New challenges in Cardiology: stem cells and COVID-19

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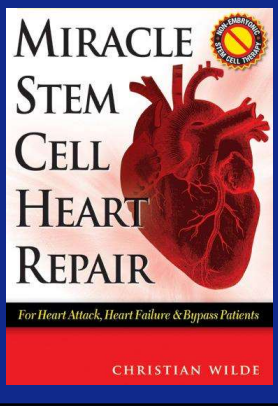
Can we rescue the damaged heart with stem cells?



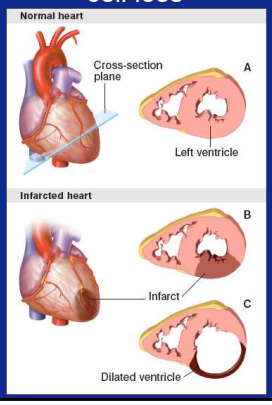
Myocyte number declines by <u>one third</u> during the lifespan of humans

Myocyte death ⟷ Myocyte renewal

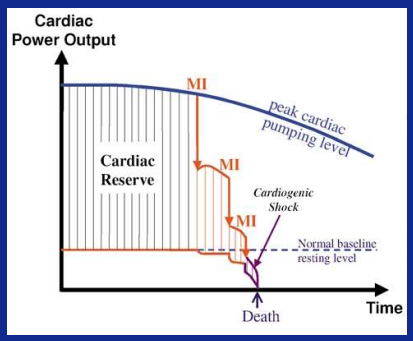
- Apoptosis
- Necrosis

Olivetti et al., Circ. Res. 68, 1560–1568, 1991.

Myocardial infarction is associated with massive cell loss



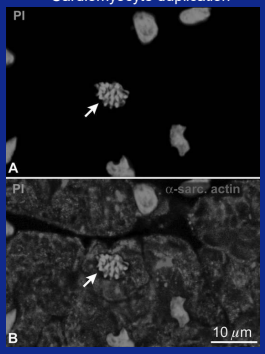
Cardiac aging is reflected in the decrease in cardiac reserve



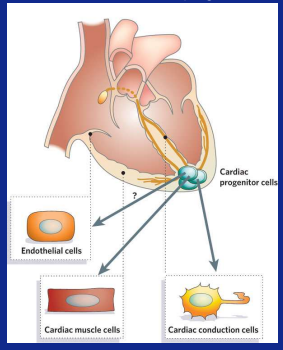
Goldspink et al., Exp. Physiol. 88, 447–458, 2003.

Physiological cardiomyocyte renewal

Cardiomyocyte duplication



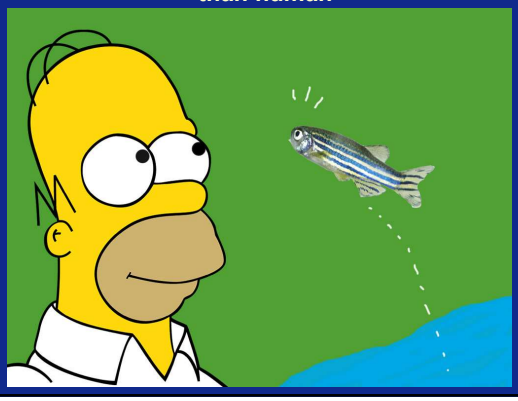
Differentiation from cardiac progenitor cells



Chimenti et al., Circ. Res. 93: 604-613, 2003

Srivastava & Ivey Nature 441, 1097-1099, 2006

Zebrafish has higher cardiac regenerative potential than human



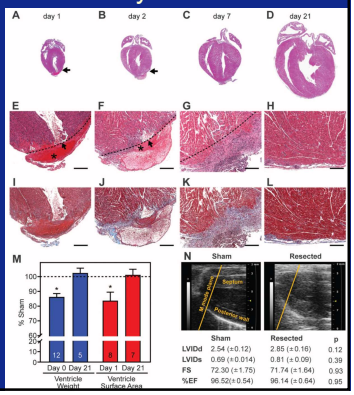
Cardiac progenitor stem cells have high regenerative potential only after birth

Characterization and functionality of cardiac progenitor cells in congenital heart patients

Mishra et al. Circulation 123 (2011)

Transient Regenerative Potential of the Neonatal Mouse Heart

Enzo R. Porrello, *et al. Science 331, 1078 (2011)*



Cardiac mass and cardiomyocyte number during aging

Myocyte death ⟷ Myocyte renewal

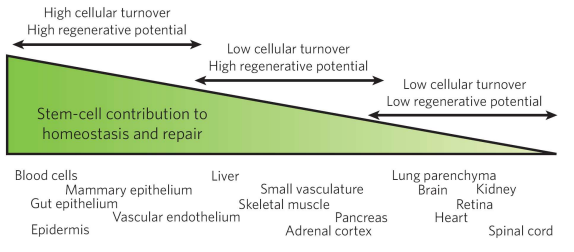
- Apoptosis
- Necrosis

- Differentiation of cardiac progenitor cells
- Cardiomyocyte duplication

Annual cardiomyocyte turnover declines from 2% to 0.5% during 60 years.

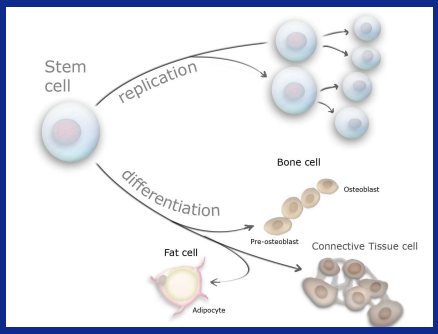
About 50% of the cardiomyocytes of an aged individual are present at birth.

Tissue heterogeneity and stem-cell functionality for homeostais and repair



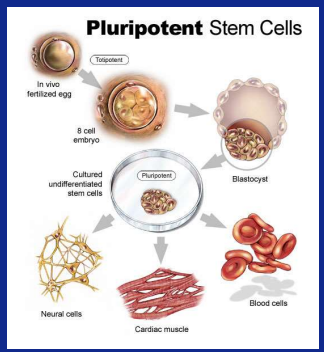
Rando, Nature 441: 1080-1086, 2006.

Stem cells



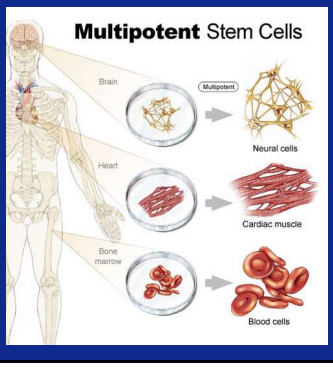
Embrionic stem cells have a high proliferative potential

Embrionic stem cells



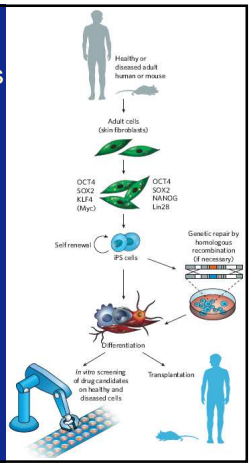
Adult stem cells can also differentiate into cardiomyocytes

Adult stem cells /
Somatic stem cells

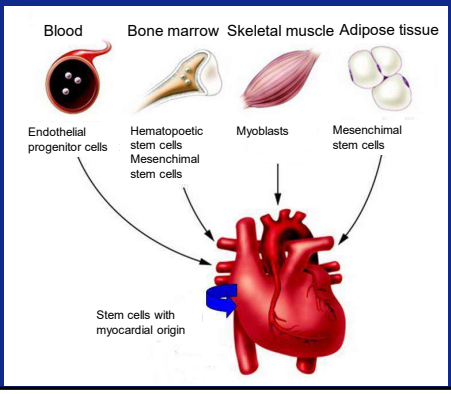


iPS
induced pluripotent stem cells

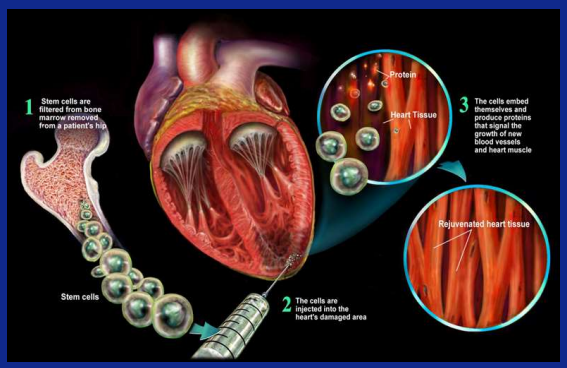
Pluripotency induced by transcription factors (Yamanaka)



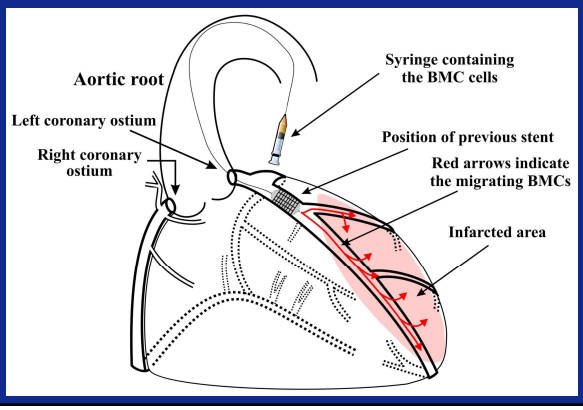
Potential stem cells for myocardial regeneration



Hematopoietic stem cell application following myocardial infarctions in humans



Intracoronary administration of BMCs

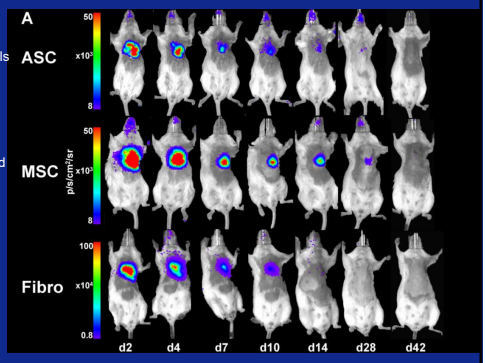


Drastic donor cell death within 4–5 weeks (bioluminescence imaging)

Adipose Stromal Cells

Bone marrow derived mesenchymal cells

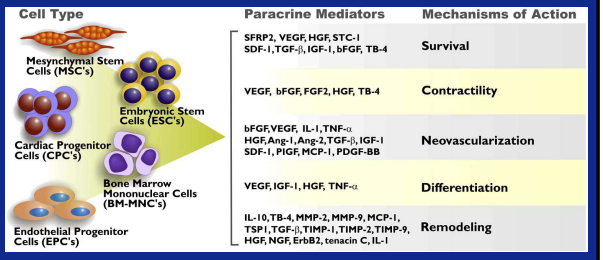
Control



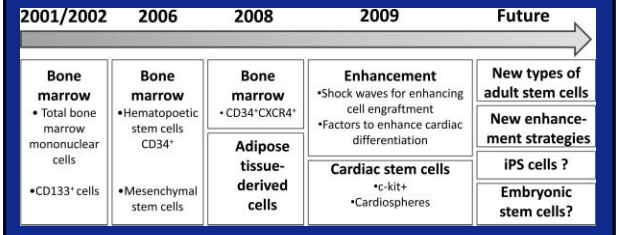
van der Bogt et al. *Transplantation*. 2009 87(5): 642–652.

Salvage of the damaged myocardium: paracrine effects?

Stem cells as „providers", „biofactories"

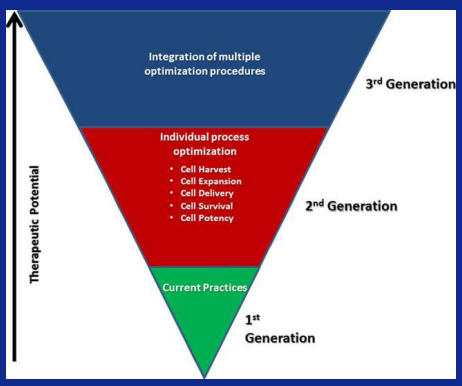


Evolution of clinical approaches



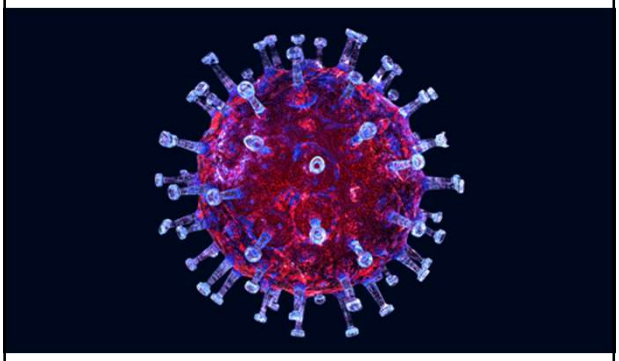
Chavakis, E., Circulation. 121(2): p. 325-35., 2010

Future directions of myocardial cell therapy

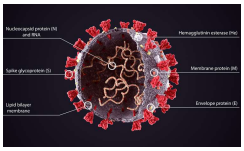


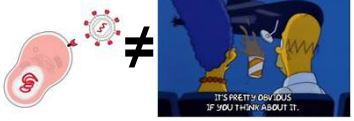
Copland et al. Semin Immunopathol. 2011 33(6):535-50.

SARS-CoV-2 coronavirus



SARS-CoV-2 Inventory

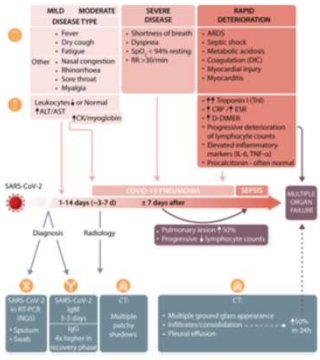


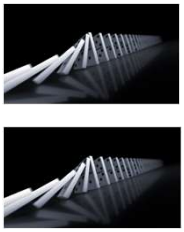


Proteins: Spike (S), Envelope (E), Membrane (M), Nucleocapsid (N), Hemagglutinin esterase (He)

Genome: 29,900 nucleotides of RNA

The clinical course of COVID-19

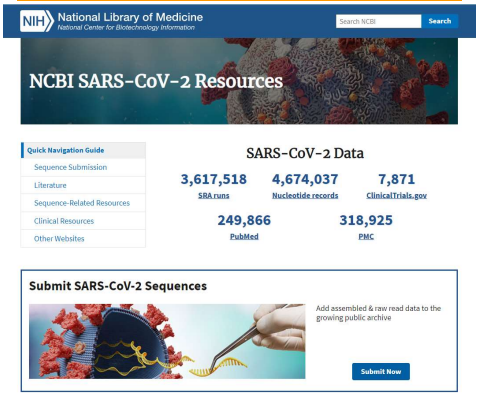




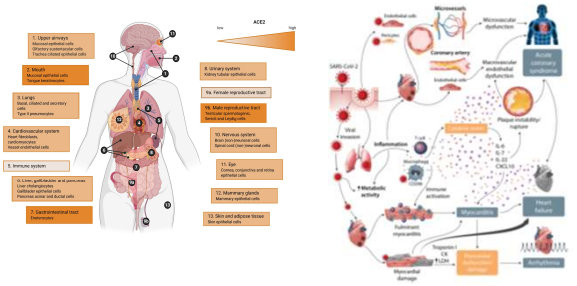
Guzik et al., Cardiovascular Research (2020) 116, 1666–1687

What makes SARS-CoV-2 a terminator?

SARS-CoV-2 Literature



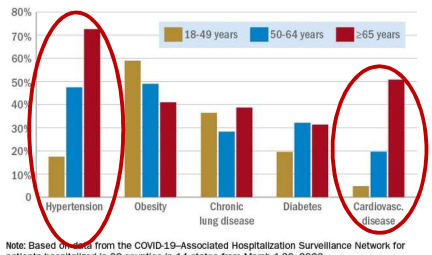
Cardiovascular involvement in COVID-19—key manifestations and hypothetical mechanisms



Guzik et al., Cardiovascular Research (2020) 116, 1666–1687

Mantra of COVID-19

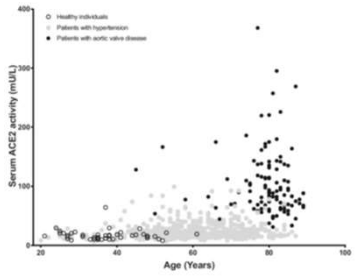
Underlying conditions among adults hospitalized with COVID-19



Note: Based on data from the COVID-19–Associated Hospitalization Surveillance Network for patients hospitalized in 99 counties in 14 states from March 1-30, 2020.

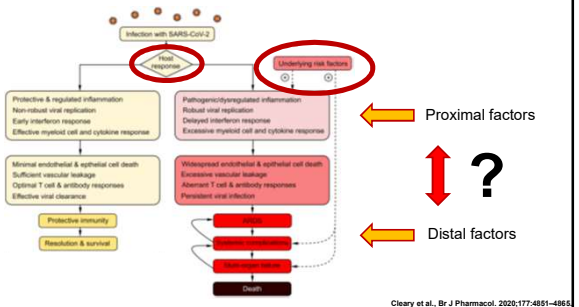
Source: MMWR. 2020 Apr 8:69(early release):1-7

Elderly patients with severe aortic stenosis have increased ACE2 activity



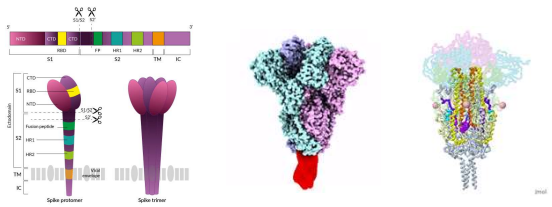
Fagyas et al. Geroscience. 2021 Jan 20:1-11.

Mild or severe COVID-19, that is the question



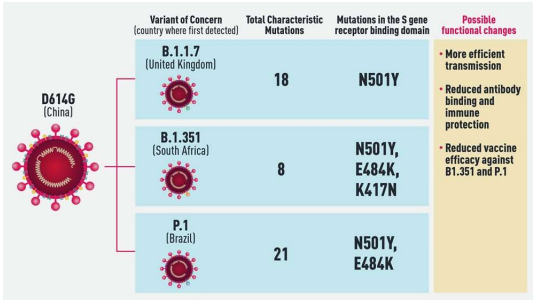
Cleary et al., Br J Pharmacol. 2020;177:4851–4865

SARS-CoV-2 spike protein



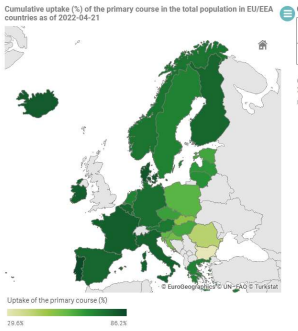
https://www.invivogen.com/sars2-spike

What do mutants teach us?



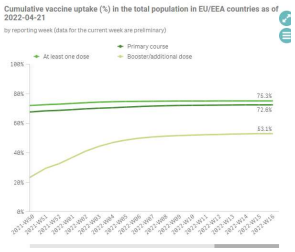
Wanner Tech Corner February 01, 2021

Vaccination against COVID-19 in Europe

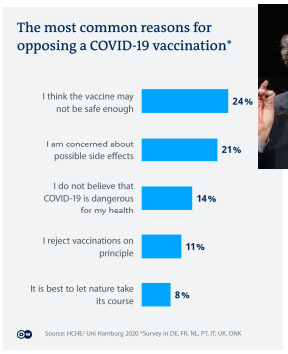


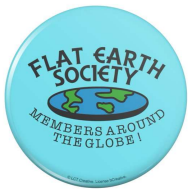
Cumulative vaccine uptake (%) in the total population in EU/EEA countries

At least one dose	Primary course	Booster/additional dose
75.3%	72.6%	53.1%

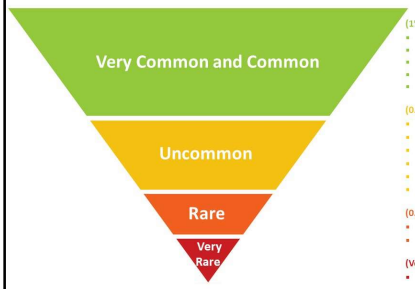


Covid vaccine skepticism





What are the side effects and risks?



(1% - more than 10% of people)
- Pain / redness / swelling at the injection site
- Headache
- Fatigue
- Muscle or joint pain
- Fever or chills

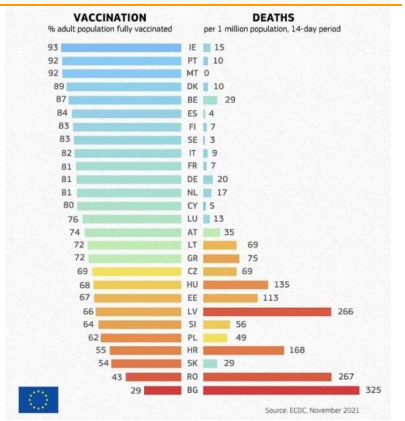
(0.1% - 1% of people)
- Excessive sweating
- Itchy skin / rash / hives
- Muscle weakness, arm or leg pain
- Feeling weak, tired, dizzy
- Abdominal pain, feeling unwell
- Enlarged lymph nodes

(0.01% - 0.1% of people)
- Severe allergic reaction
- Heart inflammation*

(Very rare)
- Blood clots**

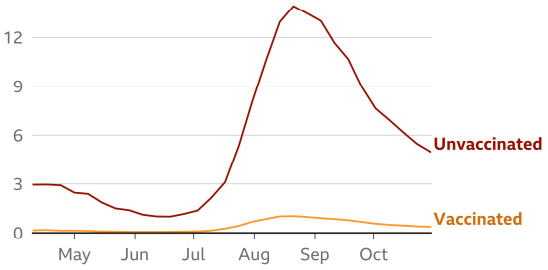
*mRNA vaccines only
**AstraZeneca and Janssen

The relationship between COVID vaccination and mortality



US Covid deaths by vaccination status

Rate of coronavirus deaths per 100,000 people by week



Data from 25 participating health departments

Source: US Centers for Disease Control and Prevention (CDC), 17 Dec

BBC

THANK YOU FOR YOUR ATTENTION!

SZÉCHENYI 2020

HUNGARIAN GOVERNMENT

European Union
European Regional Development Fund

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