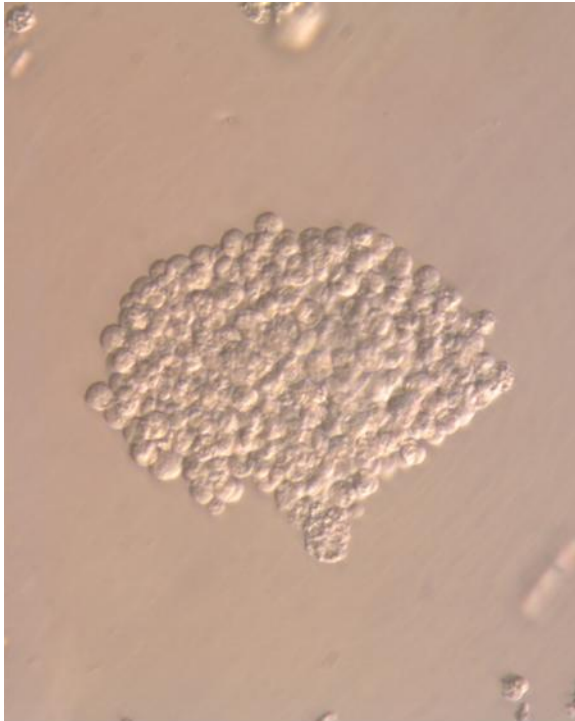


From Human Pluripotent Cells to Clinical Products

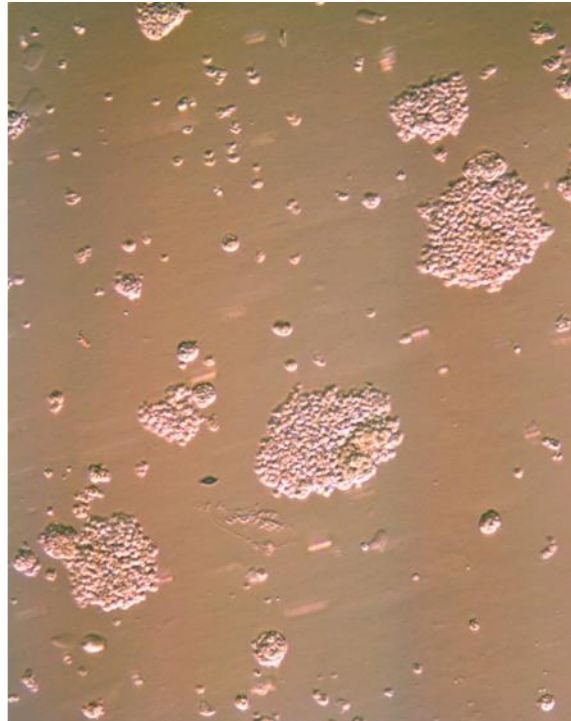




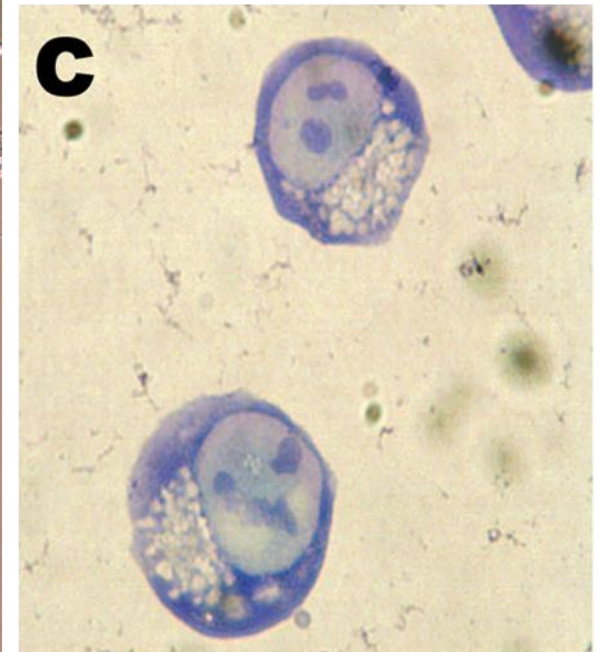
Hemangioblasts Generated from Multiple Human ES and iPS Cell Lines



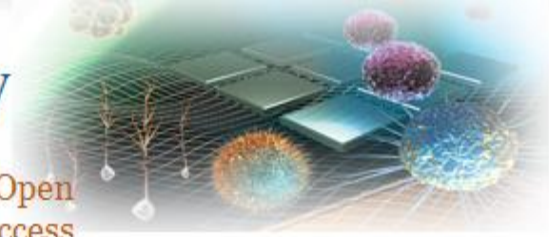
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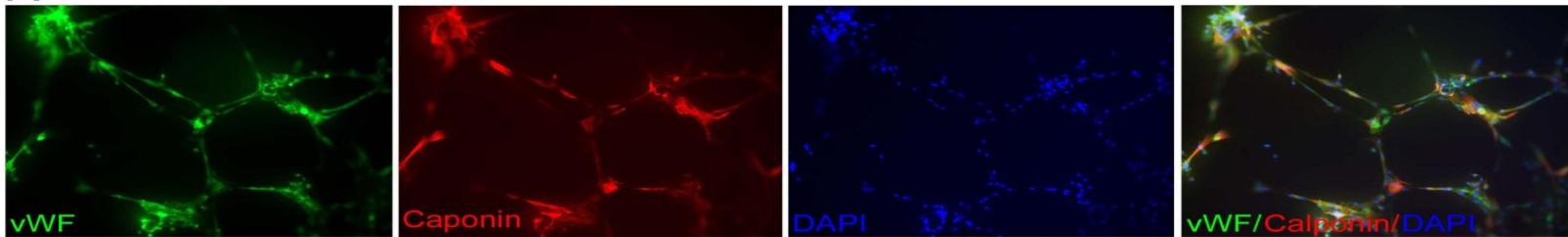


Nature Methods, 4:501-509, 2007

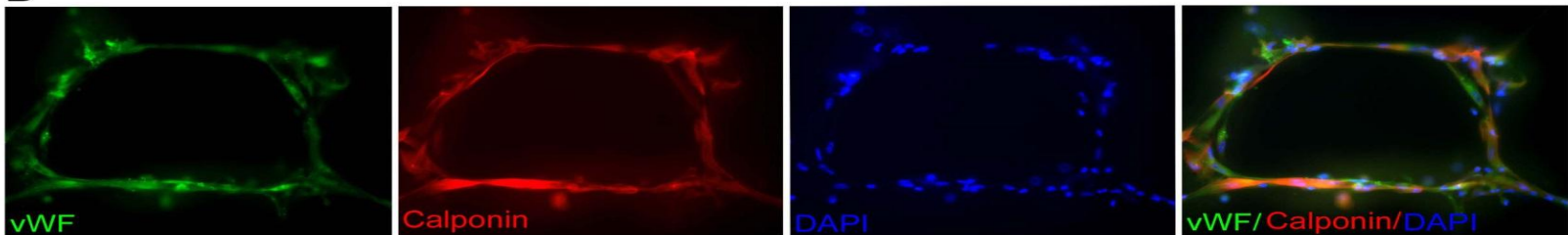


Functional Endothelial & Smooth Muscle Cells From Human PSC-Hemangioblasts

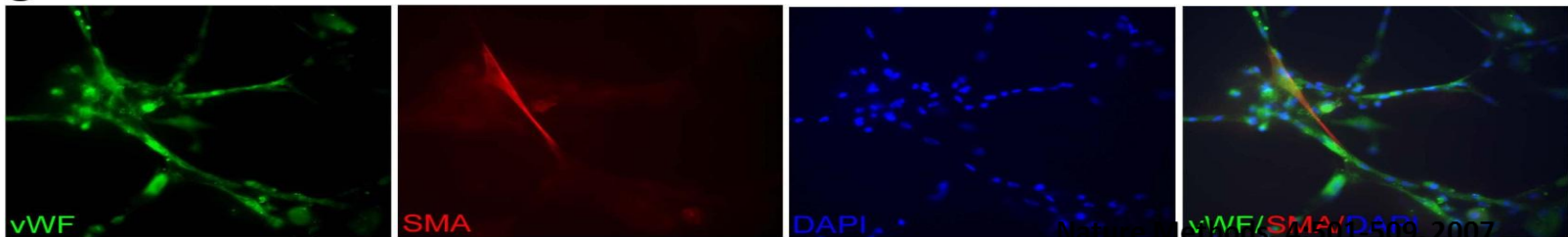
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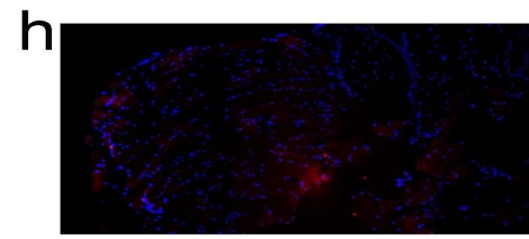
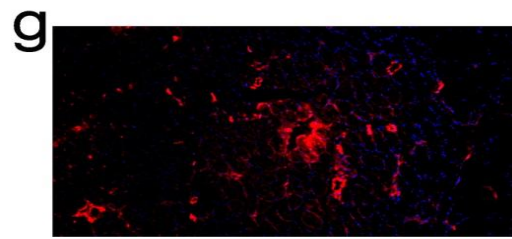
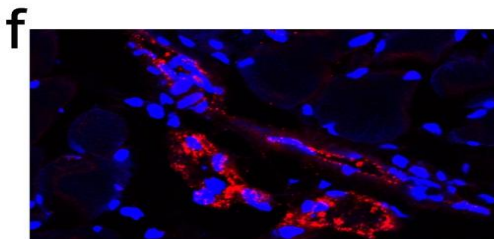
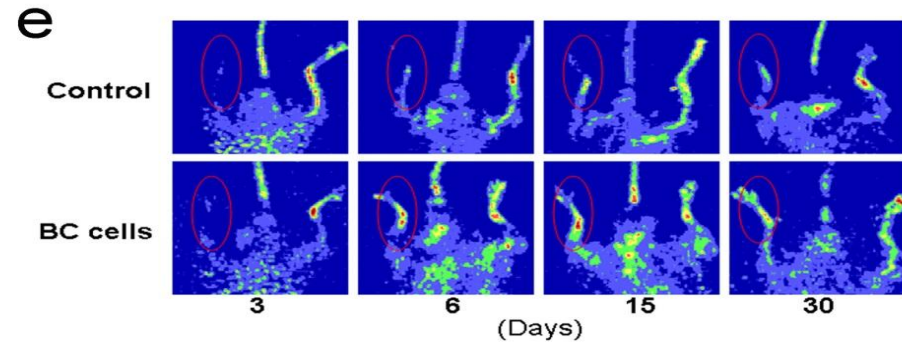
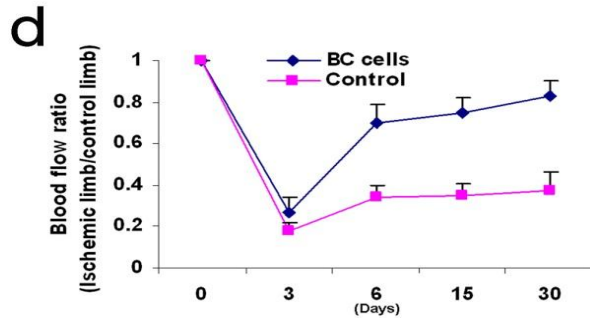
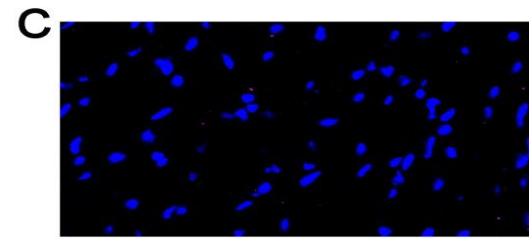
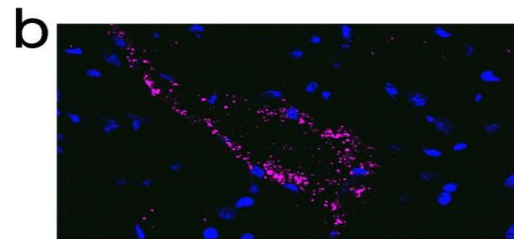
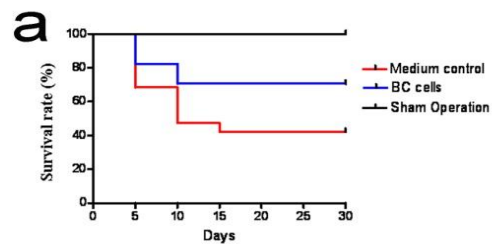
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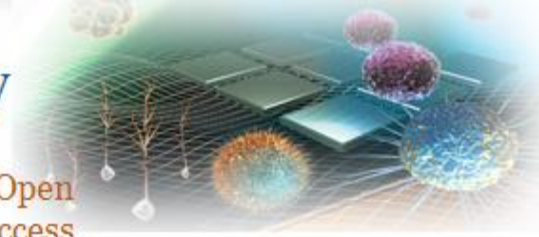


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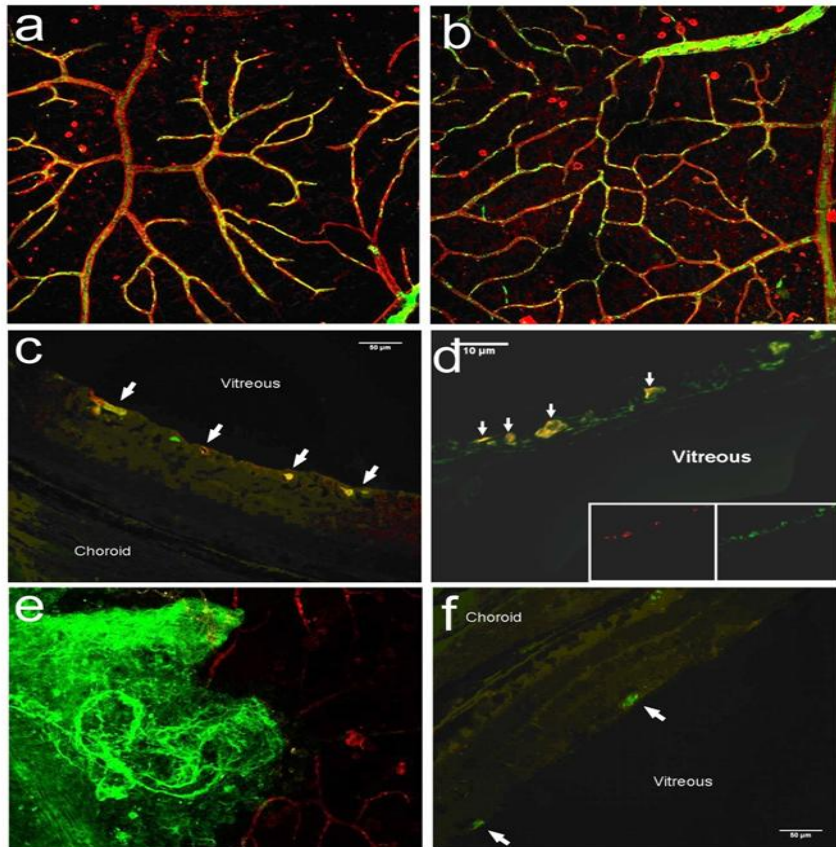
Rescue of Mice from Myocardial Infarction and Restoration of Blood Flow in Ischemic Limbs by Human PSC-Hemangioblasts



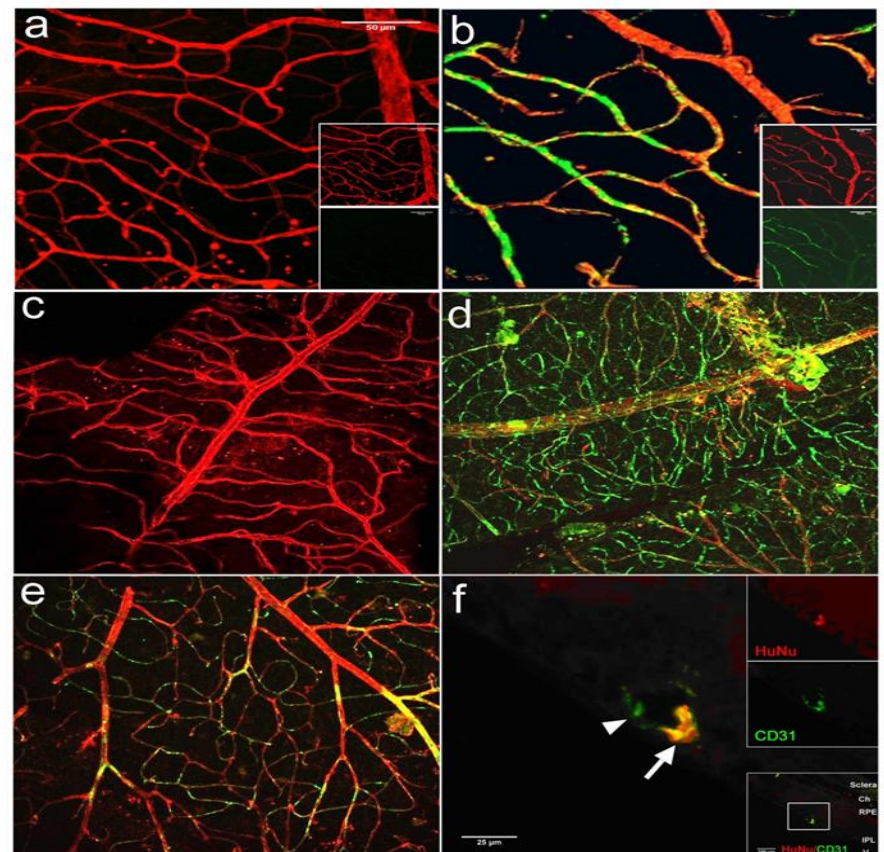


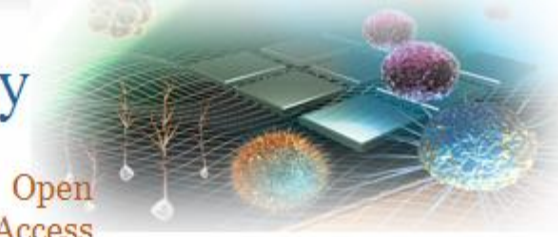
Human PSC-Hemangioblasts

Repair of retinal vasculatures in diabetic rats

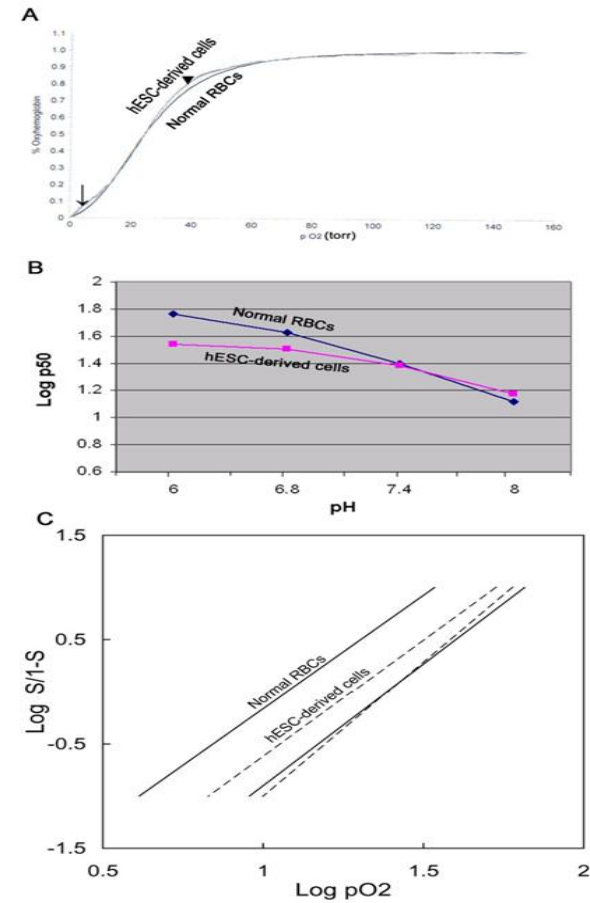
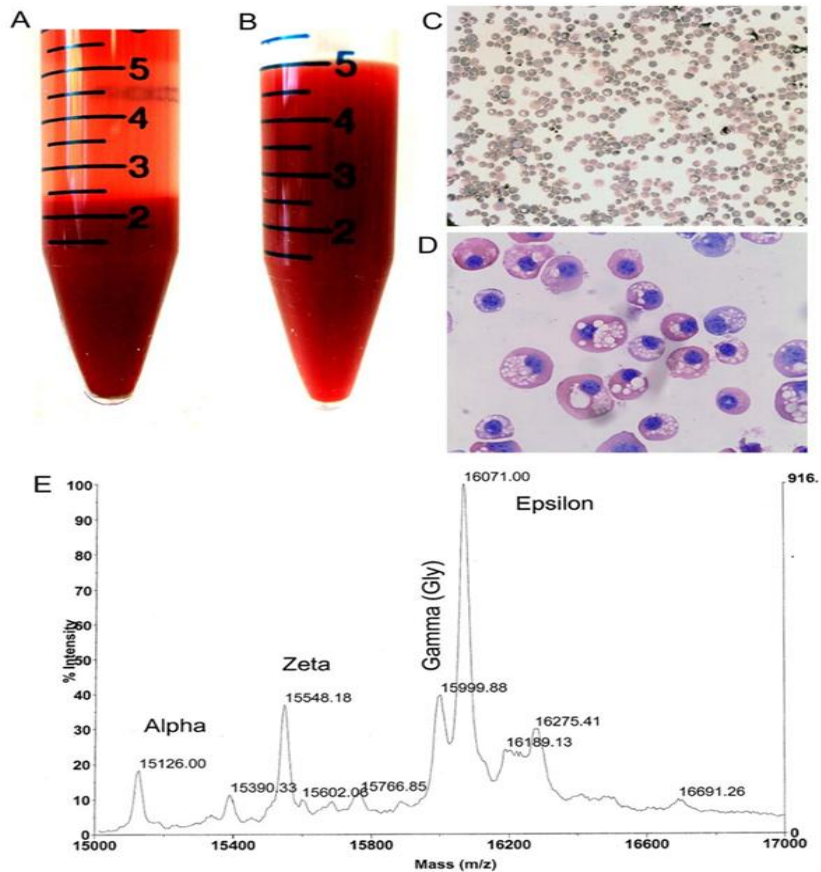


Repair of ischemic retinal vasculatures in mice





Large Scale Production to Functional Red Blood Cells from human PSCs





Media Coverage for Red Blood Cell Work

The New York Times
nytimes.com

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September 9, 2008

For Stem Cells, a Role on the Battlefield

By ANDREW POLLACK

When people envision using human embryonic stem cells for "regenerative medicine," they often talk about making neurons to treat Parkinson's disease, cardiac cells to repair the damage caused by a heart attack, or pancreatic islet cells to replace those destroyed by diabetes.



Tuesday, Aug. 19, 2008

Stem Cells May Help Transfusion Supplies

By AP/MALCOLM RITTER

Scientists say they've found an efficient way to make red blood cells from human embryonic stem cells
AP Associated Press

Related News

Stem cell advance may help transfusion supplies
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Clinical-Scale Generation of Functional Red Blood Cells from Embryonic Stem Cells

Los Angeles Times

Stem cell advance may help transfusion supplies

By MALCOLM RITTER - 1 hour ago

NEW YORK (AP) — Scientists say they've found an efficient way to make red blood cells from human embryonic stem cells, a possible step toward making transfusion supplies in the laboratory.



http://www.latimes.com/news/science/la-sci-blood20-2008aug20,0,2760531.story
From the Los Angeles Times

Researchers produce blood in lab from stem cells

The discovery marks a technical advance but has a long way to go before it can be considered an alternative to donor blood.

By Karen Kaplan
Los Angeles Times Staff Writer

1:07 PM PDT, August 19, 2008



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Scientists make red blood cells from embryonic stem cells

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Stem cell advance may help transfusion supplies

Scientists make red blood cells from embryonic stem cells: may someday



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Stem cells could allow "blood farms" company says

boston.com

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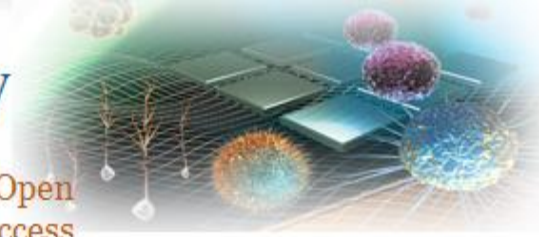
Stem cells may bring bottomless blood bank

The Boston Globe

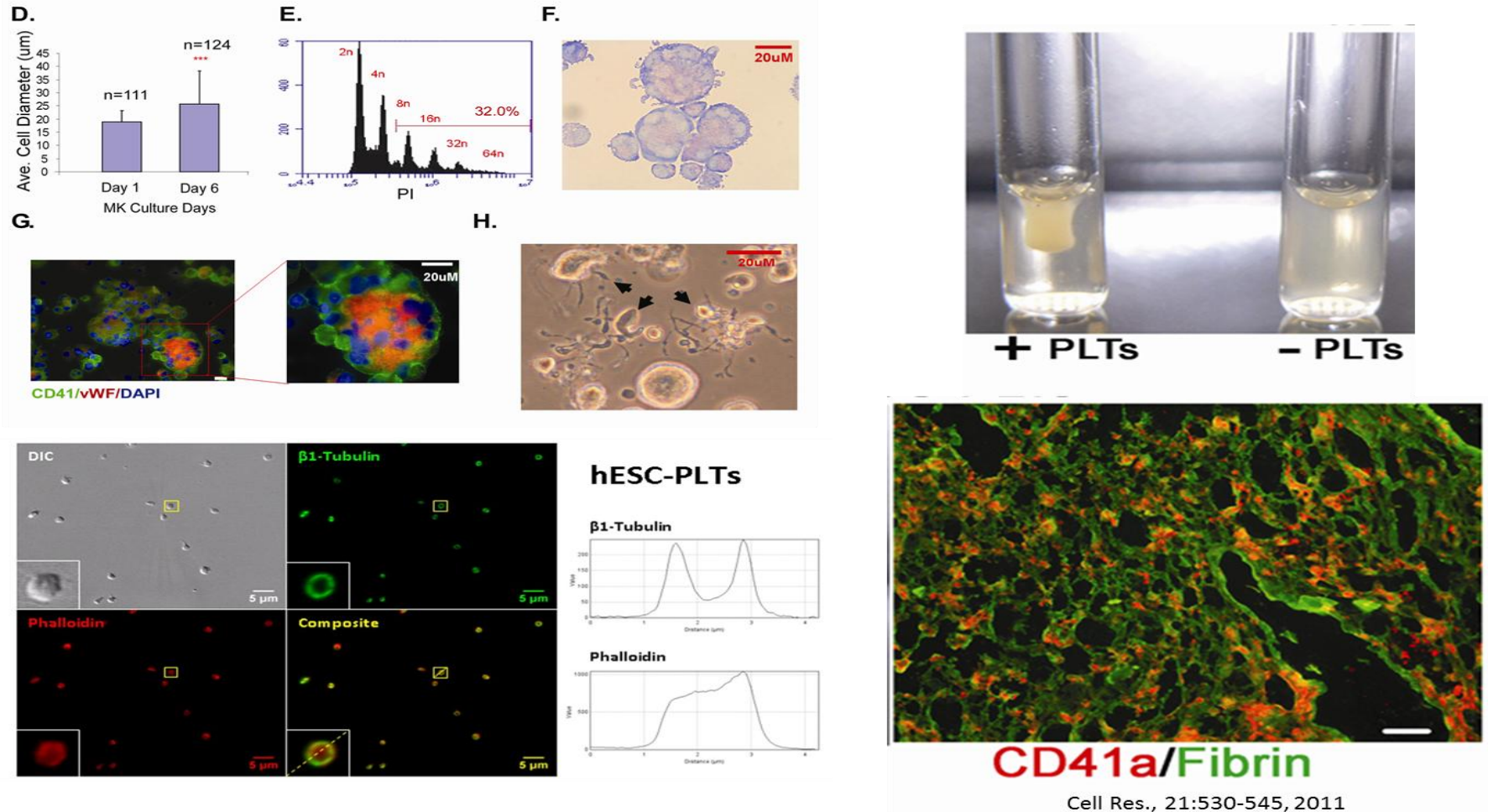
ACT says it made billions of viable cells

By Carolyn Y. Johnson, Globe Staff | August 20, 2008

Scientists at Advanced Cell Technology Inc., the Worcester stem cell company that is running out of cash, reported yesterday that they have created large numbers of red blood cells from human embryonic stem cells.



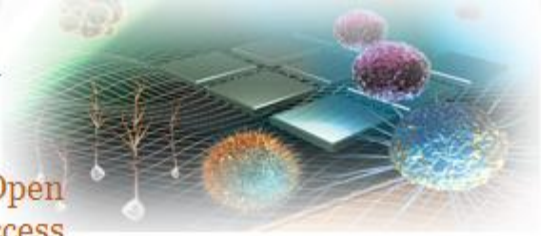
Efficient Generation of Functional Megakaryocytes and Platelets from PSC-hemangioblasts





Selected Invited Lectures

1. Invited Speaker, **The 1st International Conference on Basic and Clinical Immunogenomics**, October 3-7, 2004, Budapest, Hungary. Seminar Title: Hematopoietic precursors derived from primate ES cells exhibit an embryonic gene expression pattern.
2. Invited lecture, **Massachusetts General Hospital/Harvard Medical School**, Boston, MA, October 9, 2007. Lecture Title: Functional hemangioblasts derived from human embryonic stem cells.
3. Invited Lecture, **Institute of Hematology, Chinese Academy of Medical Sciences/Peking Union Medical College, and Union Stem Cells and Gene Engineering Co. LTD**, Tianjin, China, December 31, 2007. Lecture Title: The challenge and promise of human embryonic stem cell therapies.
4. Special Invited Lecture, **Pochon CHA University/Cha Stem Institute**, Seoul, South Korea, Oct. 15, 2008. Lecture Title: Functional red blood cells derived from human embryonic stem cells.
5. Invited Speaker, **International Forum on Stem Cells**, Tianjin, China, Oct. 16-18, 2008. Seminar Title: Biological properties of hemangioblasts derived from human embryonic stem cells.
6. Invited Speaker, **The 50th Anniversary Celebration Symposium of Beijing Institute of Ophthalmology & Ophthalmology Development Forum**, Beijing, China, May 29, 2009. Title: Human Embryonic Stem Cells---from Bench to Clinics.
7. Invited Speaker, **BioKorea 2009**, Sept. 16-18, 2009, COREX, Seoul, Korea. Title: Directed Differentiation of Human ES Cells to Functional Hemangioblastic Cells.
8. Invited Speaker, **Stem Cells for Drug Developer**, Boston, MA, April 27-28, 2011. Title: Hemangioblastic derivatives from human pluripotent stem cells: Potentials for clinical application and drug testing.
9. Invited Speaker, **Annual Meeting of Jilin Society of Pathophysiology**, Yanbian, Jilin, China, July 8-11, 2011. Title: Hemangioblastic differentiation from human pluripotent stem cells.
10. Invited Speaker, **International Forum on Stem Cells 2012**, Tianjin, China, November 01-03, 2012. Title: Human Pluripotent Stem Cells-- From Bench to Clinic: The ACT Experience.
11. Invited Speaker, **3rd Stem Cells for Drug Developer**, Boston, MA, March 20-21, 2013. Title: A Defined and Robust In Vitro System to Differentiate hPSCs into Functional Blood Cells.
12. Invited Speaker and Session Chair, **Stem Cell Summit 2013**, Boston, MA, April 29-30, 2013. Title: Robust Generation of Functional Vascular and Blood Cells from human PSCs.
13. Invited Speaker, **Therapeutics Discovery Symposia-2013: STEM CELLS & CELL SIGNALING - 2013 Meeting on Regenerative Medicine to Tissue Engineering & Therapeutics**, Boston, MA, May 01-02, 2013. Title: Blood Cells from Pluripotent Stem Cells: The Promise and Challenge for Clinical Application.
14. Invited Speaker, **World Summit on Regenerative Medicine-2013**, Xi'An, China, Oct. 19 to 22, 2013. Embryonic stem cells—discussion leader: Clinical target - sensory organs—Speaker: Commercialization of Stem Cells—Speaker



Selected Publications

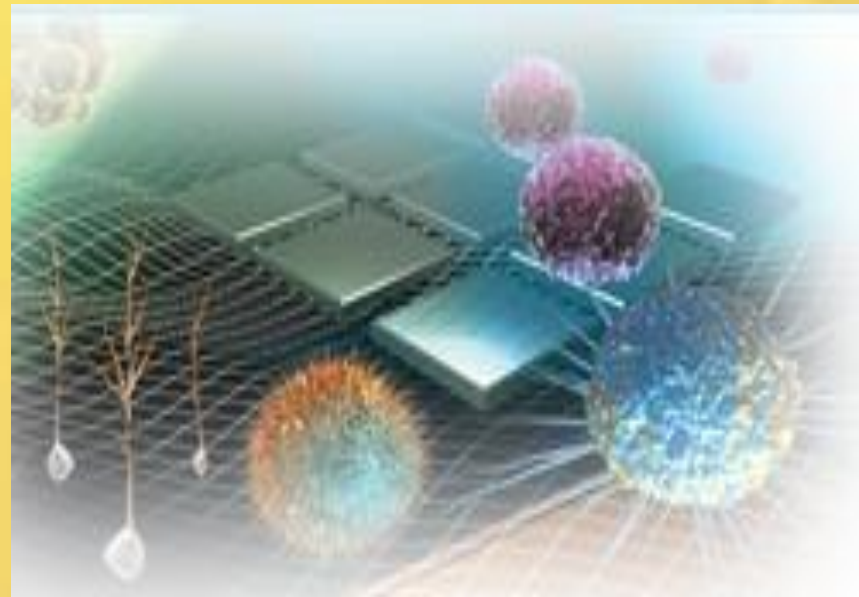
1. X. Wang, EA. Kimbrel, K. Ijichi, D. Paul, J. Chu, NA. Kouris, G. Yavanian, **S-J. Lu**, JS. Pachter, S. Crocke, R. Lanza and R-H. Xu: Human ES cell-derived MSCs outperform bone marrow MSCs in treating an EAE model of multiple sclerosis. **Stem Cell Reports**, 3:115-130, 2014.
2. **S-J. Lu***, T. Kelley, Q. Feng, A. Chen, S. Reuveny, R. Lanza and S KW. Oh. 3D Microcarrier System for Efficient Differentiation of Human Pluripotent Stem Cells into Hematopoietic Cells without Feeders and Serum. **Reg. Med.** 8:413-424, 2013. *corresponding author.
3. **S.J. Lu***, F. Li, H. Yin, Q. Feng, E.A. Kimbrel, E. Hahm, J.N. Thon, W. Wang, J. E. Italiano, J. Cho* and R. Lanza*. Platelets generated from human embryonic stem cells are functional in vitro and in the microcirculation of living mice. **Cell Res.**, 21:530-545, 2011. * corresponding authors.
4. Q. Feng, **S.J. Lu***, I. Klimanskaya, I. Gomes, Y. Chung, G. R. Honig, K-S. Kim, R. Lanza*: Hemangioblastic derivatives from human induced pluripotent stem cells exhibit limited expansion and early senescence. **Stem Cells** 28:704-712, 2010, *corresponding authors.
5. **Lu, S.J***, Feng, Q., Park, J.S. and Lanza, R. Direct differentiation of red blood cells from human embryonic stem cells. **Methods Mol. Bio.** 636:105-121, 2010. *corresponding author
6. **Lu, S.J.**, Ivanova, Y., Feng, Q., Luo, C. and Lanza, R. Hemangioblasts from human embryonic stem cells generate multilayered blood vessels with functional smooth muscle cells. **Reg. Med.** 4:37-47, 2009.
7. **Lu, S.J.**, Luo, C., Holton, C., Feng, Q., Ivanova, Y. and Lanza, R. Robust generation of hemangioblastic progenitors from human embryonic stem cells. **Reg. Med.** 3:693-704, 2008.
8. **Lu, S.J***; Feng, Q*; Park, J.S*, Vida, L.; Lee, B.S.; Strausbauch, M.; Wettstein, P.J.; Honig, G.R.; and Lanza, R. Biologic properties and enucleation of red blood cells from human embryonic stem cells**. **Blood** 112:4475-4484, 2008; with commentary in *Blood*, 112:4362-4363, 2008. *equal contribution authors. **(Ranked 16th in Discover's Top 100 Science Stories of 2008).
9. Chung, Y.; Klimanskaya, I.; Becker, S.; Li, T.; Maserati, M.; **Lu, S.J.**; Zdravkovic, T.; Ilica, D.; Genbacev, O.; Fisher, S.; Krtolica, A.; Lanza, R. Human embryonic stem cell lines generated without embryo destruction. **Cell Stem Cell**, 2: 113-117, 2008.
10. **Lu, S.J***; Hipp, J*; Feng, Q.; Hipp, J.; Lanza, R. and Atala, A. Genechip analysis of human embryonic stem cells into hemangioblasts: An in silico dissection of mixed phenotypes. **Genome Biol.** 2007, 8:R240. * equal contribution authors.

Selected Publications

11. **Lu, S.J.**; Feng, Q.; Ivanova, Y.; Luo, C.; Li, T.; Li, F., Honig, G.R. and Lanza, R. Recombinant HoxB4 fusion proteins enhance hematopoietic differentiation of human embryonic stem cells. **Stem Cells and Dev.** 16:547-559, 2007.
12. **Lu, S.J.**; Feng, Q.; Caballero, S.; Chen, Y.; Moore, M.A.S.; Grant, M.B. and Lanza, R. Generation of functional hemangioblasts from human embryonic stem cells. **Nature Methods**, 4:501-509, 2007.
- Klimanskaya, I.; Chung, Y.; Becker, S.; **Lu, S.J.**; Lanza, R. Human embryonic stem cell lines derived from single blastomeres. **Nature**, 444:481-485, 2006.
13. Chung, Y.; Klimanskaya, I.; Becker, S.; Marh, J.; **Lu, S.J.**; Johnson, J.; Meisner, L.; Lanza, R. Embryonic and extraembryonic stem cell lines derived from single mouse blastomeres. **Nature**, 439:216-219, 2006.
14. **Lu, S.J.***, Li, F., Vida, L. and Honig, G.R. CD34+CD38- hematopoietic precursors derived from human embryonic stem cells exhibit an embryonic gene expression pattern. **Blood**, 103:4134-4141, 2004.
*corresponding author.
15. **Lu, S.J.***, Quan, C., Li, F., Vida, L. and Honig, G.R. Hematopoietic progenitor cells derived from embryonic stem cells: Analysis of gene expression. **Stem Cells** 20: 428-437, 2002. *corresponding author.
16. **Lu, S.J.**, Li, F., Vida, L. and Honig, G.R. Comparative gene expression in hematopoietic progenitor cells derived from embryonic stem cells. **Exp. Hematol.**, 30: 58-66, 2002.
17. Li, F., **Lu, S.J.**, Vida, L., Thomson, J.A. and Honig, G.R. Bone morphogenetic protein-4 induces efficient hematopoietic differentiation of rhesus monkey embryonic stem cells in vitro. **Blood**, 98: 335-342, 2001.

Stem Cells Research & Therapy Related Journals

- Single Cell Biology
- Cell & Developmental Biology
- Journal of Cell Science & Therapy



Stem Cell Research & Therapy Related Conferences

- 4th International Conference and Exhibition on Cell & Gene Therapy
- 5th World Congress on Cell Science & Stem Cell Research
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