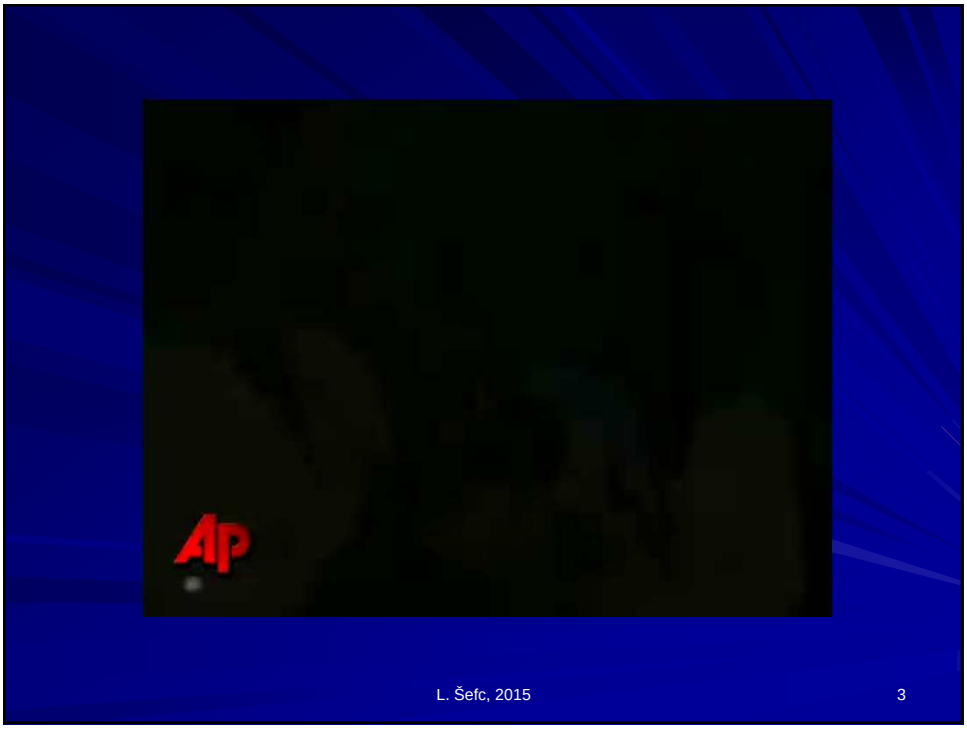
Regenerative medicine

Luděk Šefc

Regenerative Medicine

- **Process of creating living, functional tissues to repair or replace tissue or organ function lost due to age, disease, damage, or congenital defects**
- **It helps to produce extended healthy longevity.**


AP

Some history

1908 - The term "stem cell" was proposed for scientific use by the Russian histologist Alexander Maksimov (1874–1928) at congress of hematologic society in Berlin. It postulated existence of haematopoietic stem cells.

1960s - Joseph Altman and Gopal Das present scientific evidence of adult neurogenesis, ongoing stem cell activity in the brain; like André Gernez, their reports contradict Cajal's "no new neurons" dogma and are largely ignored.

1963 - McCulloch and Till illustrate the presence of self-renewing cells in mouse bone marrow.

Some history

1968 - Bone marrow transplant between two siblings successfully treats SCID.

1978 - Haematopoietic stem cells are discovered in human cord blood.

1981 - Mouse embryonic stem cells are derived from the inner cell mass by scientists Martin Evans, Matthew Kaufman, and Gail R. Martin. Gail Martin is attributed for coining the term "Embryonic Stem Cell".

1992 - Neural stem cells are cultured in vitro as neurospheres.

1997 - Leukemia is shown to originate from a haematopoietic stem cell, the first direct evidence for cancer stem cells.

1998 - James Thomson and coworkers derive the first human embryonic stem cell line at the University of Wisconsin–Madison.

2000s - Several reports of adult stem cell plasticity are published.

2005 - Researchers at UC Irvine's Reeve-Irvine Research Center are able to partially restore the ability of mice with paralyzed spines to walk through the injection of human neural stem cells.

Some history

August 2006 - Mouse Induced pluripotent stem cells: the journal Cell publishes Kazutoshi Takahashi and Shinya Yamanaka. Nobel Prize 2012

October 2007 - Mario Capecchi, Martin Evans, and Oliver Smithies win the 2007 Nobel Prize for Physiology or Medicine for their work on embryonic stem cells from mice using gene targeting strategies producing genetically engineered mice (known as knockout mice) for gene research.

November 2007 - Human induced pluripotent stem cells: Two similar papers released by their respective journals prior to formal publication: in Cell by Kazutoshi Takahashi and Shinya Yamanaka, "Induction of pluripotent stem cells from adult human fibroblasts by defined factors", and in Science by Junying Yu, et al., from the research group of James Thomson, "Induced pluripotent stem cell lines derived from human somatic cells": pluripotent stem cells generated from mature human fibroblasts.

Some history

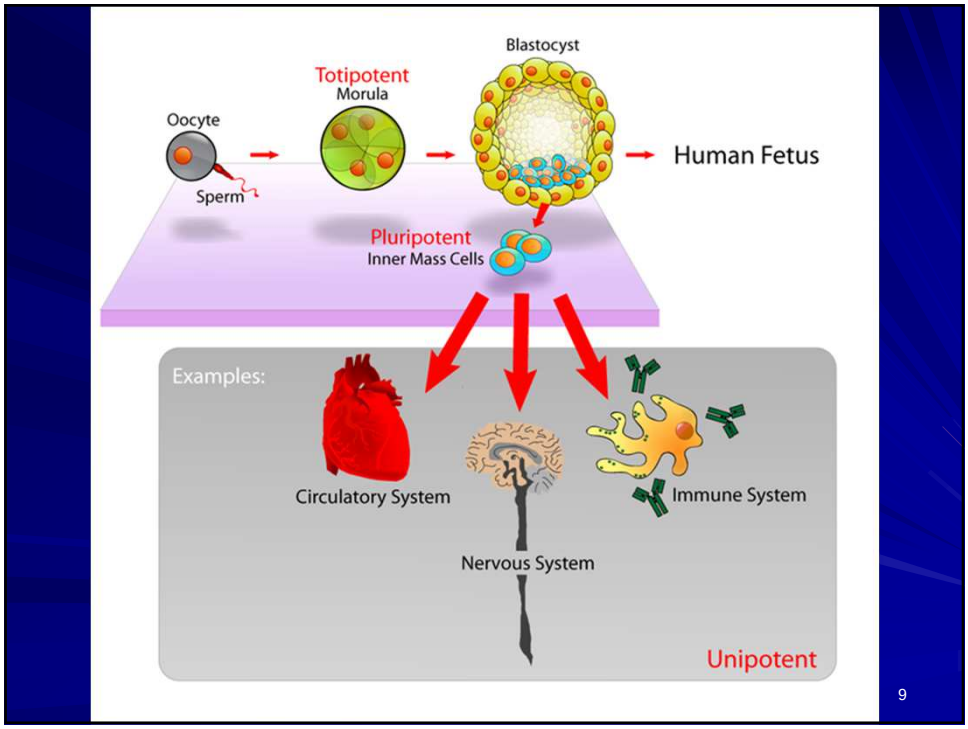
February 2008 - Generation of pluripotent stem cells from adult mouse liver and stomach: these iPS cells seem to be more similar to embryonic stem cells than the previously developed iPS cells and not tumorigenic, moreover genes that are required for iPS cells do not need to be inserted into specific sites, which encourages the development of non-viral reprogramming techniques.

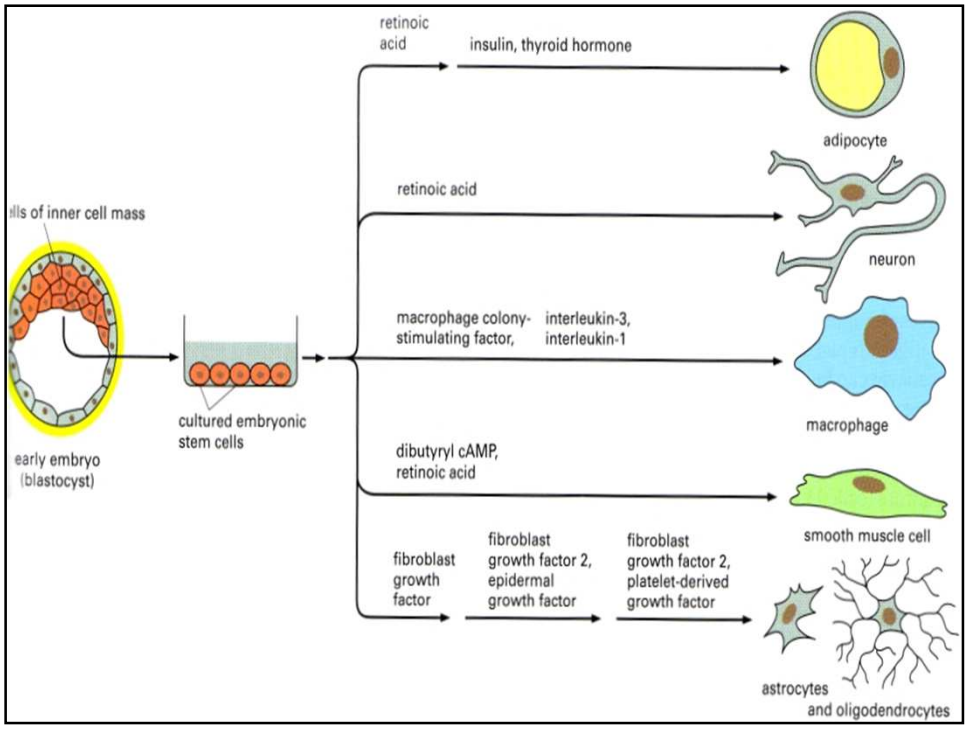
March 2008-The first published study of successful cartilage regeneration in the human knee using autologous adult mesenchymal stem cells is published by clinicians from Regenerative Sciences

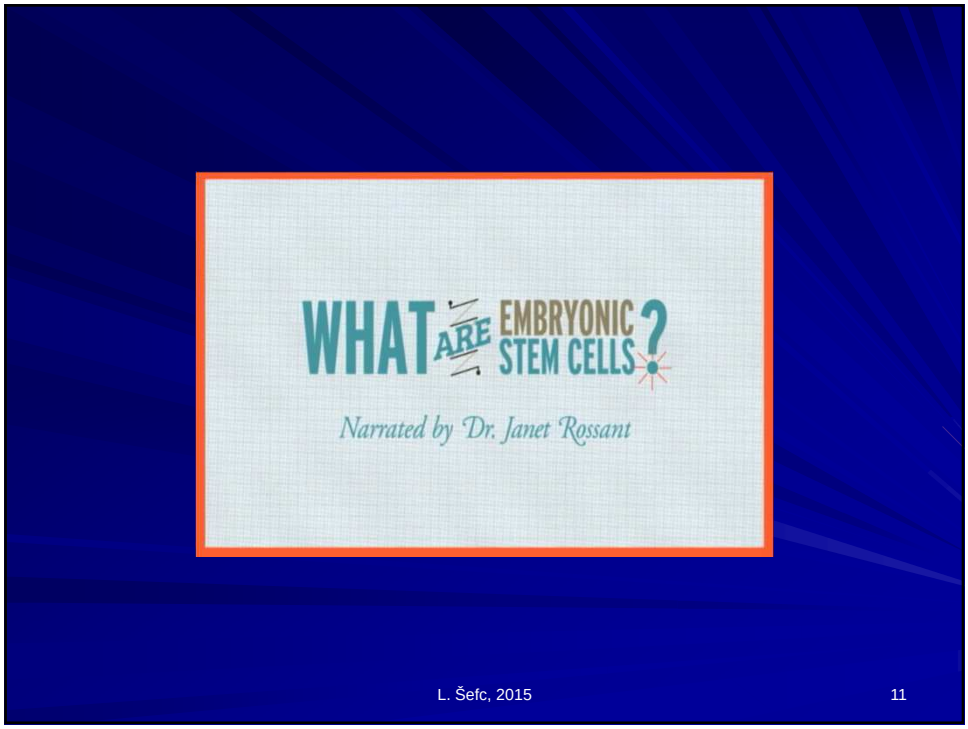
October 30, 2008 - Embryonic-like stem cells from a single human hair.

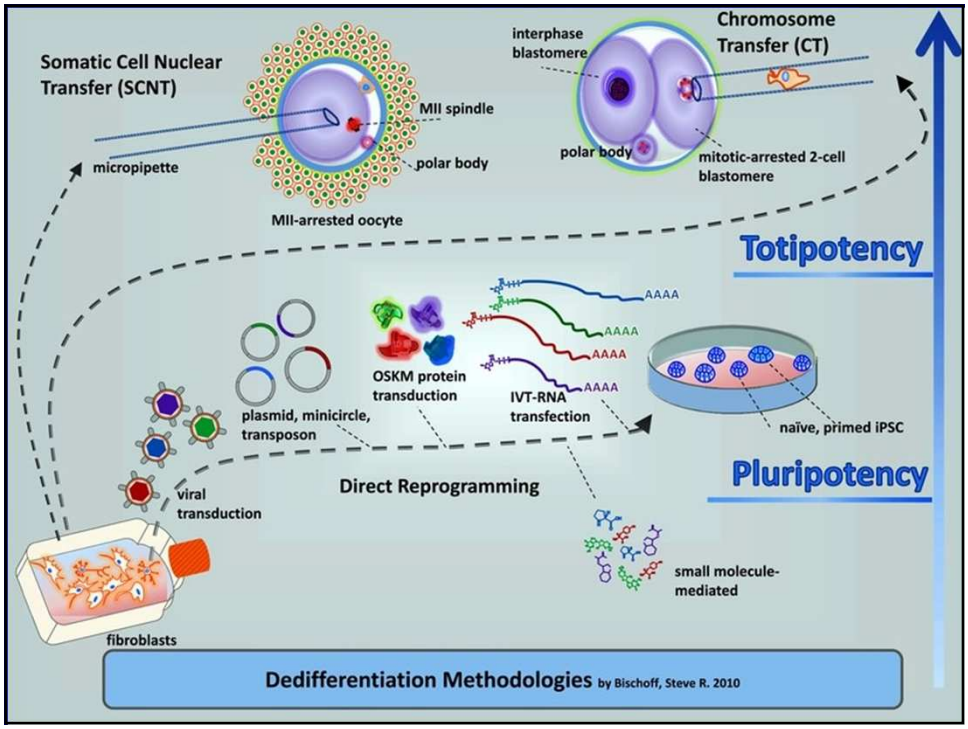
October 11, 2010 First trial of embryonic stem cells in humans.

August 2013 – Recruiting of patients into the first clinical trial using iPS cells first clinical trial using iPS cells for treatment of age-related macular degeneration (RIKEN Center for Developmental Biology in Kobe, Japan)


Blastocyst
Totipotent
Morula
Oocyte
Sperm
Human Fetus
Pluripotent
Inner Mass Cells
Examples:
Circulatory System
Immune System
Nervous System
Unipotent
9


retinoic acid
insulin, thyroid hormone
adipocyte
retinoic acid
neuron
lls of inner cell mass
macrophage colony-stimulating factor,
interleukin-3,
interleukin-1
macrophage
cultured embryonic stem cells
early embryo (blastocyst)
dibutyryl cAMP, retinoic acid
smooth muscle cell
fibroblast growth factor
fibroblast growth factor 2, epidermal growth factor
fibroblast growth factor 2, platelet-derived growth factor
astrocytes and oligodendrocytes


WHAT ARE EMBRYONIC STEM CELLS?
Narrated by Dr. Janet Rossant
L. Šefc, 2015
11


Somatic Cell Nuclear Transfer (SCNT)
micropipette
MII spindle
polar body
MII-arrested oocyte
interphase blastomere
Chromosome Transfer (CT)
polar body
mitotic-arrested 2-cell blastomere
Totipotency
AAAA
AAAA
AAAA
AAAA
OSKM protein transduction
IVT-RNA transfection
plasmid, minicircle, transposon
naïve, primed iPSC
Pluripotency
Direct Reprogramming
viral transduction
small molecule-mediated
fibroblasts
Dedifferentiation Methodologies by Bischoff, Steve R. 2010

Adult stem cells

- Hematopoietic stem cells
- Mammary stem cells
- Mesenchymal stem cells
- Endothelial stem cells
- Neural stem cells
- Olfactory adult stem cells
- Neural crest stem cells
- Testicular cells

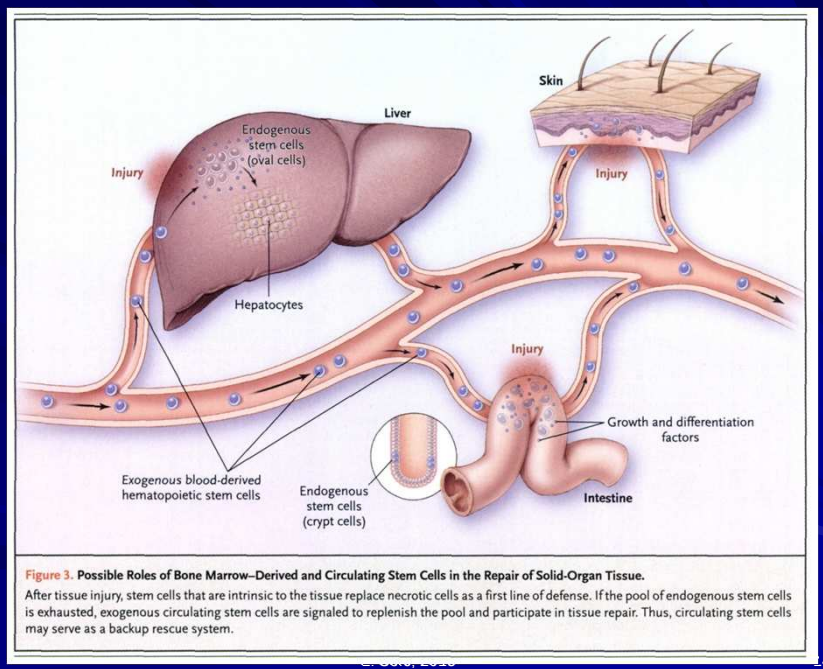
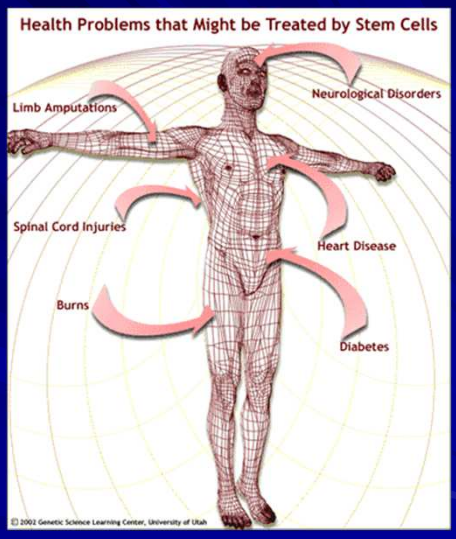


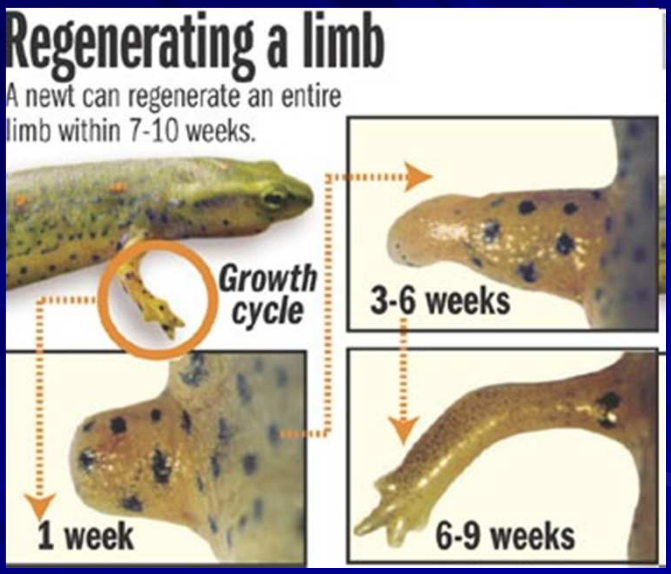
Figure 3. Possible Roles of Bone Marrow–Derived and Circulating Stem Cells in the Repair of Solid-Organ Tissue.
After tissue injury, stem cells that are intrinsic to the tissue replace necrotic cells as a first line of defense. If the pool of endogenous stem cells is exhausted, exogenous circulating stem cells are signaled to replenish the pool and participate in tissue repair. Thus, circulating stem cells may serve as a backup rescue system.

Plasticity of stem cells

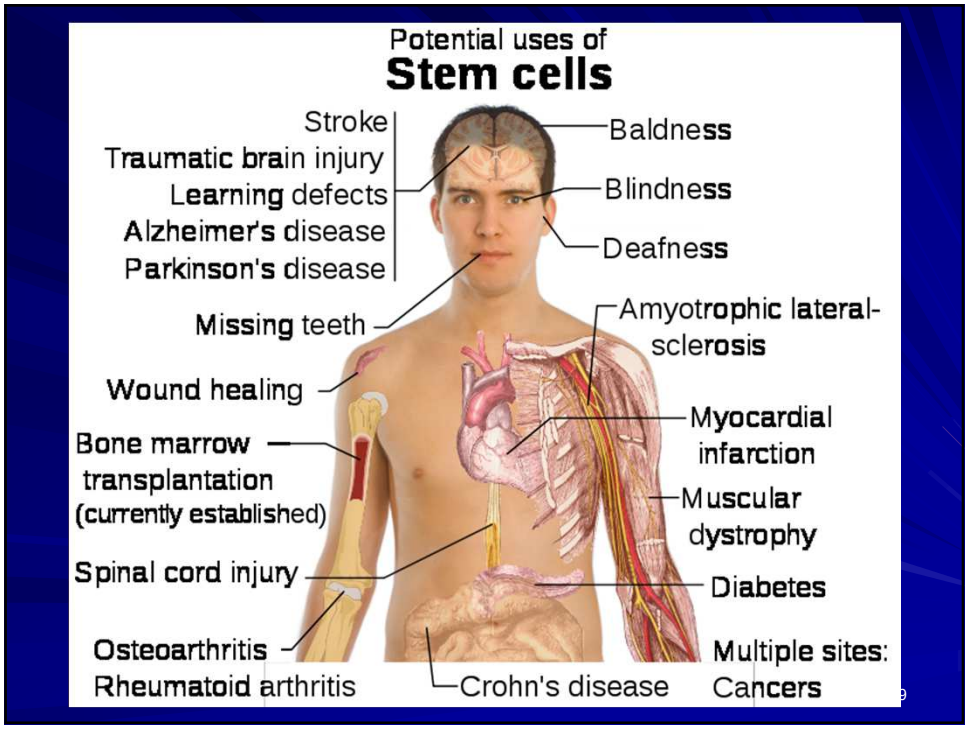
<u>Therapy use:</u>

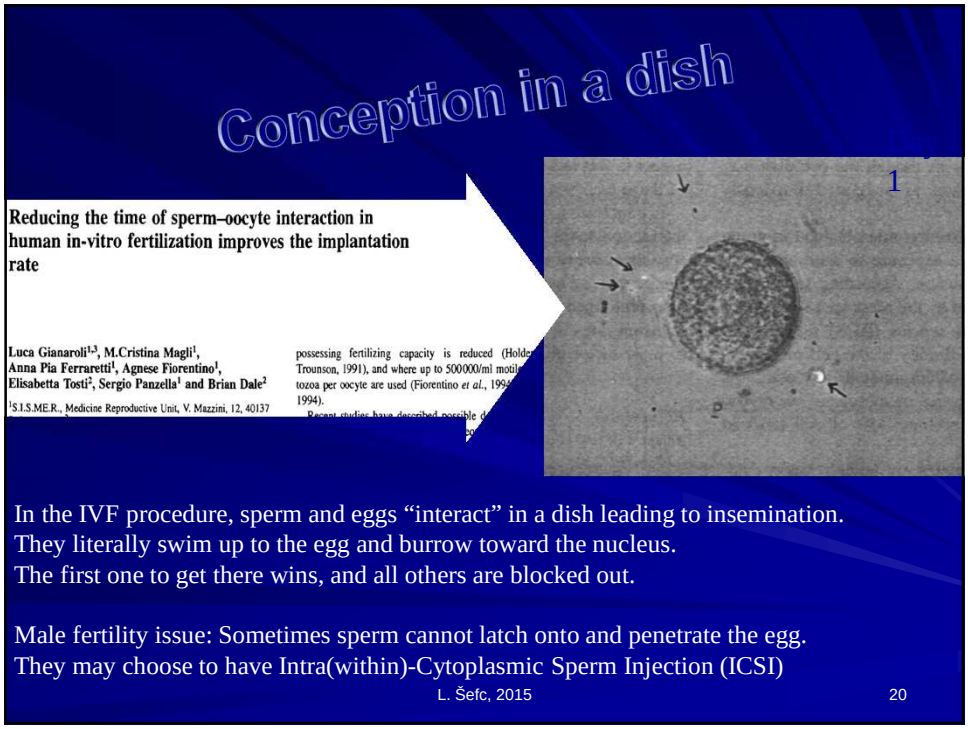
myocard infarction
neurodegenerative diseases
orthopedy
plastic surgery
gene therapy






HHMI


Potential uses of
Stem cells
Stroke
Traumatic brain injury
Learning defects
Alzheimer's disease
Parkinson's disease
Missing teeth
Wound healing
Bone marrow transplantation (currently established)
Spinal cord injury
Osteoarthritis
Rheumatoid arthritis
Baldness
Blindness
Deafness
Amyotrophic lateral-sclerosis
Myocardial infarction
Muscular dystrophy
Diabetes
Crohn's disease
Multiple sites: Cancers


Conception in a dish
Reducing the time of sperm–oocyte interaction in human in-vitro fertilization improves the implantation rate
Luca Gianaroli[1,3], M.Cristina Magli[1], Anna Pia Ferraretti[1], Agnese Fiorentino[1], Elisabetta Tosti[2], Sergio Panzella[1] and Brian Dale[2]
[1]S.I.S.ME.R., Medicine Reproductive Unit, V. Mazzini, 12, 40137
1
In the IVF procedure, sperm and eggs “interact” in a dish leading to insemination.
They literally swim up to the egg and burrow toward the nucleus.
The first one to get there wins, and all others are blocked out.
Male fertility issue: Sometimes sperm cannot latch onto and penetrate the egg.
They may choose to have Intra(within)-Cytoplasmic Sperm Injection (ICSI)
L. Šefc, 2015
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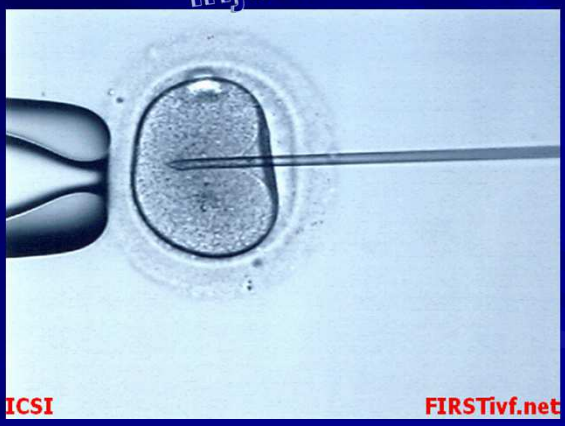
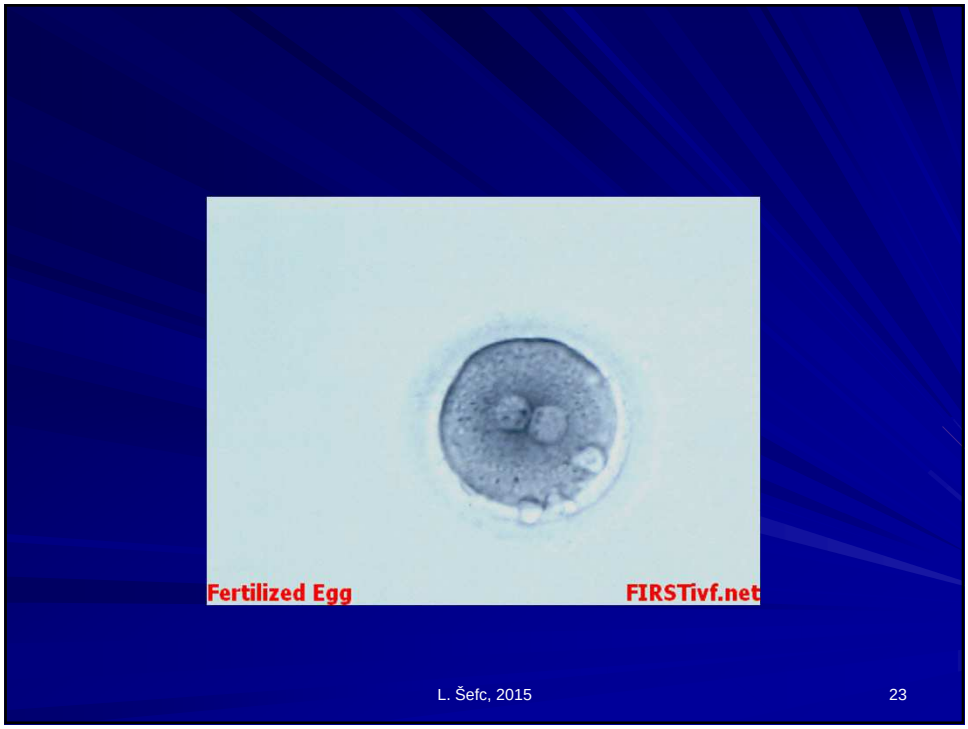
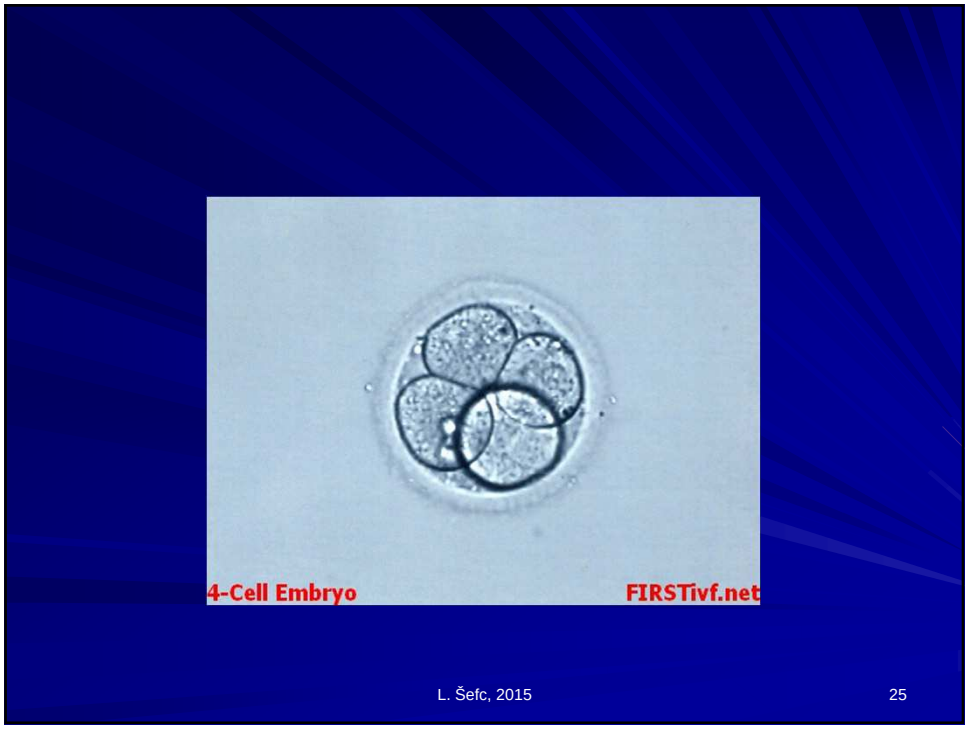
Intra-Cytoplasmic Sperm Injection

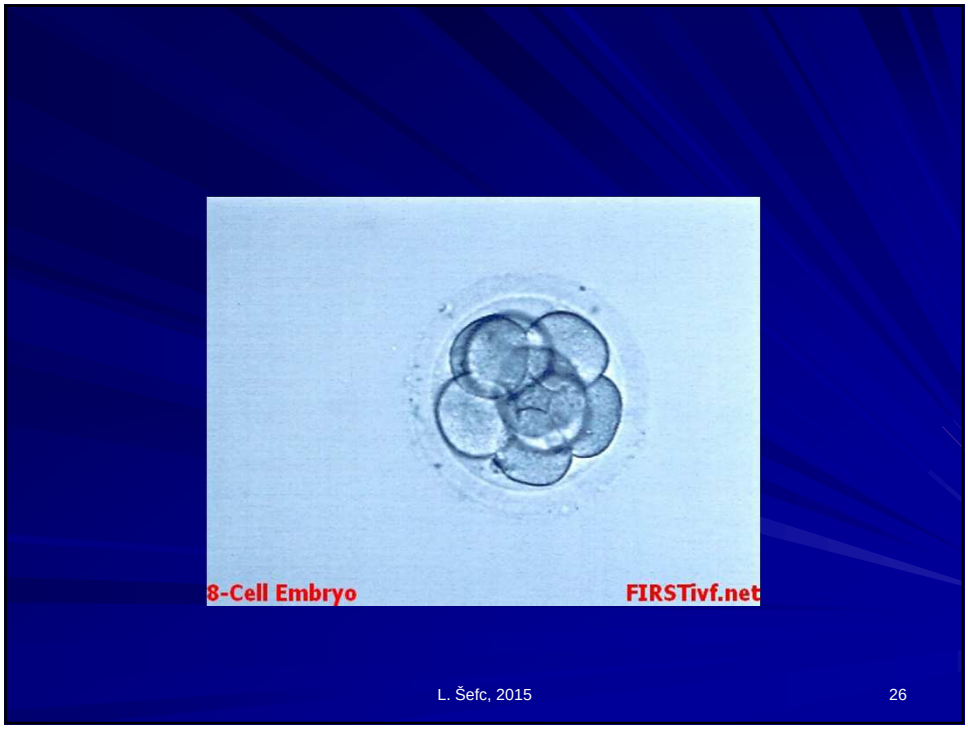
Intra-Cytoplasmic Sperm Injection

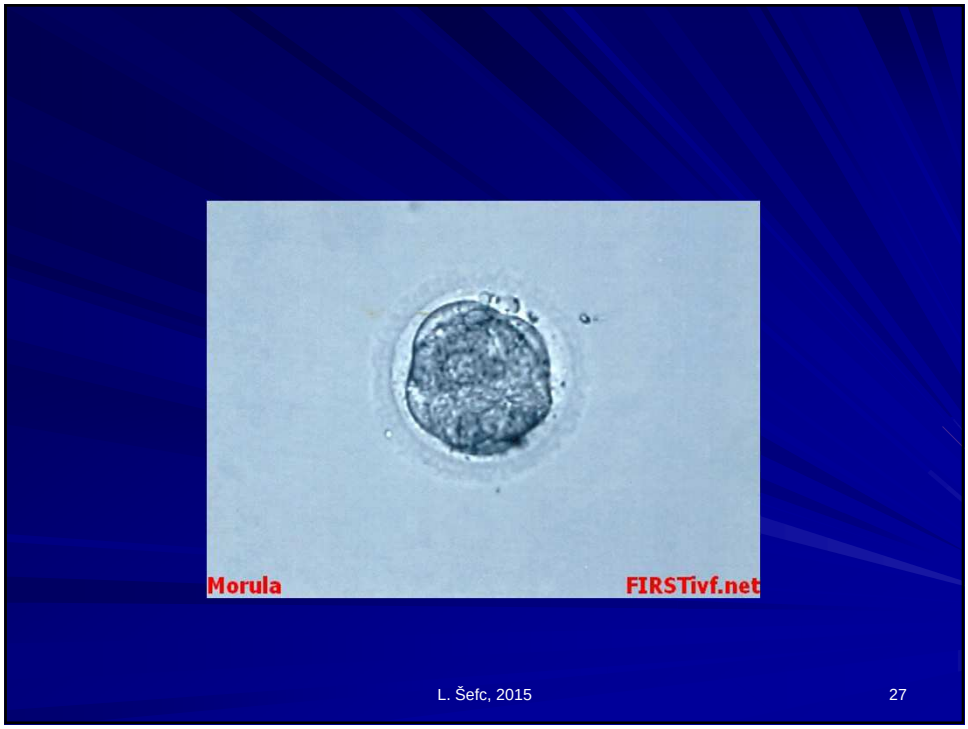


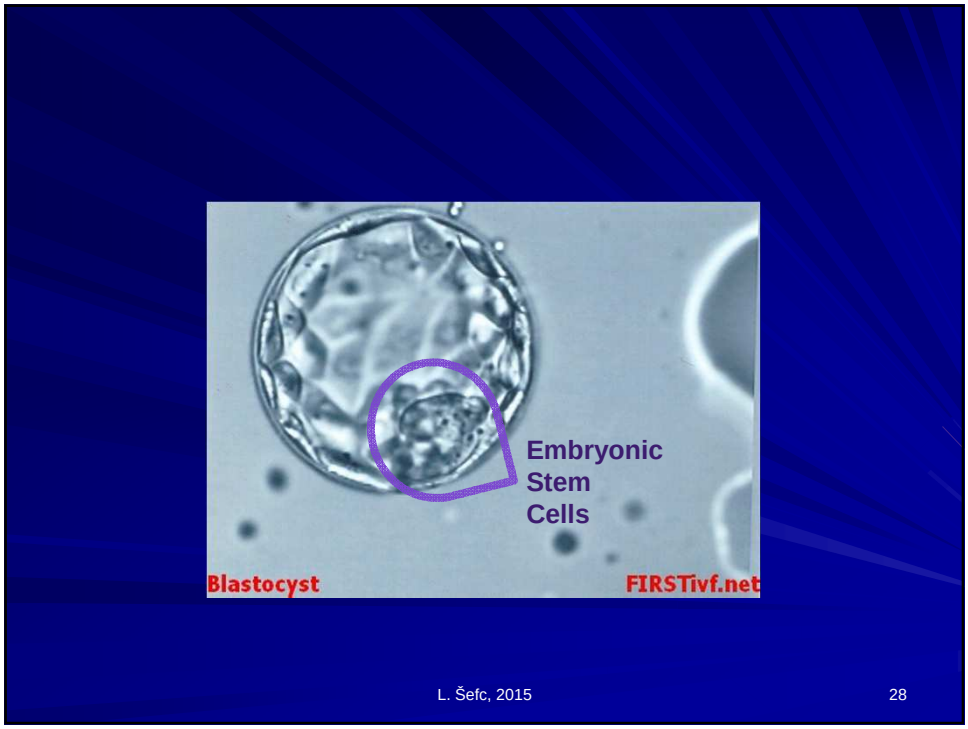

Fertilized Egg
FIRSTivf.net


2-Cell Embryo
FIRSTivf.net


4-Cell Embryo
FIRSTivf.net

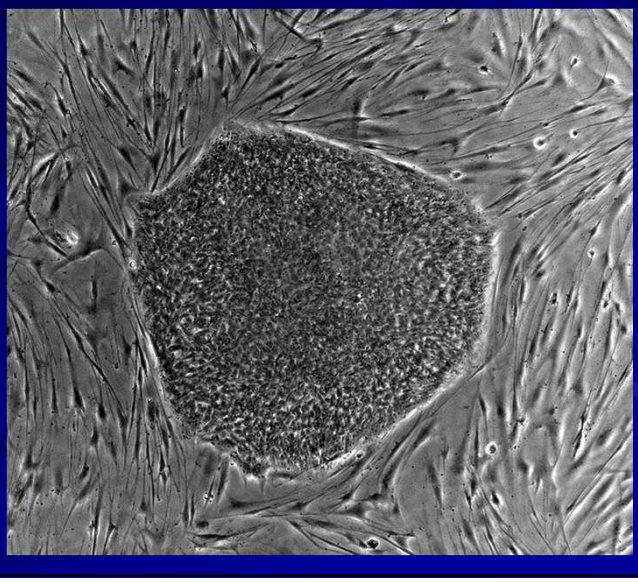

8-Cell Embryo
FIRSTivf.net


Morula
FIRSTivf.net


Embryonic
Stem
Cells
Blastocyst
FIRSTivf.net

Embryonic stem cells in the dish:

What do cultured ES cells look like?



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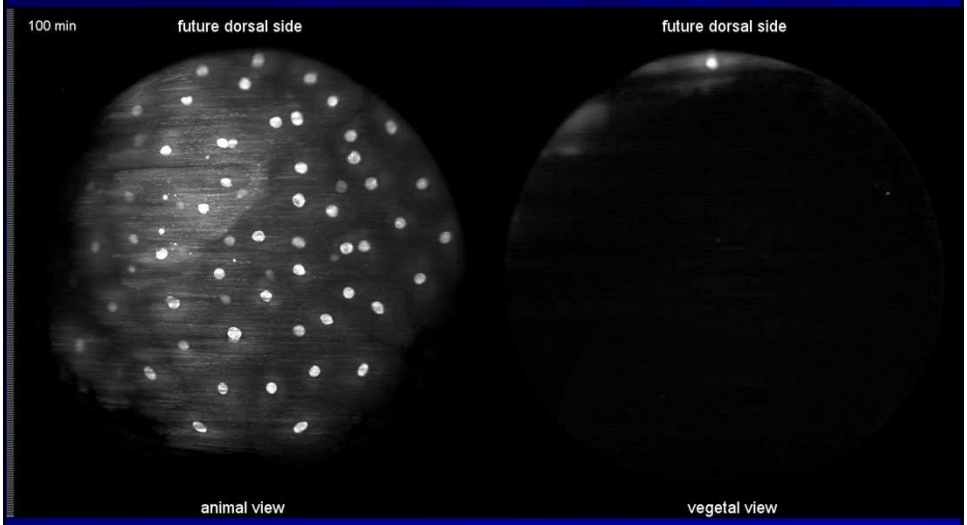
Embryonic Development: Fish embryo



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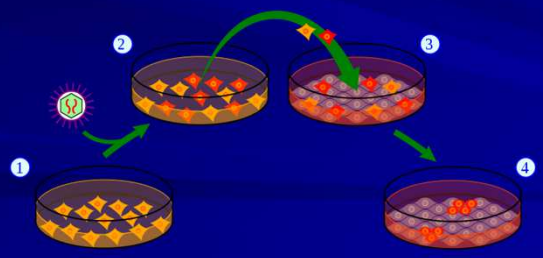
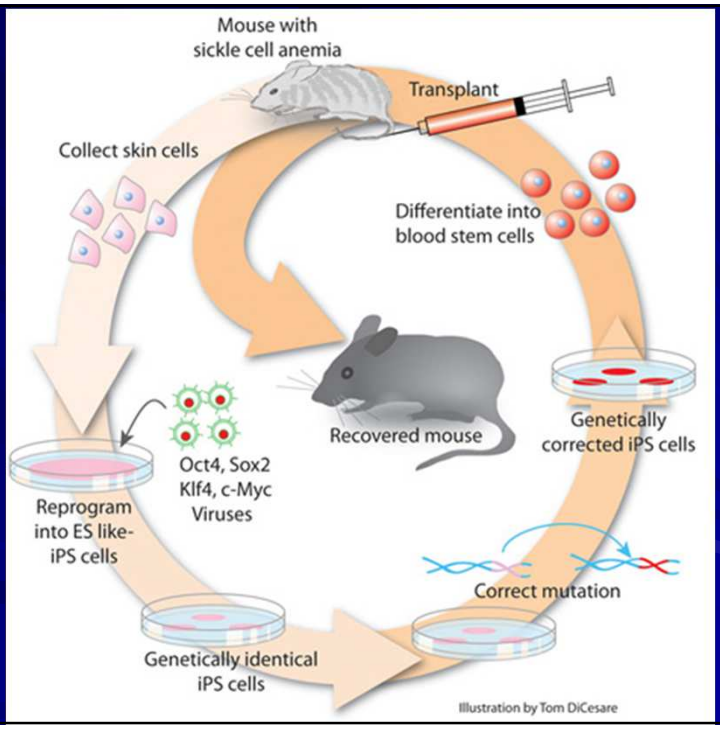
iPS cells – induced pluripotent stem cells

- 2006 – mouse, 2007 man
- viral transfection by several transcription factors – Oct-3/4, SOX2, c-Myc, Klf4





PUBLIC RELEASE: 9-MAR-2015

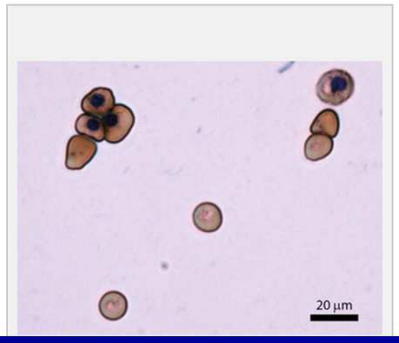
Johns Hopkins researchers engineer custom blood cells

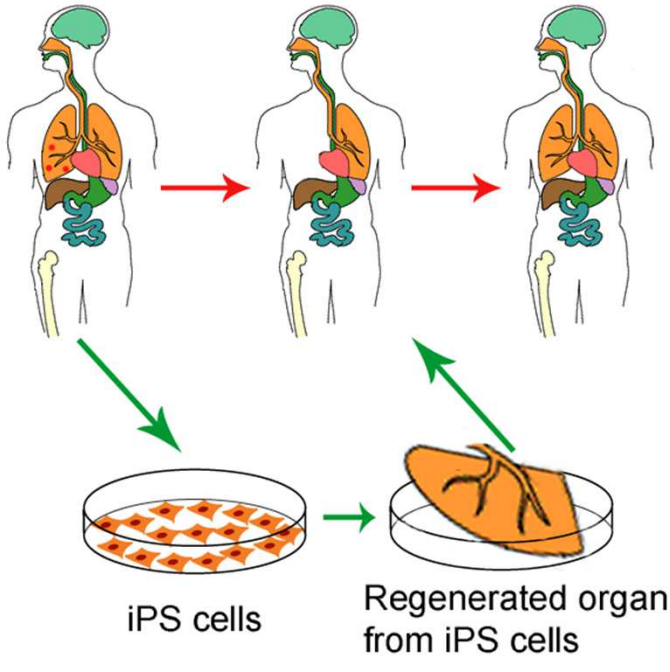
Step toward new treatment for patients with sickle cell disease

JOHNS HOPKINS MEDICINE

SHARE PRINT E-MAIL

Researchers at Johns Hopkins have successfully corrected a genetic error in stem cells from patients with sickle cell disease, and then used those cells to grow mature red blood cells, they report. The study represents an important step toward more effectively treating certain patients with sickle cell disease who need frequent blood transfusions and currently have few options.





Stem Cell Network
Réseau de cellules souches

Science
AAAS

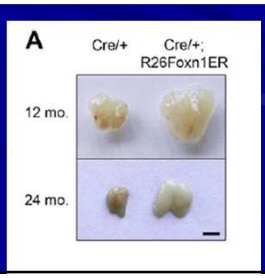
Pluripotent Stem Cells Induced from Mouse Somatic Cells by Small-Molecule Compounds
Pingping Hou *et al.*
Science **341**, 651 (2013);
DOI: 10.1126/science.1239278

 | Development (2014) 141, 1627-1637 doi:10.1242/dev.103614 Biologists

RESEARCH ARTICLE STEM CELLS AND REGENERATION

Regeneration of the aged thymus by a single transcription factor

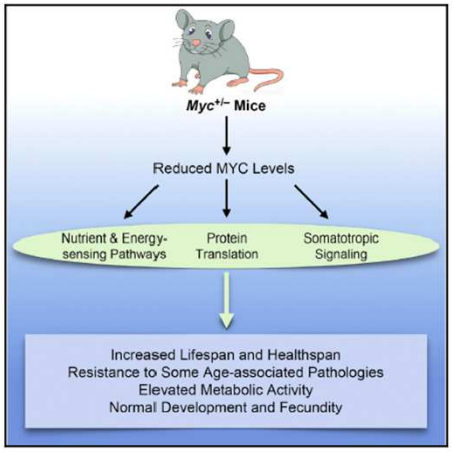
Nicholas Bredenkamp*, Craig S. Nowell‡ and C. Clare Blackburn§



Cell 160, 477–488, January 29, 2015 ©2015 Elsevier Inc.

Reduced Expression of MYC Increases Longevity and Enhances Healthspan

Graphical Abstract



Authors

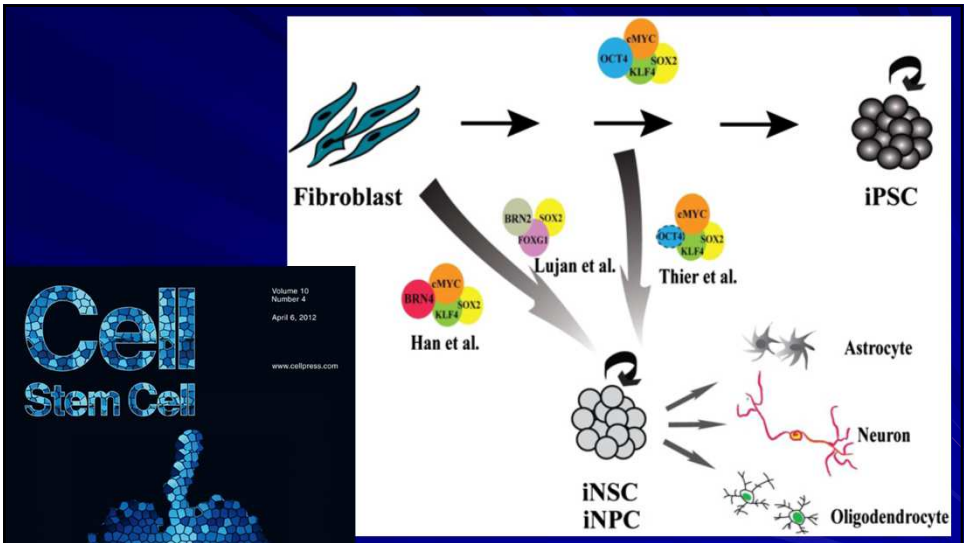
Jeffrey W. Hofmann, Xiaoai Zhao, ..., Nicola Neretti, John M. Sedivy

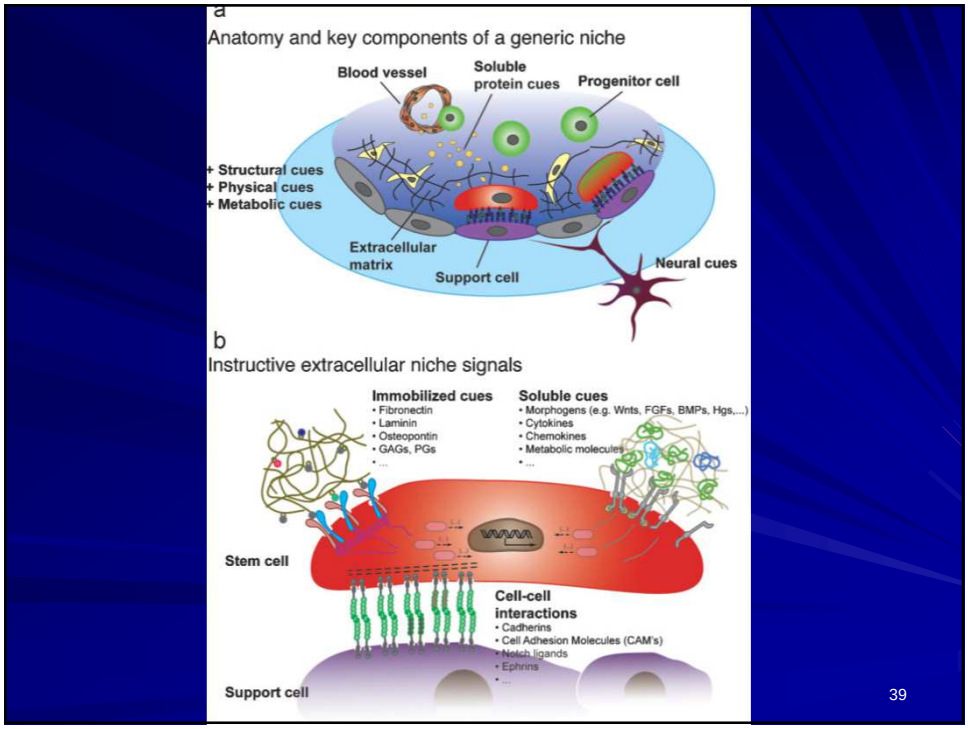
Correspondence

john_sedivy@brown.edu

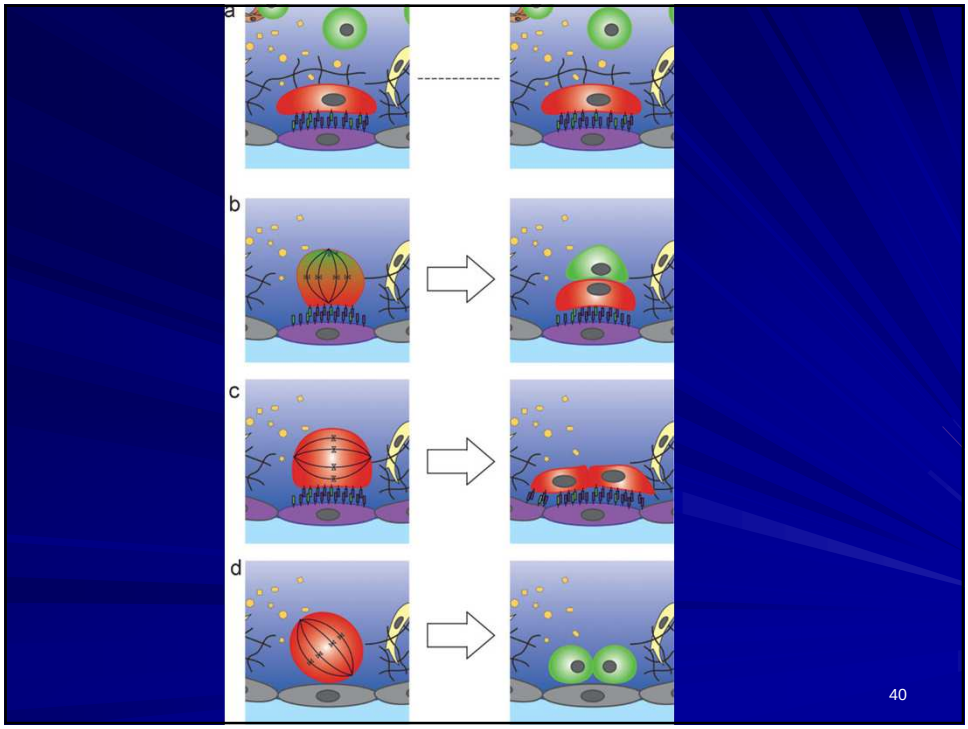
In Brief

Reduced expression of MYC increases lifespan in mice and benefits multiple aspects related to the aging process without apparent developmental trade-offs or changes in stress management pathways.



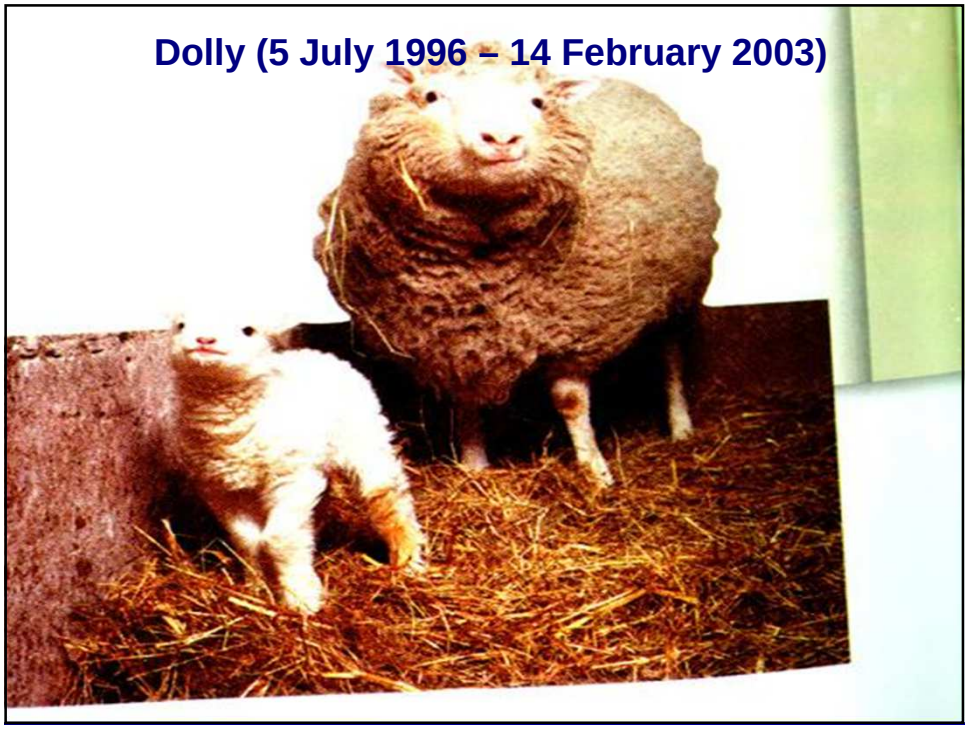

a
Anatomy and key components of a generic niche
Blood vessel
Soluble protein cues
Progenitor cell
+ Structural cues
+ Physical cues
+ Metabolic cues
Extracellular matrix
Support cell
Neural cues
b
Instructive extracellular niche signals
Immobilized cues
• Fibronectin
• Laminin
• Osteopontin
• GAGs, PGs
Soluble cues
• Morphogens (e.g. Wnts, FGFs, BMPs, Hgs,...)
• Cytokines
• Chemokines
• Metabolic molecules
Stem cell
Cell-cell interactions
• Cadherins
• Cell Adhesion Molecules (CAM's)
• Notch ligands
• Ephrins
Support cell

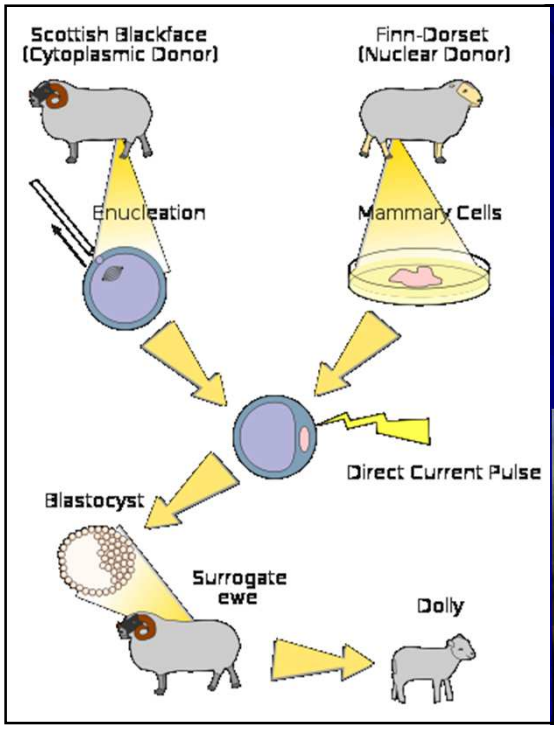
39


a
b
c
d

40

Dolly (5 July 1996 – 14 February 2003)





Cloned by Ian Wilmut, Keith Campbell and colleagues at the Roslin Institute near Edinburgh in Scotland

From 277 cell fusions, 29 early embryos developed and were implanted into 13 surrogate mothers. But only one pregnancy went to full term, and the 6.6kg Finn Dorset lamb 6LLS (alias Dolly) was born after 148 days.

Birth of 30 Genetically Modified Babies May Lead to a 'Designer' Human Race

ICTMN STAFF | 7/6/12

Now a Reality, Should Genetically Modified Babies Be Prohibited?

enetically
as sparked an
ther fertility
ul parents

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BY LEONARDO BLAIR , CP REPORTER

March 23, 2013 | 1:41 pm

After an announcement last year that a series of experiments in the United States had resulted in the birth of 30 healthy genetically modified babies, genetics experts are now debating whether or not further development of designer offspring should be banned.

43

Current treatments

Hematopoietic stem cell transplantation

For over 30 years, bone marrow stem cells, and more recently, umbilical cord blood stem cells, have been used to treat cancer patients with conditions such as leukemia and lymphoma. During chemotherapy, most growing cells are killed by the cytotoxic agents. These agents, however, cannot discriminate between the leukemia or neoplastic cells, and the hematopoietic stem cells within the bone marrow. It is this side effect of conventional chemotherapy strategies that the stem cell transplant attempts to reverse; a donor's healthy bone marrow reintroduces functional stem cells to replace the cells lost in the host's body during treatment.

L. Šefc, 2015

Thalesemia

- The genetic defect results in reduced rate of synthesis of one of the globin chains that make up hemoglobin
- Hematopoietic stem cell transplantation (HSCT) is the only curative approach

L. Šefc, 2015 46

Transplantation. 2010 Mar 15;89(5):485-91.

Tissue-engineered tracheal transplantation.

Baiguera S, Birchall MA, Macchiarini P.

Source

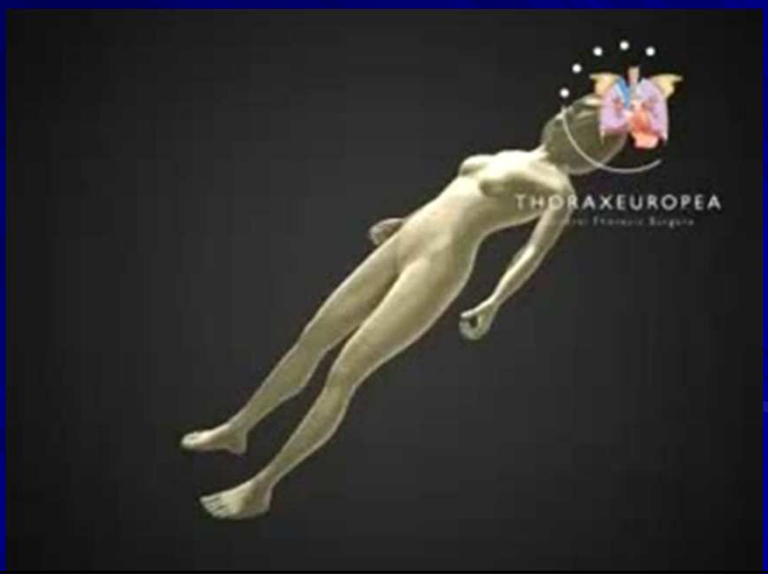
BIOAIR (Laboratory of Biomolecular and Bioengineering Airways), University of Florence, Florenz, Italy.

Abstract

Regenerative medicine offers new tools with which to tackle disorders for which there is currently no good therapeutic option. The trachea is an ideal organ in which to explore the clinical potential of tissue engineering because severe large airway disease is poorly managed by conventional treatments, and the success of a graft is determined only by its ability to conduct air lifelong: that is, whether it can become a sustainable biological conduit. We define the component parts of tissue engineering and review the experimental methods used to produce airway implants to date, including a recent successful, **first-in-man experience.**

Trachea transplantation

Example of adult stem cell-based tissue regeneration



Urethra engineering

Tissue-engineered autologous urethras for patients who need reconstruction: an observational study

Atlantida Raya-Rivera, Diego R Esquiliano, James J Yoo, Esther Lopez-Bayghen, Shay Soker, Anthony Atala

www.thelancet.com Published online March 8, 2011 DOI:10.1016/S0140-6736(10)62354-9

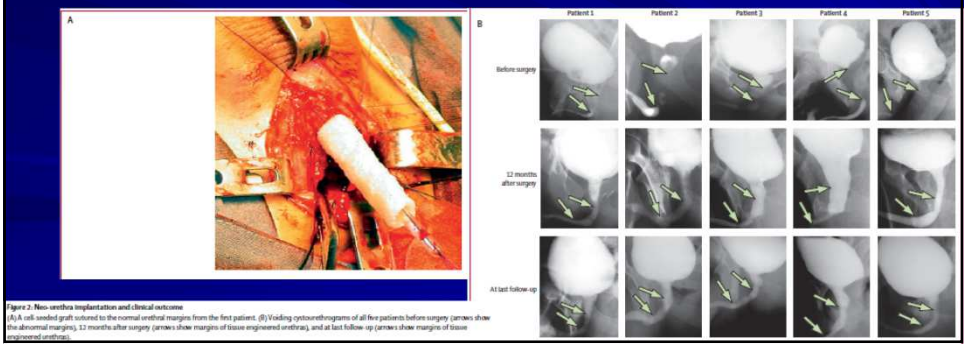


Figure 2: Neo-urethra implantation and clinical outcome
(A) A cell-seeded graft sutured to the normal urethral margins from the first patient. (B) Voiding cystourethrograms of all five patients before surgery (arrows show the abnormal margins), 12 months after surgery (arrows show margins of tissue engineered urethras), and at last follow-up (arrows show margins of tissue engineered urethras).

Potential treatments

Heart damage

Several clinical trials targeting heart disease have shown that adult stem cell therapy is safe, effective, and equally efficient in treating old and recent infarcts. Adult stem cell therapy for treating heart disease was commercially available in at least five continents at the last count (2007).

<u>Possible mechanisms of recovery include:</u>

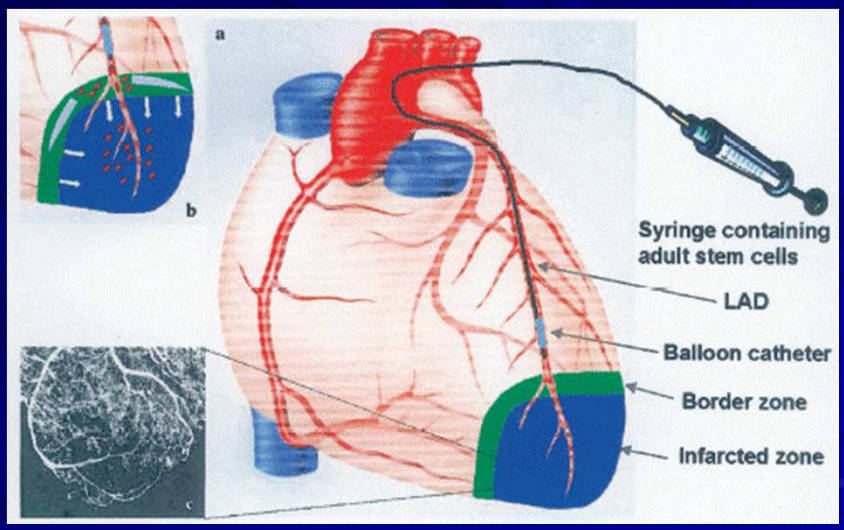
Generation of heart muscle cells

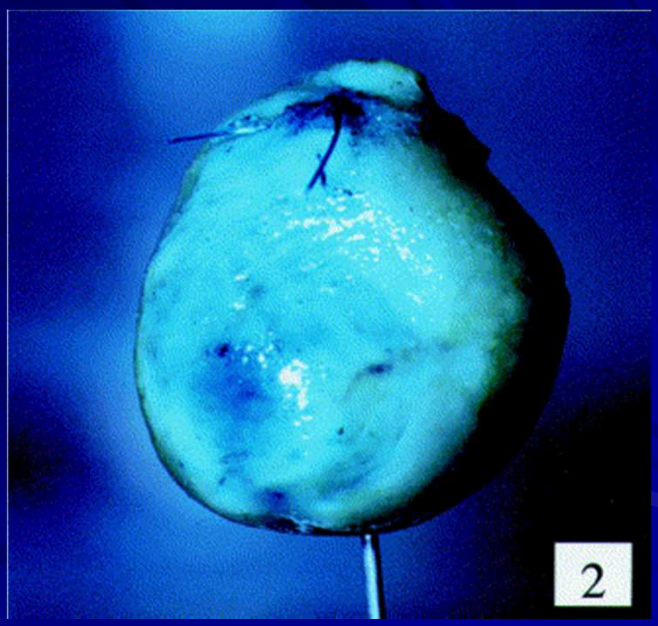
Stimulation of growth of new blood vessels to repopulate damaged heart tissue

Secretion of growth factors

Assistance via some other mechanism

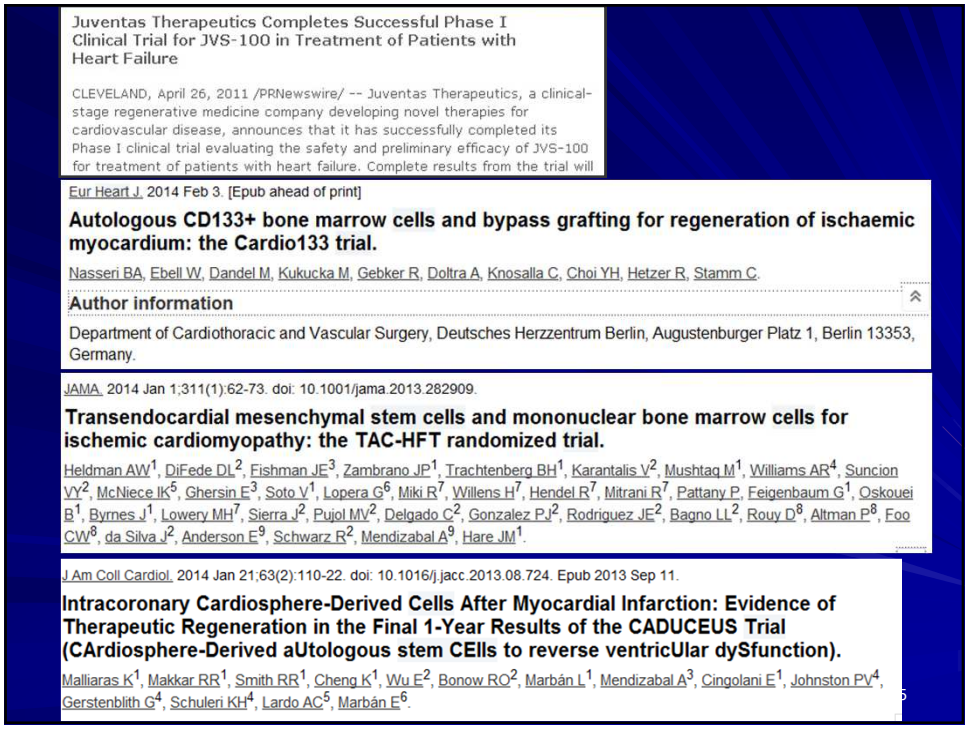
It may be possible to have adult bone marrow cells differentiate into heart muscle cells.





Experimental model system

Heart muscle cells beating in a petri dish



Juventas Therapeutics Completes Successful Phase I Clinical Trial for JVS-100 in Treatment of Patients with Heart Failure

CLEVELAND, April 26, 2011 /PRNewswire/ -- Juventas Therapeutics, a clinical-stage regenerative medicine company developing novel therapies for cardiovascular disease, announces that it has successfully completed its Phase I clinical trial evaluating the safety and preliminary efficacy of JVS-100 for treatment of patients with heart failure. Complete results from the trial will

Eur Heart J. 2014 Feb 3. [Epub ahead of print]

Autologous CD133+ bone marrow cells and bypass grafting for regeneration of ischaemic myocardium: the Cardio133 trial.

Nasseri BA, Ebell W, Dandel M, Kukucka M, Gebker R, Doltra A, Knosalla C, Choi YH, Hetzer R, Stamm C.

Author information

Department of Cardiothoracic and Vascular Surgery, Deutsches Herzzentrum Berlin, Augustenburger Platz 1, Berlin 13353, Germany.

JAMA. 2014 Jan 1;311(1):62-73. doi: 10.1001/jama.2013.282909.

Transendocardial mesenchymal stem cells and mononuclear bone marrow cells for ischemic cardiomyopathy: the TAC-HFT randomized trial.

Heldman AW[1], DiFede DL[2], Fishman JE[3], Zambrano JP[1], Trachtenberg BH[1], Karantalis V[2], Mushtaq M[1], Williams AR[4], Suncion VY[2], McNiece IK[5], Ghersin E[3], Soto V[1], Lopera G[6], Miki R[7], Willens H[7], Hendel R[7], Mitrani R[7], Pattany P, Feigenbaum G[1], Oskouei B[1], Byrnes J[1], Lowery MH[7], Sierra J[2], Pujol MV[2], Delgado C[2], Gonzalez PJ[2], Rodriguez JE[2], Bagno LL[2], Rouy D[8], Altman P[8], Foo CW[8], da Silva J[2], Anderson E[9], Schwarz R[2], Mendizabal A[9], Hare JM[1].

J Am Coll Cardiol. 2014 Jan 21;63(2):110-22. doi: 10.1016/j.jacc.2013.08.724. Epub 2013 Sep 11.

Intracoronary Cardiosphere-Derived Cells After Myocardial Infarction: Evidence of Therapeutic Regeneration in the Final 1-Year Results of the CADUCEUS Trial (CArdiosphere-Derived aUtologous stem CElls to reverse ventricULar dySfunction).

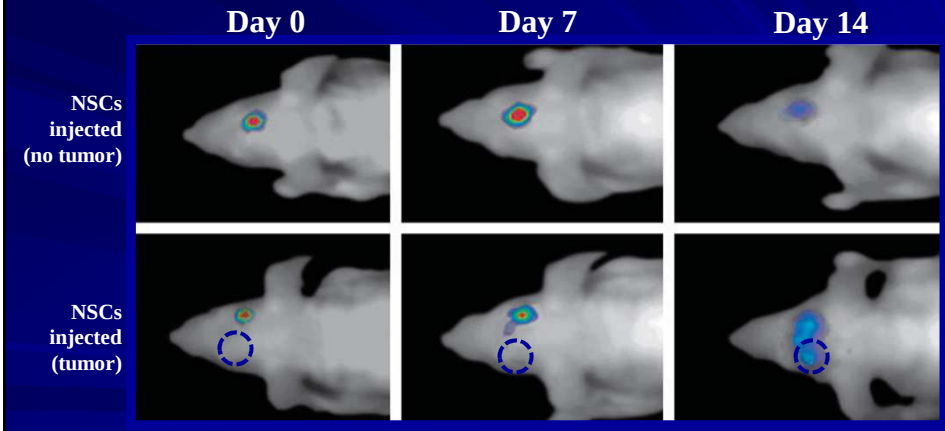
Malliaras K[1], Makkar RR[1], Smith RR[1], Cheng K[1], Wu E[2], Bonow RO[2], Marbán L[1], Mendizabal A[3], Cingolani E[1], Johnston PV[4], Gerstenblith G[4], Schuleri KH[4], Lardo AC[5], Marbán E[6].

Cancer

The development of gene therapy strategies for treatment of intra-cranial tumours offers much promise, and has shown to be successful in the treatment of some dogs; although research in this area is still at an early stage. Using conventional techniques, brain cancer is difficult to treat because it spreads so rapidly. Researchers at the Harvard Medical School transplanted human neural stem cells into the brain of rodents that received intracranial tumours. Within days, the cells migrated into the cancerous area and produced cytosine deaminase, an enzyme that converts a non-toxic pro-drug into a chemotheraputic agent. As a result, the injected substance was able to reduce the tumor mass by 81 percent. The stem cells neither differentiated nor turned tumorigenic. Some researchers believe that the key to finding a cure for cancer is to inhibit proliferation of cancer stem cells. Accordingly, current cancer treatments are designed to kill cancer cells. However, conventional chemotherapy treatments cannot discriminate between cancerous cells and others. Stem cell therapies may serve as potential treatments for cancer

Stem cells for drug delivery

More focused delivery, fewer side affects



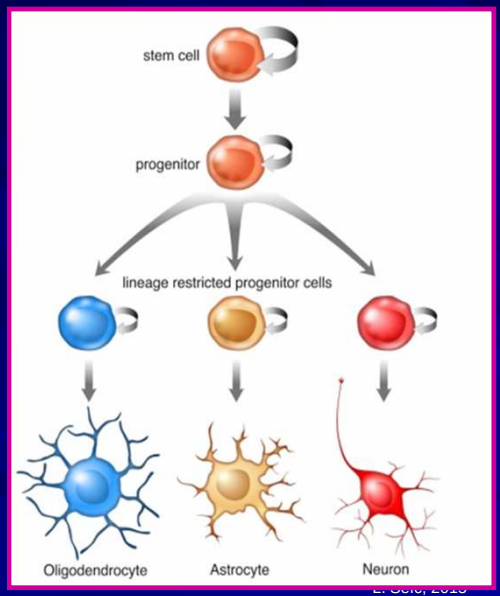
Shah et al. *Dev Neurosci* 2004

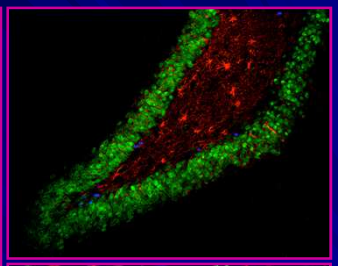
Brain damage

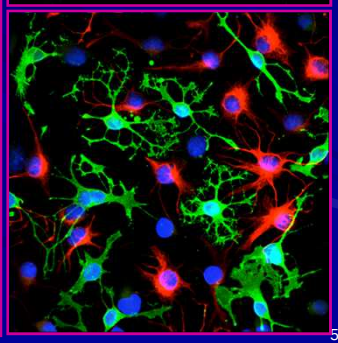
Stroke and traumatic brain injury lead to cell death, characterized by a loss of neurons and oligodendrocytes within the brain. Healthy adult brains contain neural stem cells which divide to maintain general stem cell numbers, or become progenitor cells. In healthy adult animals, progenitor cells migrate within the brain and function primarily to maintain neuron populations for olfaction (the sense of smell). Interestingly, in pregnancy and after injury, this system appears to be regulated by growth factors and can increase the rate at which new brain matter is formed. Although the reparative process appears to initiate following trauma to the brain, substantial recovery is rarely observed in adults, suggesting a lack of robustness.

Stem cells may also be used to treat brain degeneration, such as in Parkinson's and Alzheimer's disease.

Stem cells in the adult brain







Spinal cord injury

A team of Korean researchers reported on November 25, 2003, that they had transplanted multipotent adult stem cells from umbilical cord blood to a patient suffering from a spinal cord injury and that following the procedure, she could walk on her own, without difficulty. The patient had not been able to stand up for roughly 19 years. For the unprecedented clinical test, the scientists isolated adult stem cells from umbilical cord blood and then injected them into the damaged part of the spinal cord.

According to the October 7, 2005 issue of The Week, University of California, Irvine researchers transplanted multipotent human fetal-derived neural stem cells into paralyzed mice, resulting in locomotor improvements four months later. The observed recovery was associated with differentiation of transplanted cells into new neurons and oligodendrocytes- the latter of which forms the myelin sheath around axons of the central nervous system, thus insulating neural impulses and facilitating communication with the brain.

Spinal cord injury

Example of embryonic stem cell-based therapy

Stem Cells. 2012 Mar 13. doi: 10.1002/stem.1079. [Epub ahead of print]

Lumbar Intraspinal Injection of Neural Stem Cells in Patients with ALS: Results of a Phase I Trial in 12 Patients.

Glass JD, Boulis NM, Johe K, Rutkove SB, Federici T, Polak M, Kelly C, Feldman EL.

Department of Neurology, Emory University School of Medicine, Atlanta, GA 30322 USA. jglas03@emory.edu.

Ann Neurol. 2014 Feb 7. doi: 10.1002/ana.24113. [Epub ahead of print]

Intraspinal Neural Stem Cell Injections in ALS Subjects: Phase I Trial Outcomes.

Feldman EL, Boulis NM, Hur J, Johe K, Rutkove SB, Federici T, Polak M, Bordeau J, Sakowski SA, Glass JD.

Author information

Department of Neurology, University of Michigan, Ann Arbor, MI, USA.

- A Phase I Study to Assess the Feasibility, Safety, and Tolerability of Autologous Mesenchymal Stem Cell Transplantation in Patients With Relapsing Forms of Multiple Sclerosis (Clinical Trials.Gov Identifier: NCT00813969)

STEM CELLS AND DEVELOPMENT
Volume 22, Number 15, 2013
© Mary Ann Liebert, Inc.
DOI: 10.1089/scd.2013.0089

COMPREHENSIVE REVIEW

The Rise of Cell Therapy Trials for Stroke: Review of Published and Registered Studies

Paulo Henrique Rosado-de-Castro,[1] Pedro Moreno Pimentel-Coelho,[2] Lea Mirian Barbosa da Fonseca,[1] Gabriel Rodriguez de Freitas,[2,3] and Rosalia Mendez-Otero[2]

Bridging of peripheral nerve gaps

Cell Transplant. 2013 Nov 21. [Epub ahead of print]

Stem Cell Salvage of injured peripheral nerve.

Grimoldi N, Colleoni F, Tiberio F, Vetrano IG, Cappellar A, Costa A, Belicchi M, Razini P, Giordano R, Spagnoli D, Pluderi M, Gatti S, Morbin M, Gaini SM, Rebulla P, Bresolin N, Torrente Y.

Abstract

We previously developed a collagen tube filled with autologous skin?derived stem cells (SDSCs) for bridging long rat sciatic nerve gaps. Here we present a case report describing a compassionate use of this graft for repairing poly?injured motor and sensory nerves of upper arms of a patient. Preclinical assessment was performed with collagen?SDSCs implantation in rats after sectioning sciatic nerve. For the patient, during the 3?year follow?up period, functional recovery of injured median and ulnar nerves was assessed by pinch gauge test and static two?point discrimination and touch test with monofilaments, along with electrophysiological and MRI examinations. Preclinical experiments in rats revealed rescue of sciatic nerve and no side effects of patient?derived SDSCs transplantation (30 and 180 days of treatment). In the patient treatment, motor and sensory functions of the median nerve demonstrated ongoing recovery post?implantation during the follow?up period. The results indicate that the collagen/SDSCs artificial nerve graft could be used for surgical repair of larger defects in major lesions of peripheral nerves, increasing patient quality of life by saving the upper arms from amputation.

PMID: 24268028 [PubMed - as supplied by publisher]

Bridging of peripheral nerve gaps

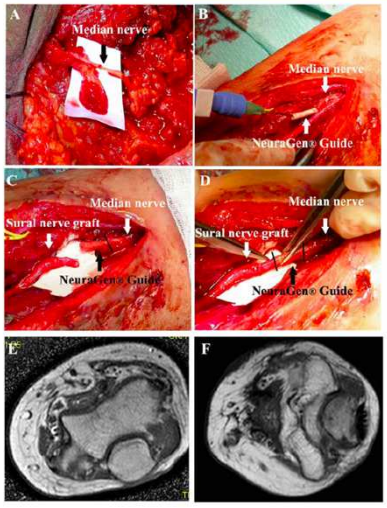


FIGURE 1

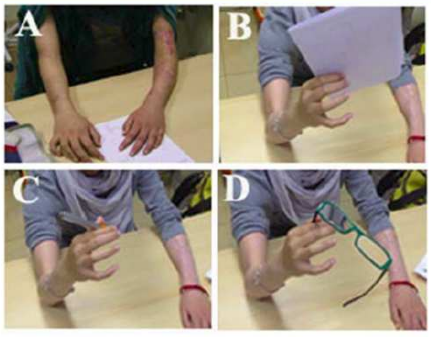
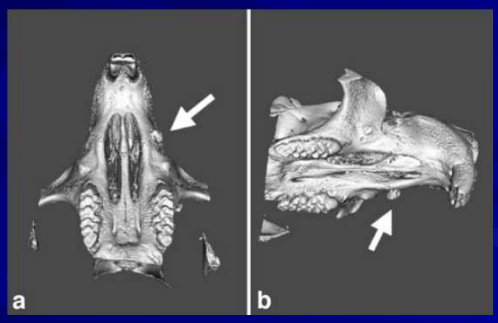


FIGURE 3

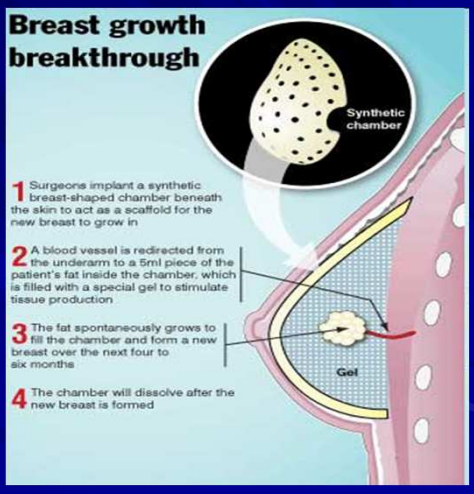
Missing teeth

Amanda H.-H. Yen & Paul T. Sharpe. Cell Stem cells and tooth tissue engineering Tissue Res (2008) 331:359–372

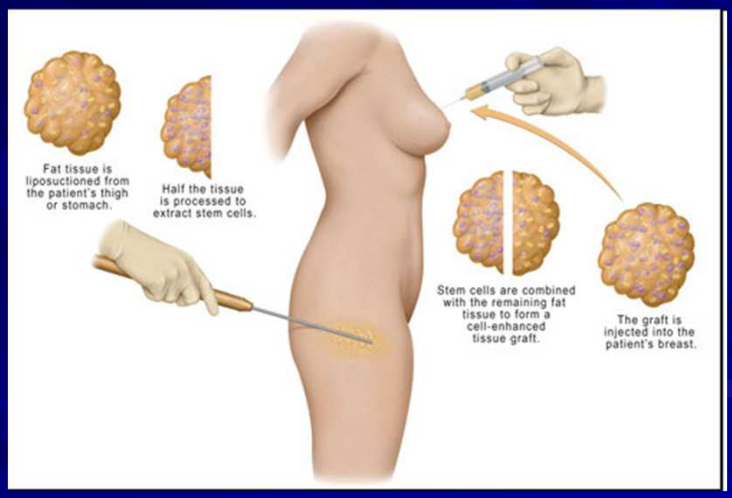


Implanted tooth germ grown in the diastema. Transplanted mouse incisor tooth germ (E13) after 20 days in the maxillary diastema of an adult mouse. The tooth has erupted. a Horizontal view. b Lateral view

Breast regrowth



Breast augmentation



TheScientificWorldJOURNAL (2011) 11, 2567–2578
ISSN 1537-744X; doi:10.1100/2011/323989

TheScientificWorldJOURNAL
www.thescientificworld.com

Tissue Engineering of the Penis

Manish N. Patel and Anthony Atala

Wake Forest Institute for Regenerative Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, USA

Received 10 July 2010; Accepted 27 August 2010

Diabetes

NEW STRAITS TIMES THURSDAY, APRIL 12, 2007

Stem cells may end d

WASHINGTON: Diabetics using stem-cell therapy have been able to stop taking insulin injections for the first time, after their bodies started to produce the hormone naturally again.

In a breakthrough trial, 15 young patients with newly-diagnosed Type 1 diabetes were given drugs to suppress their immune systems, followed by transfusions of stem cells drawn from their own blood.

The results show that insulin-dependent diabetics can be freed from reliance on needles by an injection of their own stem cells. The therapy could signal a revolution in the treatment of the condition, which affects millions.

People with Type 1 diabetes have to give themselves regular injections to control blood-sugar levels, as their ability to create the hormone naturally is destroyed by an immune disorder.

All but two of the volunteers in the trial, details of which were published yesterday in the *Journal of the American Medical Association*, did not need daily insulin injections up to three years after stopping their treatment regimes.

The findings were released yesterday as the future of US stem-cell research was being debated in Washington.

Stem cells are immature, unprogrammed cells that have the ability to grow into different kinds of tissue and can be sourced from people of all ages.

Previous studies have suggested that stem-cell therapies offer huge potential to treat a variety of diseases, such as Alzheimer's, Parkinson's and motor neuron disease.

A study by British scientists in November also reported that stem-cell injections could repair organ damage in heart attack victims.

BEHIND THE B

1 Beta cells that make insulin in the pancreas are destroyed by white blood cells

White blood cell

Pancre

But research using the most versatile kind of stem cells — those acquired from human embryos — is currently opposed by powerful critics, including US President George W. Bush.

The journal the first clini the efficacy Type 1 diabe the chronic normally em hood or early

WS 17

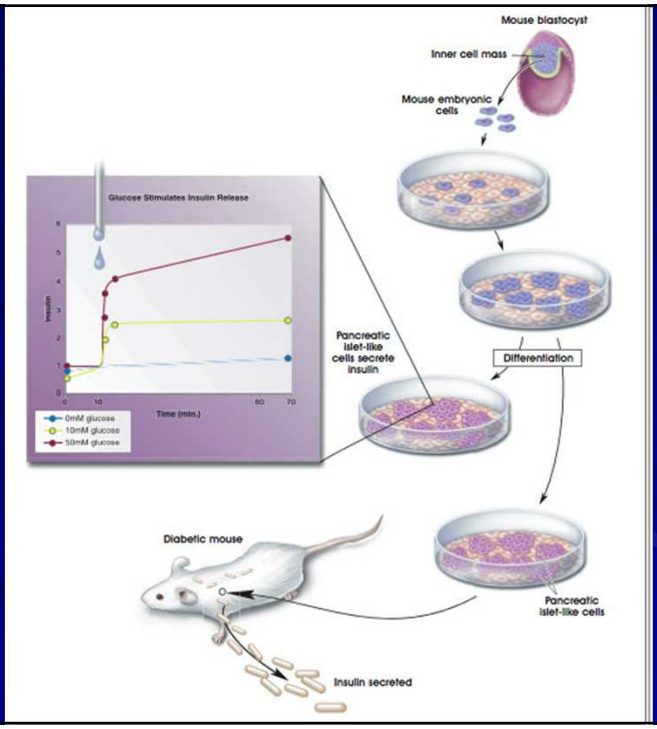
n control their els with pills or

dy, by a joint an and Ameri- found that one ents to undergo had not used ntal synthetic e years. raging results n a small num- with early-on- wrote the au- Julio Voltarelli, versity of São o Preto, Brazil. per cent of pa- different peri- independence -related toxicity o mortality." ably be five to fore we see a ing available," urt, a co-author n Northwestern nberg School of cago. —DM

Shimon Efrat *Editor*

STEM CELL THERAPY FOR DIABETES

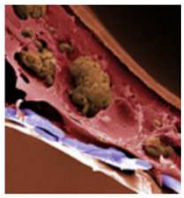
Humana Press



70

Next Phase to Begin for the Bioartificial Pancreas, Islet Sheet

by ELIZABETH SNOUFFER *on* 03/26/2012



Electron micrograph of a canine Islet Sheet.

Next week on Thursday 5th April 2012, the first large mammal (dog) pre-clinical study to determine the efficacy of the Islet Sheet, or bioartificial pancreas, is slated to take place at Cedars-Sinai lab in Los Angeles.

The Islet Sheet Project expects to begin clinical trials in 2013. This can be life-changing news for people with type 1 diabetes and their loved ones. We're committed to real progress, not promises. Please read on … and join us.

"We believe this technology has significant potential to be considered a 'cure' for type 1 diabetes."

— The authors of *Targeting a Cure for Type 1 Diabetes*

Whole-Organ Tissue Engineering: Decellularization and Recellularization of Three-Dimensional Matrix Scaffolds

Stephen F. Badylak,[1,2] Doris Taylor,[3,4] and Korkut Uygun[5,6]

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[2]McGowan Institute for Regenerative Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania 15219

[3]Center for Cardiovascular Repair, University of Minnesota, Minneapolis, Minnesota 55455; email: dataylor@umn.edu

[4]Department of Integrative Biology and Physiology, University of Minnesota, Minneapolis, Minnesota 55455

[5]Center for Engineering in Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts 02114; email: kuygun@partners.org

[6]Shriners Hospitals for Children, Boston, Massachusetts 02114

Annu. Rev. Biomed. Eng. 2011. 13:27–53

The *Annual Review of Biomedical Engineering* is online at bioeng.annualreviews.org

This article's doi: 10.1146/annurev-bioeng-071910-124743

1523-9829/11/0815-0027$20.00

NATURE COMMUNICATIONS | ARTICLE

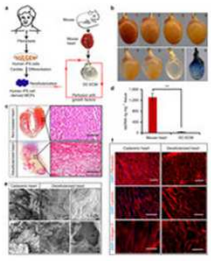
Repopulation of decellularized mouse heart with human induced pluripotent stem cell-derived cardiovascular progenitor cells

Tung-Ying Lu, Bo Lin, Jong Kim, Mara Sullivan, Kimimasa Tobita, Guy Salama & Lei Yang

Affiliations | Contributions | Corresponding author

Nature Communications **4**, Article number: 2307 | doi:10.1038/ncomms3307
Received 18 March 2013 | Accepted 15 July 2013 | Published 13 August 2013

Figure 1: Decellularization of mouse heart.



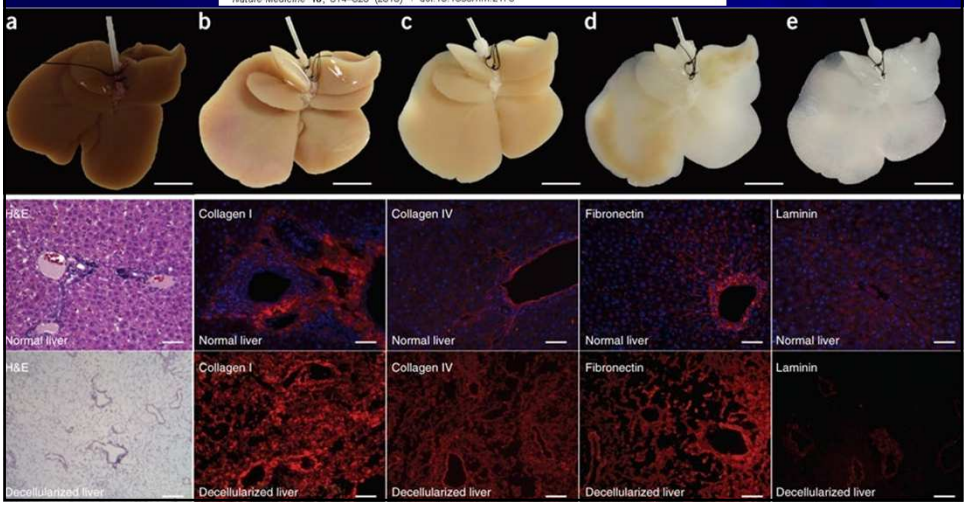
NATURE MEDICINE | TECHNICAL REPORT

Organ reengineering through development of a transplantable recellularized liver graft using decellularized liver matrix

Basak E Uygun, Alejandro Soto-Gutierrez, Hiroshi Yagi, Maria-Louisa Izamis, Maria A Guzzardi, Carley Shulman, Jack Milwid, Naoya Kobayashi, Arno Tilles, Francois Berthiaume, Martin Hertl, Yaakov Nahmias, Martin L Yarmush & Korkut Uygun

Affiliations | Contributions | Corresponding author

Nature Medicine **16**, 814–820 (2010) | doi:10.1038/nm.2170



Published Online June 24 2010
Science 30 July 2010:
Vol. 329 no. 5991 pp. 538-541
DOI: 10.1126/science.1189345

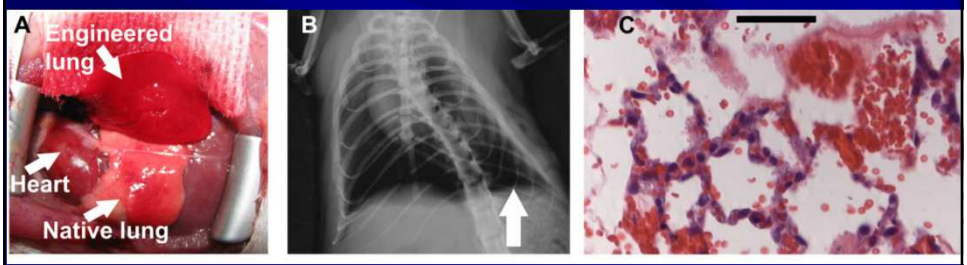
RESEARCH ARTICLE

Tissue-Engineered Lungs for in Vivo Implantation

Thomas H. Petersen[1,2], Elizabeth A. Calle[1], Liping Zhao[3], Eun Jung Lee[3], Liqiong Gui[3], MichaSam B. Raredon[1], Kseniya Gavrilov[4], Tai Yi[5], Zhen W. Zhuang[6], Christopher Breuer[5], Erica Herzog[6] and Laura E. Niklason[1,3,*]

± Author Affiliations

*To whom correspondence should be addressed. E-mail: laura.niklason@yale.edu



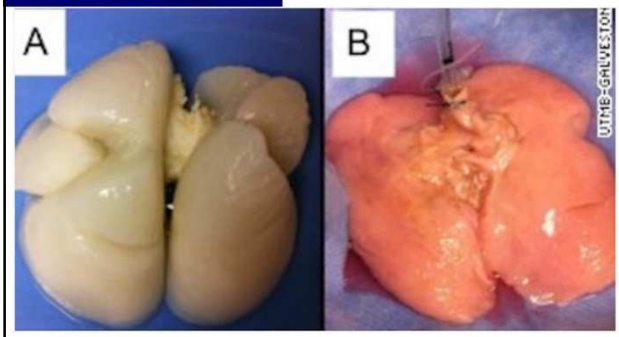
utmb Health | Institute for Translational Sciences

2nd Annual
Clinical & Translational Research Forum
February 12, 2014

T0: Basic Science Discovery - Preclinical basic and animal studies directed at mechanisms, targets and presentations of human disease	
Presented by:	**Vega, Stephanie P., B.S.** GSBS Student – Microbiology & Immunology Microbiology & Immunology

Tissue Engineered Human Lung Model System

Vega SP, GSBS, Internal Medicine & Infectious Disease, Argueta LB, GSBS, Internal Medicine & Infectious Disease, Eastaway AC, SOM, Niles JA, Internal Medicine & Infectious Disease, Cortiella J, Anesthesiology, Nichols JE, GSBS, SOM, Internal Medicine & Infectious Disease



The lab-grown lung before and after being reseeded with cells. Image credit: UTMB

76

Sci Transl Med. 2014 Jan 29;6(221):221ra14. doi: 10.1126/scitranslmed.3006894.

Bioengineering dermo-epidermal skin grafts with blood and lymphatic capillaries.

Marino D, Luginbühl J, Scola S, Meuli M, Reichmann E.

Author information

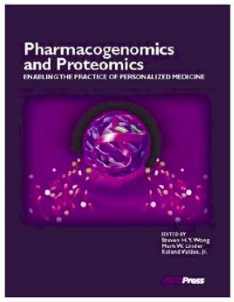
Tissue Biology Research Unit, Department of Surgery, University Children's Hospital Zurich, August Forel-Strasse 7, 8008 Zurich, Switzerland.

Veterinary use of nuclear transfer – cloning of near-extincted species

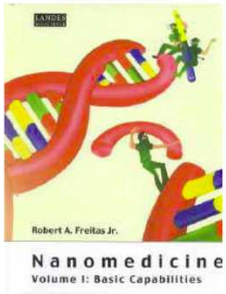
The progression of medicine and the evolution of nanomedicine

Conventional "Modern" Medicine → "Personalized" or "Molecular" Medicine + Nanomedicine Single-cell Medicine

Best guess on how to treat this particular patient…



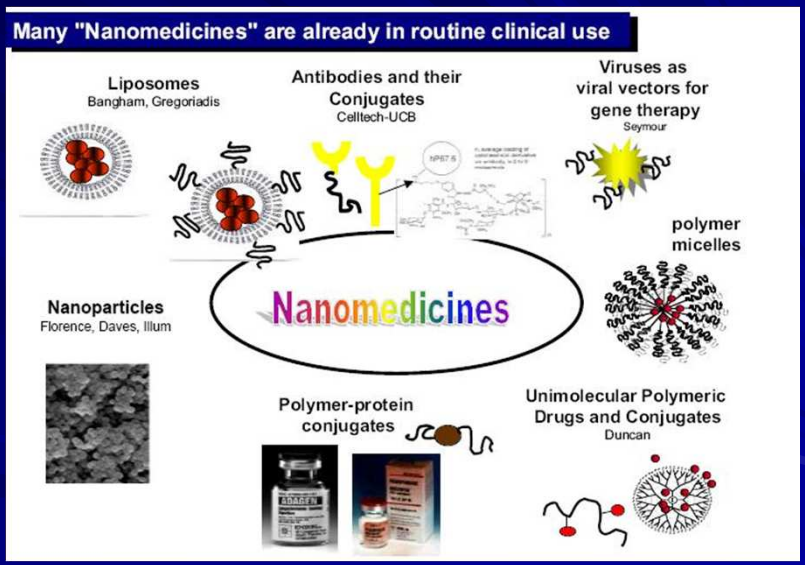
Should this patient receive this drug? Predictive medicine based on genomic info.



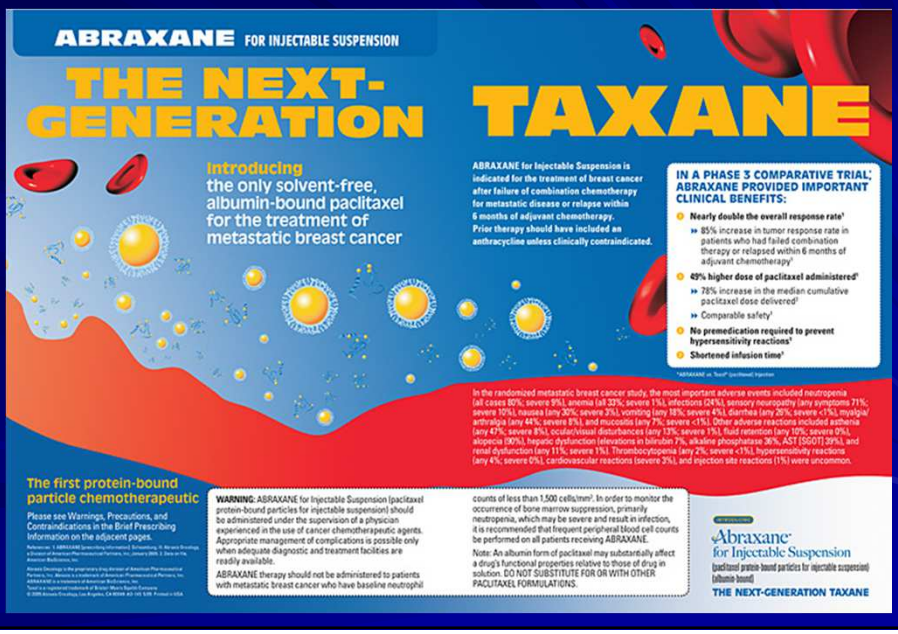
How can we target that drug to single cells to reduce side effects? 17

Nanomedicine

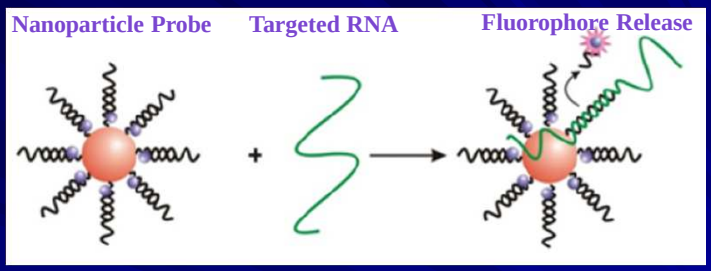
Many "Nanomedicines" are already in routine clinical use

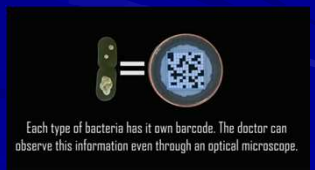


Drug carriers



Detection of pathogens





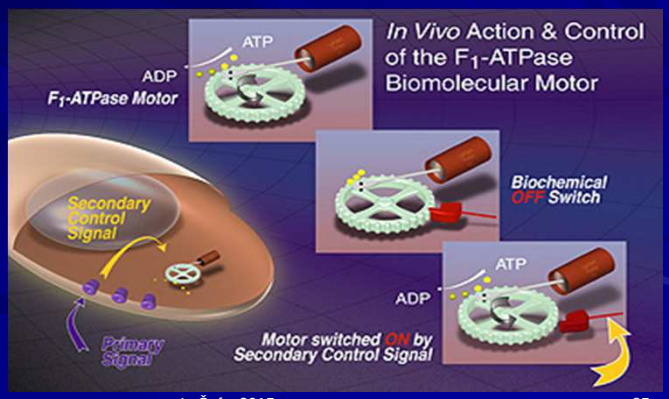
Power for nanorobots

Powering an Inorganic Nanodevice with a Biomolecular Motor

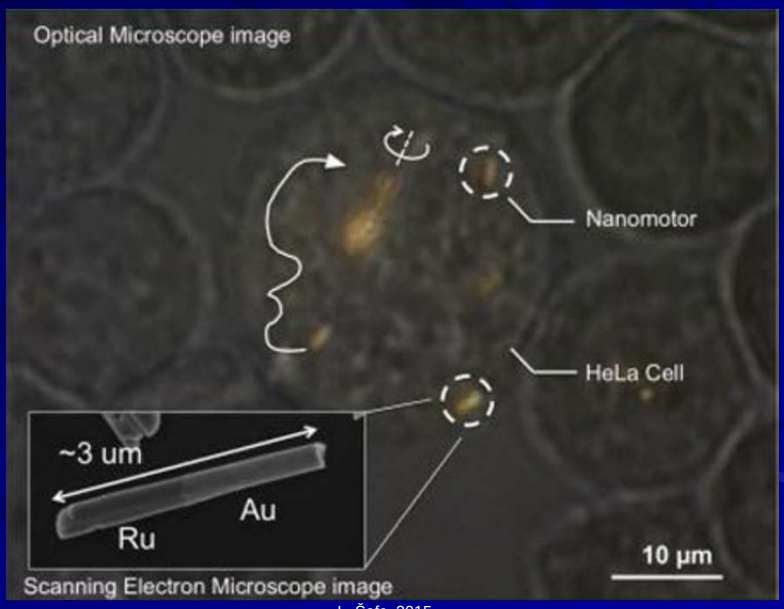
Ricky K. Soong[1,2], George D. Bachand[1,2], Hercules P. Neves[1,2], Anatoli G. Olkhovets[1,3], Harold G. Craighead[1,3], Carlo D. Montemagno[1,2,*]

Author Affiliations

[1] Nanobiotechnology Center,
[2] Department of Agricultural and Biological Engineering,
[3] School of Applied and Engineering Physics, Cornell University, Ithaca, NY 14853, USA.



Pohon nanorobotů



Power for nanorobots

nature COMMUNICATIONS

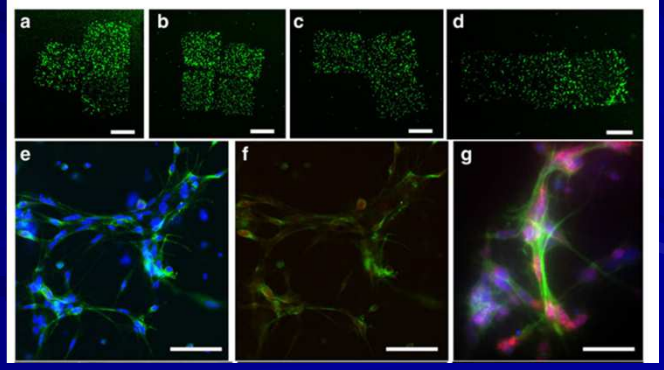
ARTICLE

Received 26 Sep 2013 | Accepted 16 Dec 2013 | Published 28 Jan 2014 DOI: 10.1038/ncomms4124

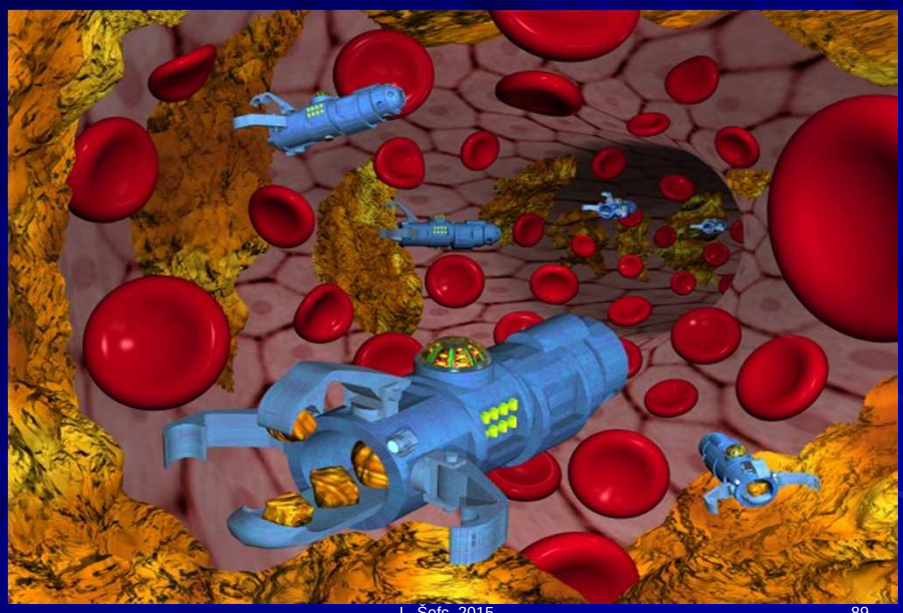
Untethered micro-robotic coding of three-dimensional material composition

S. Tasoglu[1,*], E. Diller[2,*], S. Guven[1], M. Sitti[2] & U. Demirci[1,3]

And the assembly of shapes using mouse stem cells:



Nanorobot cleaning atherosclerotic deposit

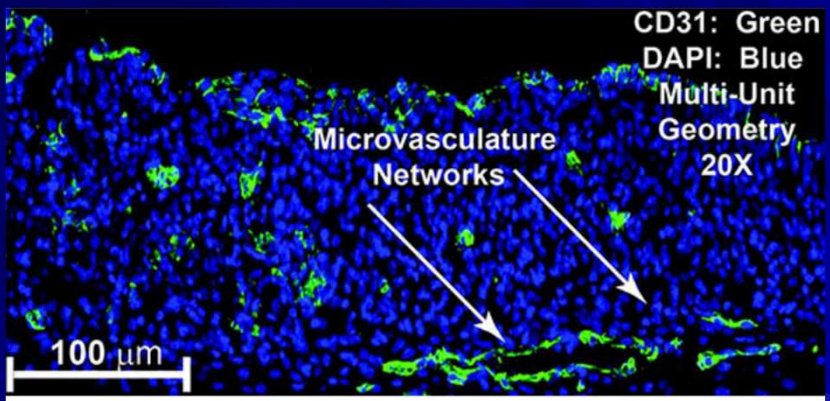


3D printers

organovo CHANGING THE SHAPE OF MEDICAL RESEARCH AND PRACTICE

3D HUMAN TISSUES | SCIENCE & TECHNOLOGY | PARTNERSHIP

3D printers



The image above shows bioprinted human liver with CD31+ microvessels (green) forming within the tissue.

3D printers

bladder

3D printers

NANO LETTERS
Letter
pubs.acs.org/NanoLett

3D Printed Bionic Ears

Manu S. Mannoor,[†] Ziwen Jiang,[†] Teena James,[‡] Yong Lin Kong,[†] Karen A. Malatesta,[†] Winston O. Soboyejo,[†] Naveen Verma,[§] David H. Gracias,[‡] and Michael C. McAlpine*[,†]

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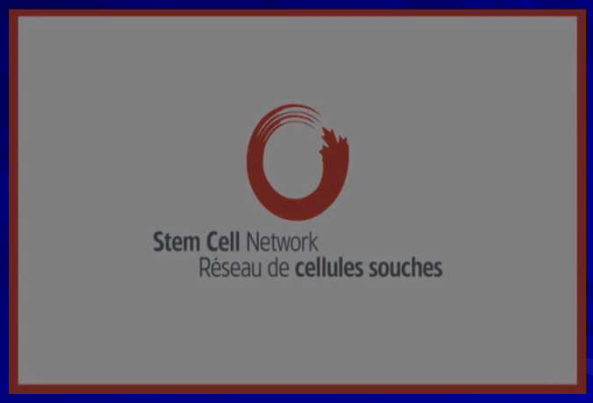
3D printers

Robocop



Science is discovering the unknown

- Stem cell field is still in its infancy
- Human embryonic stem cell research is a decade old, adult stem cell research has 30 year head start
- Holds hope for curing or improving treatments for 70+ diseases