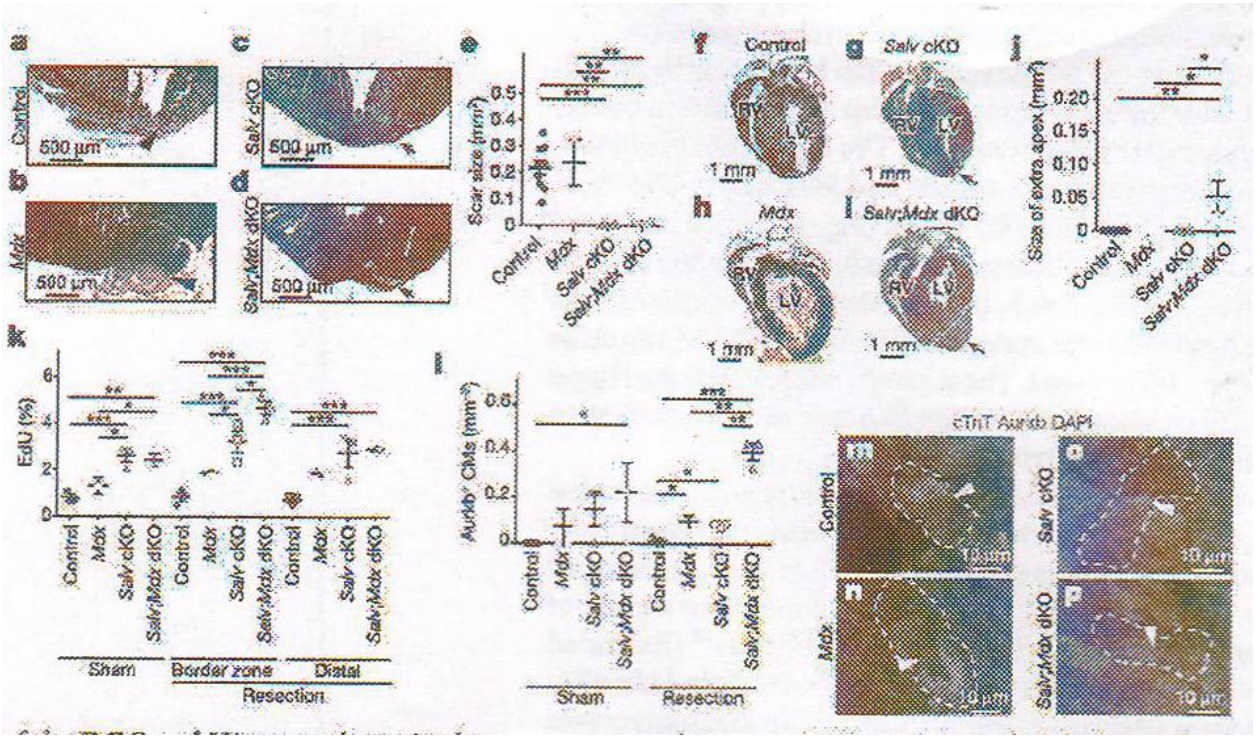
CARDIOMYOCYTE PROLIPHERATION

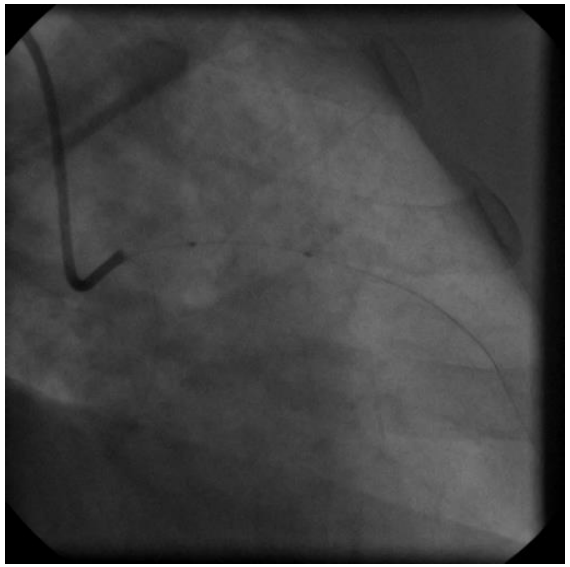


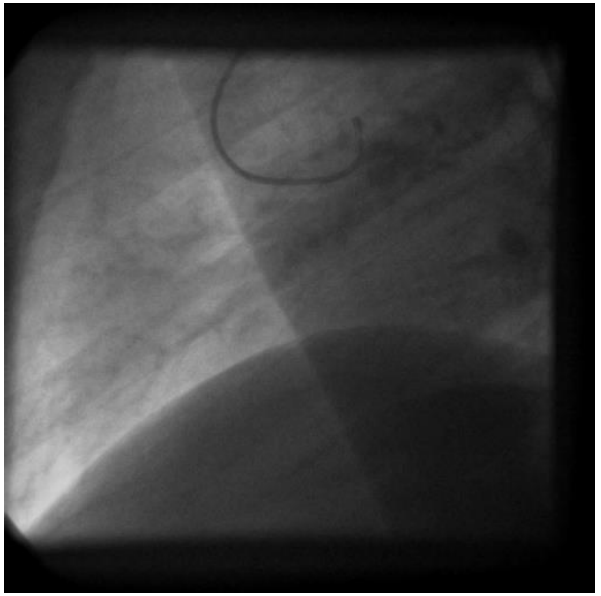
dva protichůdné názory na růst kardiomyocytů:

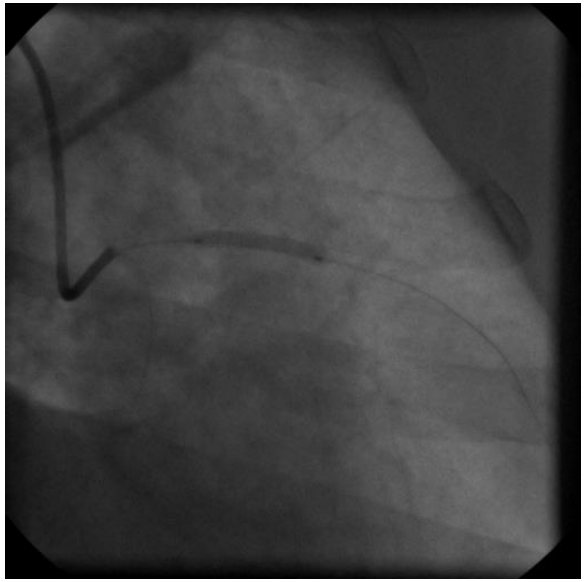
- první vidí srdce jako statický orgán, charakterizovaný konečným počtem kardiomyocytů žijících po dobu života organismu;

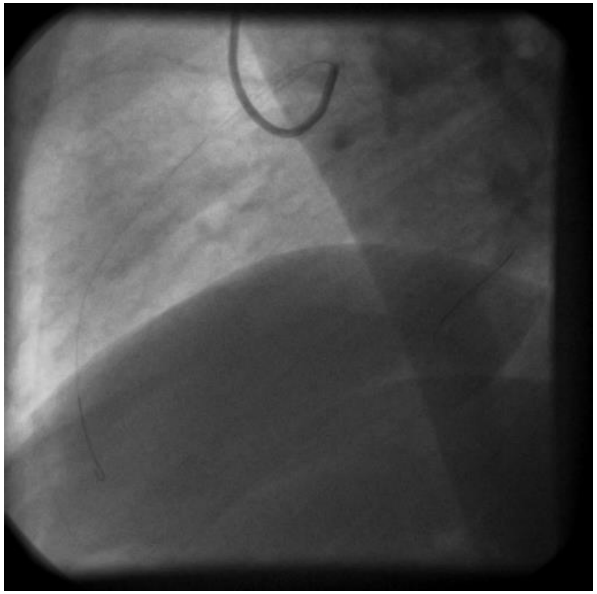
- druhý vidí srdce jako vysoce plastický orgán s kardiomyocyty schopnými mitózy a subcelulární obnovy na subcelulární úrovni zvláště po poranění

INDIKACE INTRAKORONÁRNÍHO PODÁNÍ KMENOVÝCH BUNĚK 2004



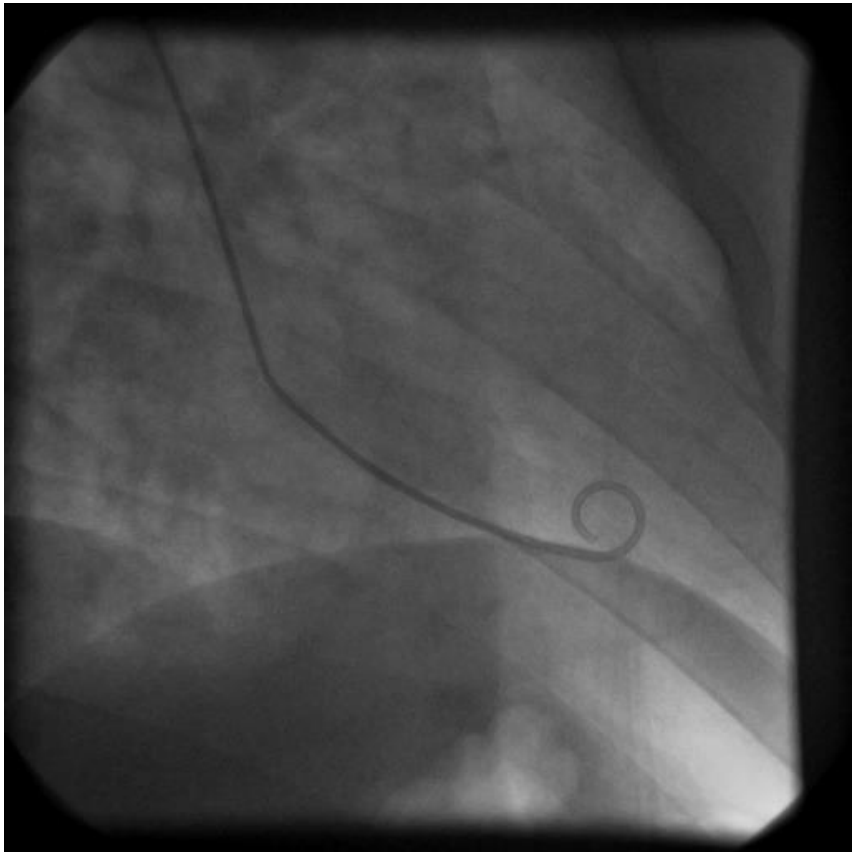


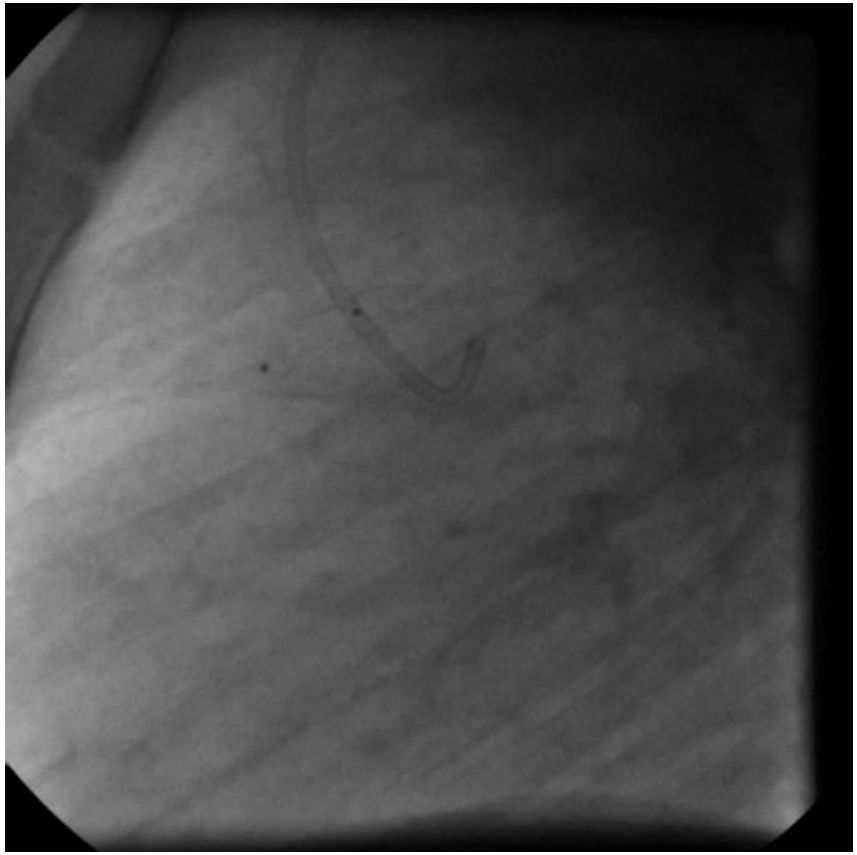




INTRAKORONÁRNÍ PODÁNÍ KMENOVÝCH BUNĚK 2004

J.P. 1960



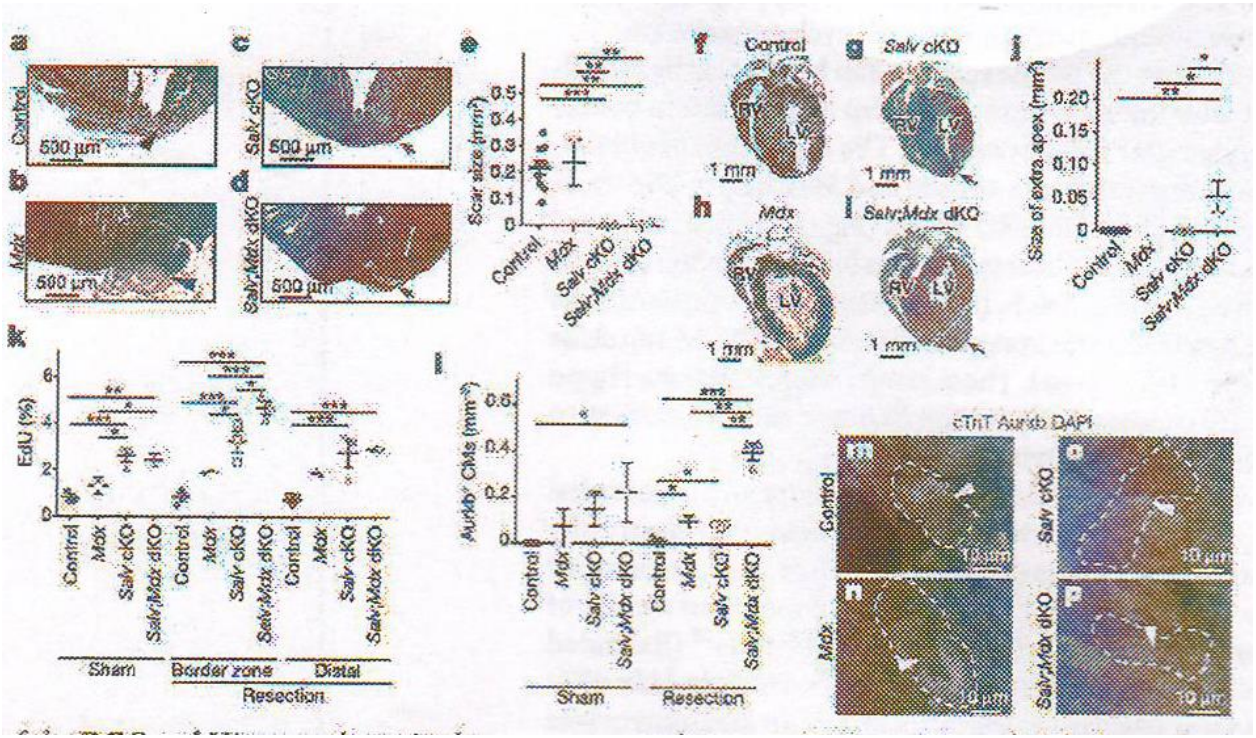


HLASOVÁNÍ

1. KDO SI MYSLÍ, ŽE U ČLOVĚKA SE KARDIOMYOCYTY BĚHEM ŽIVOTA OBNOVUJÍ ?

2. KDO SI MYSLÍ, ŽE MUSÍME DOŽÍT SE STEJNÝMI KARDIOMYOCYTY, S NIMIŽ JSME SE NARODILI?

CARDIOMYOCYTE PROLIPHERATION



CARDIOMYOCYTE PROLIPHERATION

Kardiomyocyty v experimentu na myších mají proliferativní schopnost do 7. dne po narození, potom se růst srdce děje pouze hypertrofií kardiomyocytů

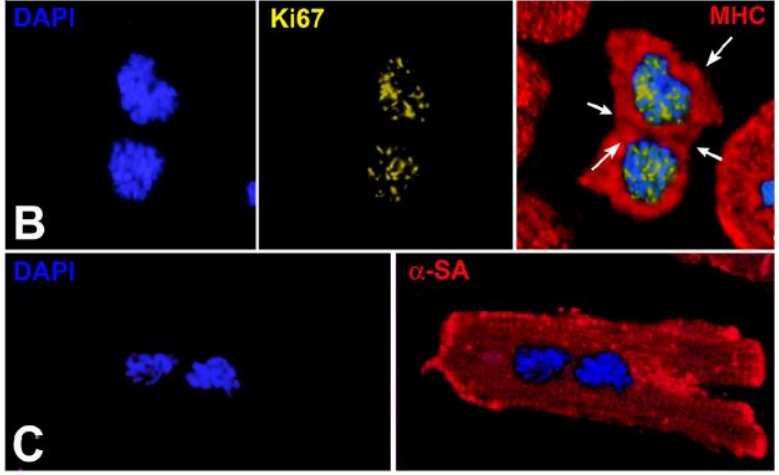


Figure 1.
Myocyte cytokinesis. **Panels A** and **B:**
labeled by the cell cycle protein Ki67 (
chain, MHC, red). Arrows point to cyto
binucleated mouse myocyte (α-sarcom

nature
International journal of science

Letter | Published: 05 April 2001

Bone marrow cells regenerate infarcted myocardium

Donald Orlic, Jan Kajstura, Stefano Chimenti, Igor Jakoniuk, Stacie M. Anderson, Baosheng Li, James Pickel, Ronald McKay, Bernardo Nadal-Ginard, David M. Bodine, Annarosa Leri & Piero Anversa

Nature **410**, 701–705 (05 April 2001) | Download Citation

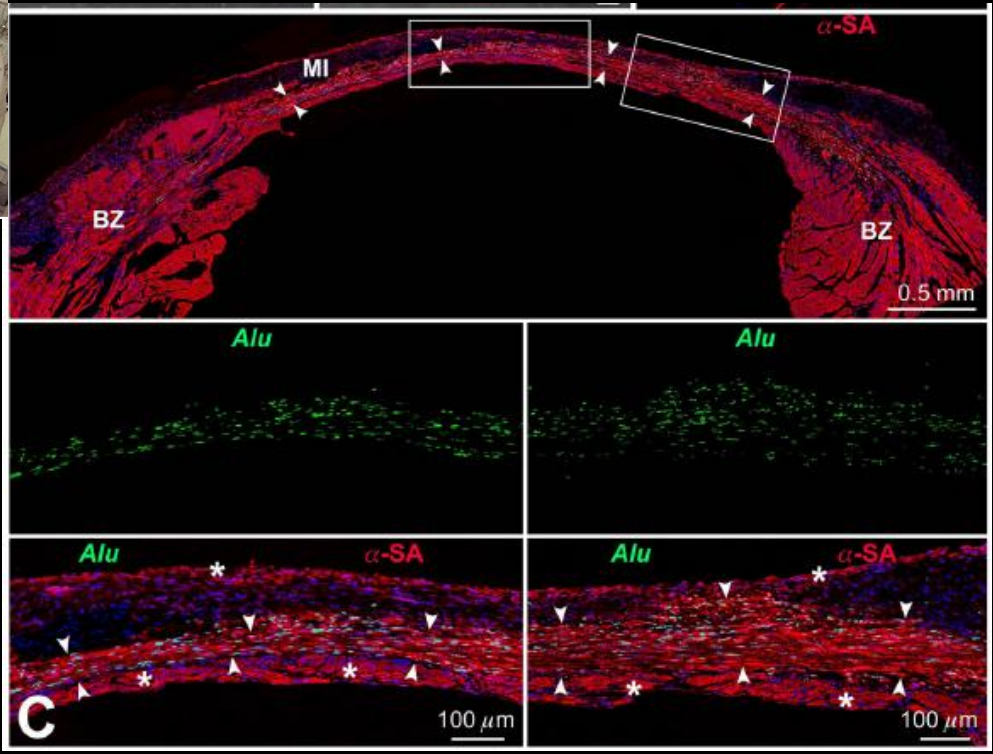
Published in final edited form as:
Circ Res. 2012 September 14; 111(7): 894–906. doi:10.1161/CIRCRESAHA.112.273649.

Tracking Chromatid Segregation to Identify Human Cardiac Stem Cells that Regenerate Extensively the Infarcted Myocardium

Jan Kajstura, **Yingnan Bai**, **Donato Cappetta**, **Junghyun Kim**, **Christian Arranto**, **Fumihiro Sanada**, **Domenico D'Amario**, **Alex Matsuda**, **Silvana Bardelli**, **João Ferreira-Martins**, **Toru Hosoda**, **Annarosa Leri**, **Marcello Rota**, **Joseph Loscalzo**, and **Piero Anversa**
Departments of Anesthesia and Medicine, and Division of Cardiovascular Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115

Abstract

Rationale—According to the immortal DNA strand hypothesis, dividing stem cells selectively segregate chromosomes carrying the old template DNA, opposing accumulation of mutations resulting from non-repaired replication errors and attenuating telomere shortening.




University of Miami
Hospital
"We all have stem cells. But only my UHealth
doctors used mine to heal my heart."

nature
International journal of science

Letter | Published: 21 March 2004

Haematopoietic stem cells do not transdifferentiate into cardiac myocytes in myocardial infarcts

Charles E. Murry ✉, Mark H. Soonpaa, Hans Reinecke, Hidehiro Nakajima, Hisako O. Nakajima, Michael Rubart, Kishore B. S. Pasumarthi, Jitka Ismail Virag, Stephen H. Bartelmez, Veronica Poppa, Gillian Bradford, Joshua D. Dowell, David A. Williams & Loren J. Field

Nature **428**, 664–668 (08 April 2004) | Download Citation ⬇

Abstract

The mammalian heart has a very limited regenerative capacity and, hence, heals by scar formation[1]. Recent reports suggest that

ır 21.

e into cardiac myocytes in myocardial

akajima HO, Rubart M, Pasumarthi KB, JD, Williams DA, Field LJ.

4 HSB, University of Washington, ton.edu

ve capacity and, hence, heals by scar etic stem cells can transdifferentiate e, hepatocytes, epithelial cells, neurons, tissue injury or placement in a new arts contain myocytes derived from nated from bone marrow. Although

results indicate that haematopoietic stem cells do not readily acquire a cardiac phenotype, and raise a cautionary note for clinical studies of infarct repair.

nature
International journal of science

Letter | Published: 21 March 2004

Haematopoietic stem cells adopt mature haematopoietic fates in ischaemic myocardium

Leora B. Balsam, Amy J. Wagers, Julie L. Christensen, Theo Kofidis, Irving L. Weissman & Robert C. Robbins

Nature **428**, 668–673 (08 April 2004) | Download Citation

Abstract

Under conditions of tissue injury, myocardial replication and regeneration have been reported[1]. A growing number of investigators

4 Mar 21.

topoietic fates in ischaemic myocardium.

Weissman IL, Robbins RC.

d University School of Medicine, Stanford,

lication and regeneration have been
e implicated adult bone marrow (BM) in
reservoir for cardiac precursor cells. It
to myocardium, and whether they do so
udied the ability of c-kit-enriched BM
- Sca-1+ long-term reconstituting
dium in an infarct model. Cells were
uorescent protein (GFP) and injected

Our data suggest that even in the microenvironment of the injured heart, c-kit-enriched BM cells, Lin- c-kit+ BM cells and c-kit+ Thy1.1(lo) Lin- Sca-1+ long-term reconstituting haematopoietic stem cells adopt only traditional haematopoietic fates.

Circulation. 2012 Oct 9;126(15):1869-81. doi: 10.1161/CIRCULATIONAHA.112.118380. Epub 2012 Sep 6.

Cardiomyogenesis in the aging and failing human heart.

Kajstura J[1], Rota M, Cappetta D, Ogórek B, Arranto C, Bai Y, Ferreira-Martins J, Signore S, Sanada F, Matsuda A, Kostyla J, Caballero MV, Fiorini C, D'Alessandro DA, Michler RE, del Monte F, Hosoda T, Perrella MA, Leri A, Buchholz BA, Loscalzo J, Anversa P.

Author information

The average age of cardiomyocytes, vascular endothelial cells (ECs), and fibroblasts and their turnover rates were measured by retrospective ^{14}C birth dating of cells in 19 normal hearts 2 to 78 years of age and in 17 explanted failing hearts 22 to 70 years of age. We report that the human heart is characterized by a significant turnover of ventricular myocytes

- Paper published in Circulation seemed to offer final proof that the heart could regenerate. He worked with a scientist at Lawrence Livermore National Laboratory, Bruce Buchholz, who measured carbon isotope levels in 36 hearts from people ranging in age from 2 to 78. **Because of nuclear testing done in the 1950s, older people were exposed to more radioactive isotopes than younger people.**
- **If the body cannot produce new heart cells, the amounts of radioactive carbon should have been higher in the heart cells of older people.**

RETRACTED ARTICLE

See: Retraction Notice

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Author information

Retraction in

Notice of retraction. [Circulation. 2014]

Abstract

BACKGROUND: Two opposite views of cardiac growth are currently held; one views the heart as a static organ characterized by a large number of cardiomyocytes that are present at birth and live as long as the organism, and the other views the heart a highly plastic organ in which the myocyte compartment is restored several times during the course of life.

METHODS AND RESULTS: The average age of cardiomyocytes, vascular endothelial cells (ECs), and fibroblasts and their turnover rates were measured by retrospective (14)C birth dating of cells in 19 normal hearts 2 to 78 years of age and in 17 explanted failing hearts 22 to 70 years of age. We report that the human heart is characterized by a significant turnover of ventricular myocytes, ECs, and fibroblasts, physiologically and pathologically. Myocyte, EC, and fibroblast renewal is very high shortly after birth, decreases during postnatal maturation, remains relatively constant in the adult organ, and increases dramatically with age. From 20 to 78 years of age, the adult human heart entirely replaces its myocyte, EC, and fibroblast compartment ≈8, ≈6, and ≈8 times, respectively. Myocyte, EC, and fibroblast regeneration is further enhanced with chronic heart failure.

CONCLUSIONS: The human heart is a highly dynamic organ that retains a remarkable degree of plasticity throughout life and in the presence of chronic heart failure. However, the ability to regenerate cardiomyocytes, vascular ECs, and fibroblasts cannot prevent the manifestations of myocardial aging or oppose the negative effects of ischemic and idiopathic dilated cardiomyopathy.

The New York Times

November 1, 2018

He Promised to Restore Damaged Hearts. Harvard Says His Lab Fabricated Research.

nature
International journal of science

Letter | Published: 05 April 2001

Bone marrow cells regenerate infarcted myocardium

Donald Orlic, Jan Kajstura, Stefano Chimenti, Igor Jakoniuk, Stacie M. Anderson, Baosheng Li, James Pickel, Ronald McKay, Bernardo Nadal-Ginard, David M. Bodine, Annarosa Leri & Piero Anversa

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Author information

Retraction in
Notice of retraction. [Circulation. 2014]

But the Harvard University said 31 scientific papers produced by Dr. Anversa's laboratories, going back to 2001, should be retracted

Department of Justice announced that Brigham and Women's Hospital and another Harvard-affiliated hospitals, would pay $10 million to settle allegations leading to inaccurately characterized cardiac stem cells, reckless or deliberately misleading record-keeping, and discrepancies and fabrications of data and images

Published in final edited form as:
Circulation. 2017 August 15; 136(7): 680–686. doi:10.1161/CIRCULATIONAHA.117.029343.

Cardiomyocyte Regeneration: A Consensus Statement

Thomas Eschenhagen, MD[1,*], Roberto Bolli, MD[2], Thomas Braun, MD[3], Loren J. Field, PhD[4], Bernd K. Fleischmann, MD[5], Jonas Frisén, MD, PhD[6], Mauro Giacca, MD[7], Joshua M. Hare, MD[8], Steven Houser, PhD[9,*], Richard T. Lee, MD[10], Eduardo Marbán, MD[11], James F. Martin, MD, PhD[12], Jeffery D. Molkentin, PhD[13], Charles E. Murry, MD, PhD[14], Paul R. Riley, PhD[15], Pilar Ruiz-Lozano, PhD[16], Hesham A. Sadek, MD, PhD[17,*], Mark A. Sussman, PhD[18], and Joseph A. Hill, MD, PhD[17,*]

- **Cell therapy is an exciting option for repairing the injured heart, one which has attracted considerable interest over the past 15 years. Consensus exists that the injection/infusion or tissue-based implantation of various cell types may exert therapeutic effects**, and there is general agreement that additional molecular, translational and clinical studies are required to define the optimal cell source, method of delivery, and underlying mechanism(s) of action.

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- During a brief postnatal window of **7 days in rodents**, myocardial injury induces a regenerative response resulting in **replacement of lost cardiomyocytes by new ones**. It remains **unclear** whether this regenerative window exists **in large animals or in humans**.

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- While cardiomyocytes appear to continue to renew throughout life, the quantitatively dominant mechanism of growth in the mammalian postnatal heart is an **increase in cardiomyocyte size**

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- In the healthy, uninjured adult human and murine heart, the total number of cardiomyocytes remains essentially stable, and **cardiomyocyte turnover** is currently estimated **at 0.5–2% per year in both species**.

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- Following cardiac injury in adult mammals cardiomyocyte renewal rates may be higher than under normal conditions

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- **After heart or bone marrow transplantation**

chimera

- Sex-mismatched heart transplantation in patients with end-stage heart failure or **sex-mismatched** bone marrow **transplantation** provide opportunities to ascertain experimentally **cardiomyocyte renewal deriving from extra-cardiac sources**.

- While data are not completely consistent, the preponderance of studies suggest that the level of cardiomyocyte **chimerism after sex-mismatched transplantation is <1%, and may arise at least partially from fusion events**.

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Therapeutic manipulation of cardiomyocyte renewal

- The degree of new cardiomyocyte formation depends on the cell type, as well as on retention and survival of those cells within the heart. **Retention of unselected bone marrow cells** in the heart is low (a study in patients determined a rate of **<3%** for unselected bone marrow cells and approximately **10-fold higher with CD34+ cells 1 hour after coronary infusion**). It may be higher following cell injection into the myocardium. Co-injection of scaffolding materials and use of tissue engineering approaches may increase this rate.

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Therapeutic manipulation of cardiomyocyte renewal

- The **degree of engraftment and differentiation of transplanted cells into cardiomyocytes does not appear to match the extent of functional improvement**, suggesting that other mechanisms account for at least part of the beneficial effects of cell therapy

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Therapeutic manipulation of cardiomyocyte renewal

- Mechanisms of benefit of cellular transplantation experiments **remain obscure** but may **involve paracrine actions**, including exosome-derived effects on pre-existing cardiac tissue, as well as **cell-specific post-translational protein modifications**

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Therapeutic manipulation of cardiomyocyte renewal

- Transplantation of cardiomyocytes derived from pluripotent stem cells can generate new myocardium **that beats in synchrony with the host myocardium** and may contribute to systolic force generation, although the extent of this contribution **has not been precisely determined**.

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Therapeutic manipulation of cardiomyocyte renewal

- Prevailing evidence suggests that **unfractionated bone marrow-derived cells do not become cardiomyocytes when infused or injected into the heart**.

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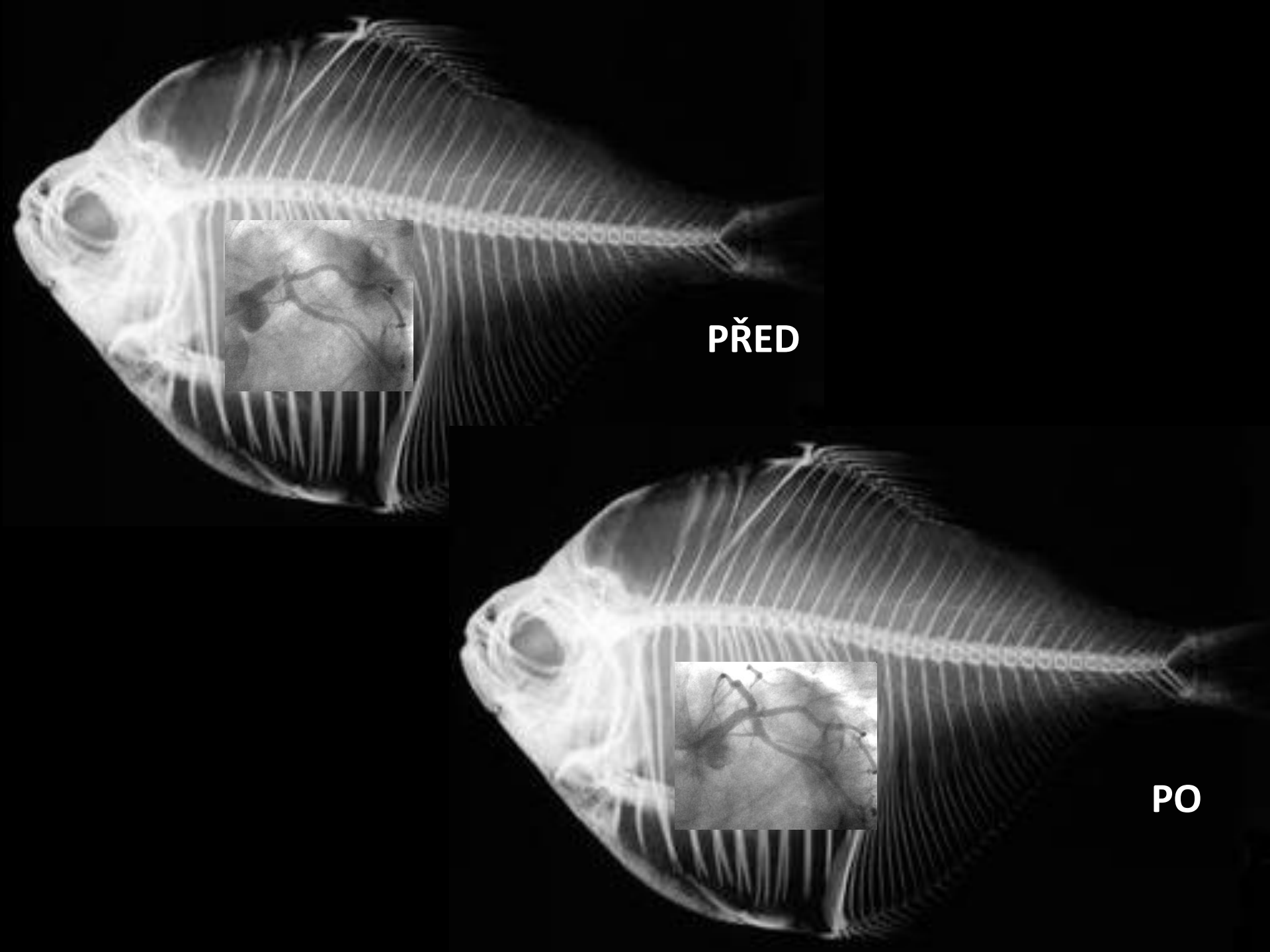
Therapeutic manipulation of cardiomyocyte renewal

- **Pluripotent cells**
- **Pluripotent stem cells (embryonic stem cells [ESCs] or induced pluripotent stem cells [iPSCs]) proliferate in an undifferentiated state indefinitely, and upon exposure to specific culture conditions can differentiate into almost all cell types of the organism including cardiomyocytes**.
- **Undifferentiated pluripotent stem cells can form teratomas** when injected into the heart of immunocompromised organisms.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