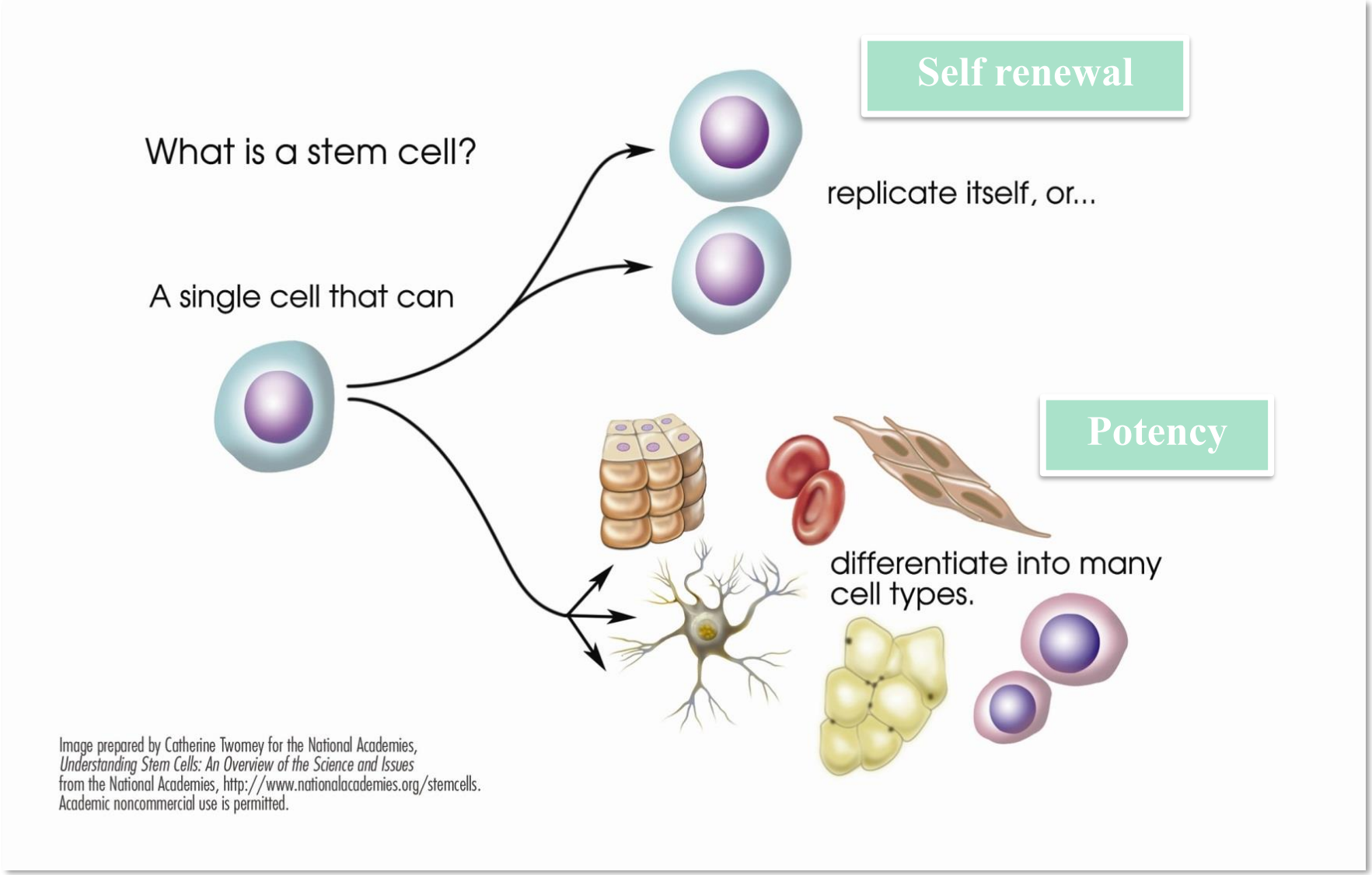
Basics of Cell Therapy

Professor Sian E. Harding

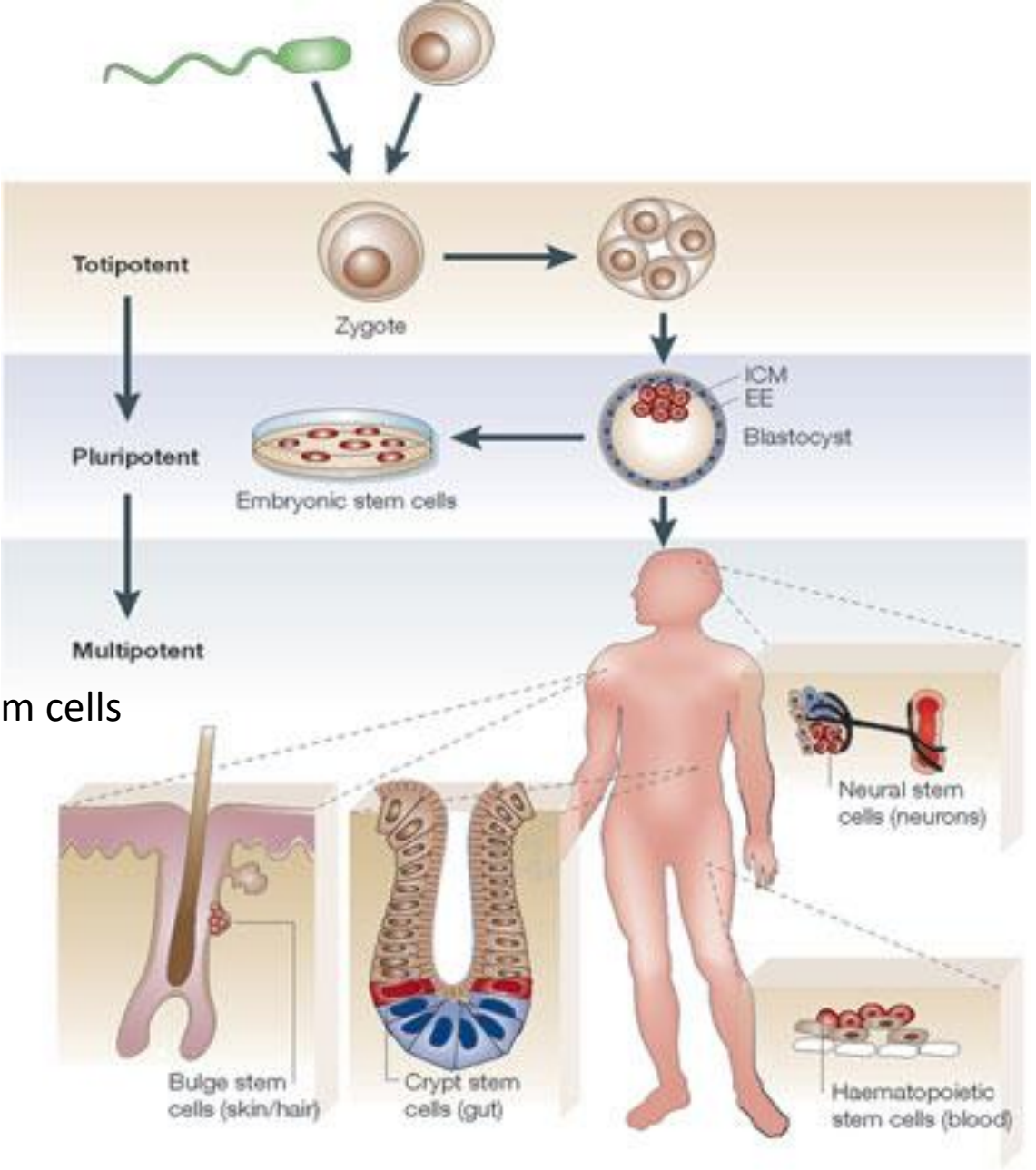
Director, Imperial BHF Centre for Cardiac Regeneration

Can stem cells repair the body?

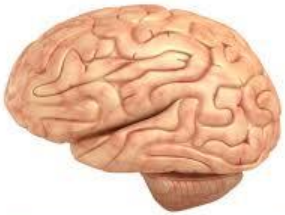


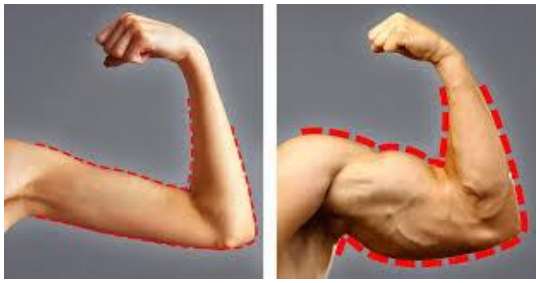
Differentiation: is the process by which a less specialized cell becomes a more specialized cell type

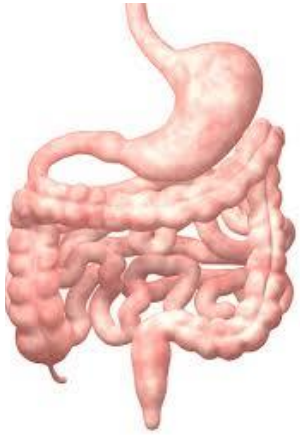
Adult stem cells



What tissues in your body regenerate themselves?







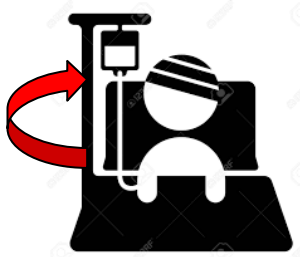
Clinical trials are aiming to replace or boost natural regeneration

Which stem cells shall we use?

Stem cells given back to the same patient = autologous

<u>Advantages</u>

- Not rejected by the immune system
- Do not need to be stored



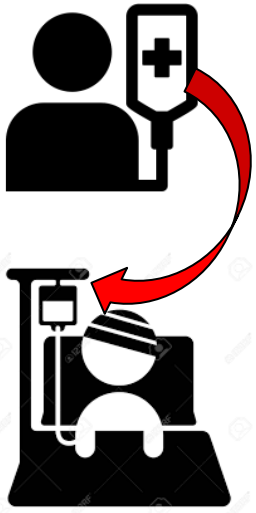
<u>Disadvantages</u>

- May be affected by the patient's disease
- May need to be transported to a lab to be modified
- Cannot be prepared in advance

Stem cells transplanted from one person to another = allogeneic

<u>Advantages</u>

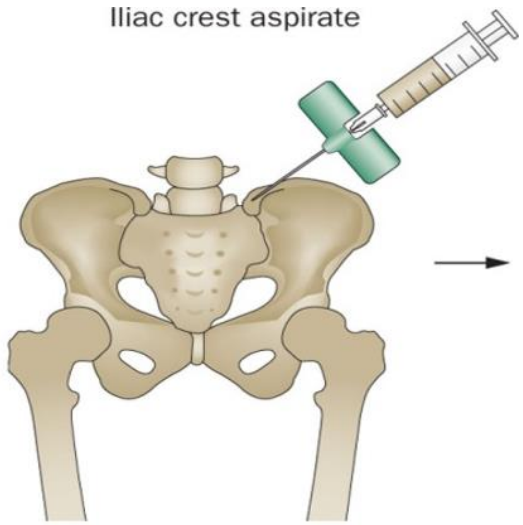
- Can be tested for quality
- Can be prepared in advance, made into a tissue engineered product



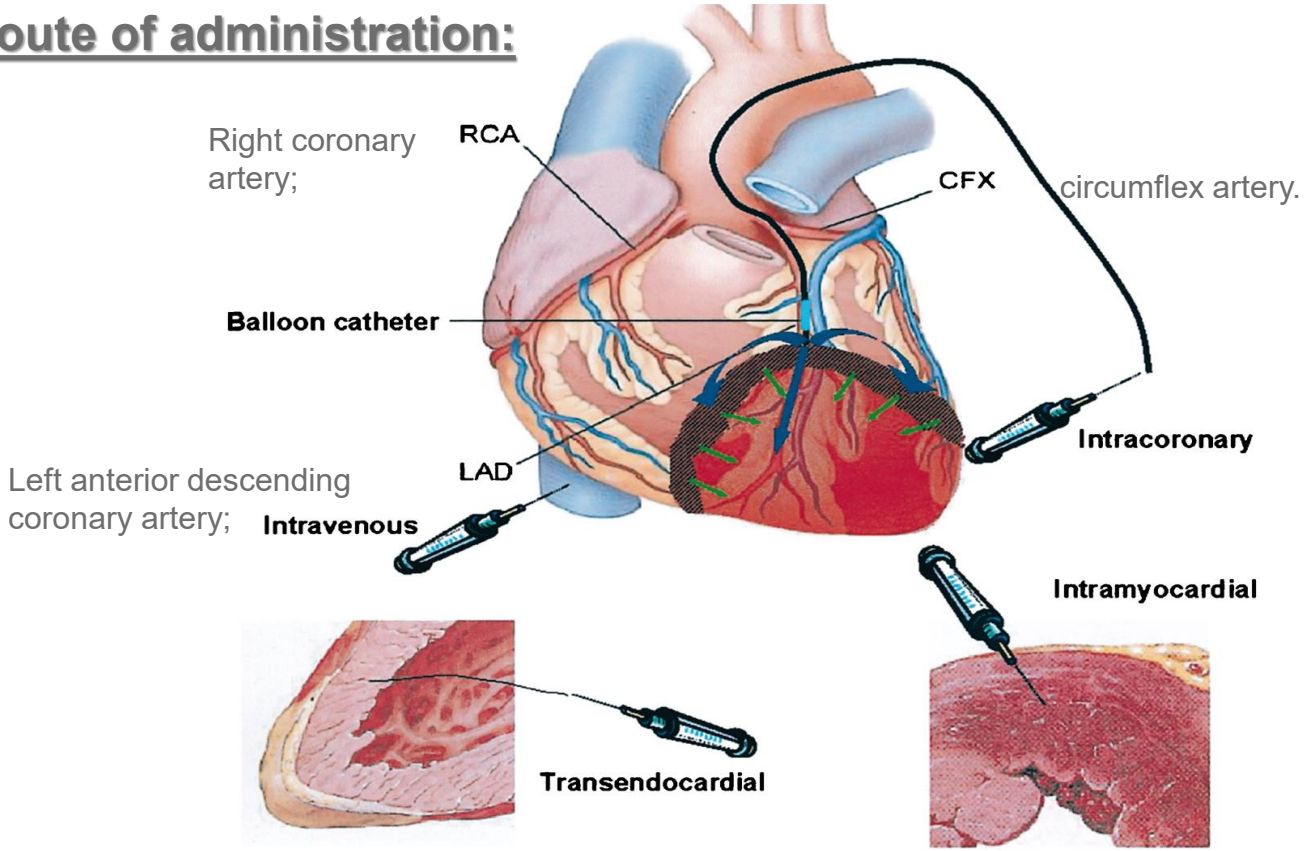
<u>Disadvantages</u>

- May be rejected by the immune system and need immunosuppression

Bone Marrow contain stem cells which are being injected back into damaged organs



Route of administration:

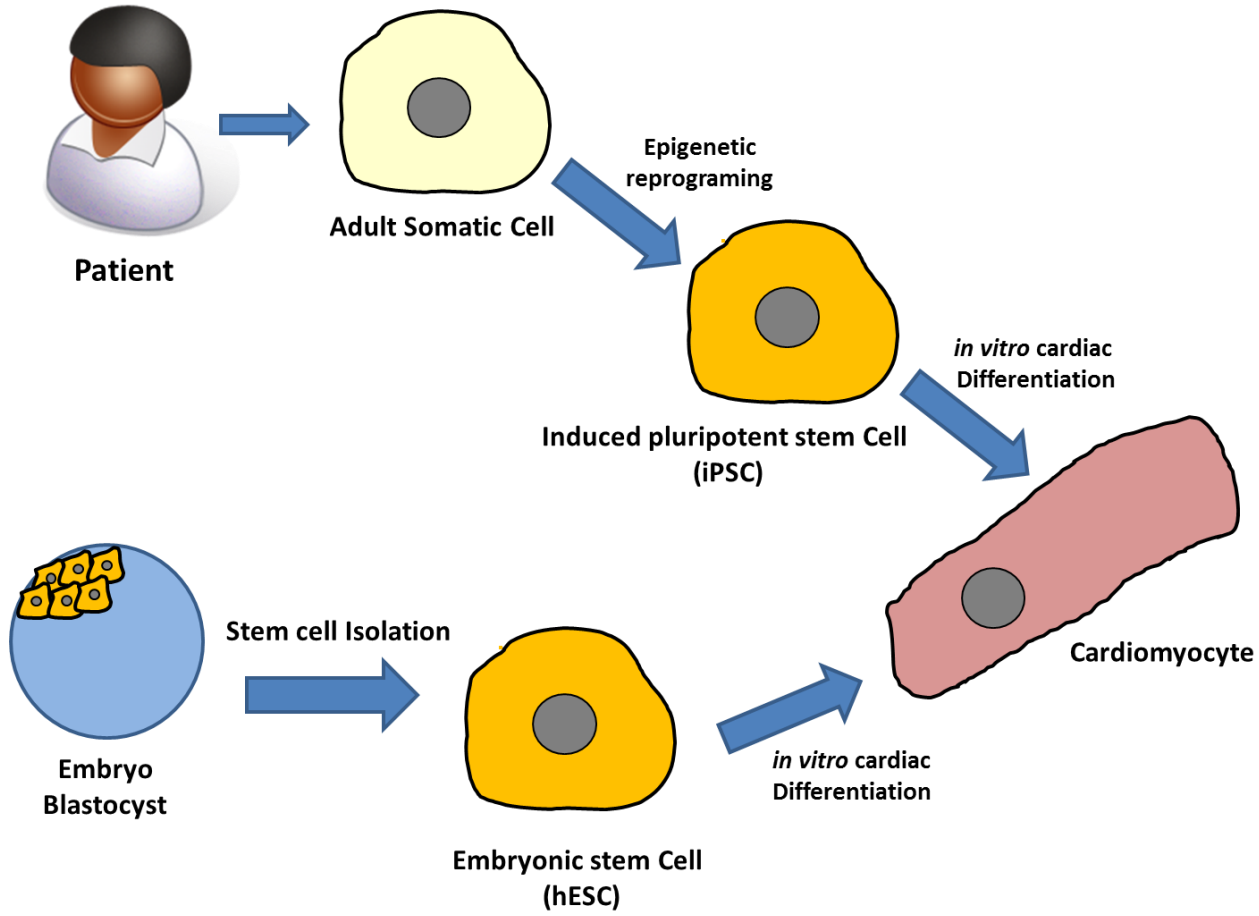


UCL BAMI trial

Mesenchymal stem cells
– reduce inflammation and suppress immune response?
Can be used for patient-to-patient transfer?

Bone marrow stromal cells
Adipose tissue
Amniotic fluid
Cord blood
Cardiospheres

Pluripotent stem cells can make any cell type *(except placenta)*



Human embryonic stem cells discovered in 1998

In vitro fertilization day 1

Embryos frozen at 1-7 days
(at this point, ~80% embryos do not implant either naturally or after IVF)

Unused embryos must be destroyed

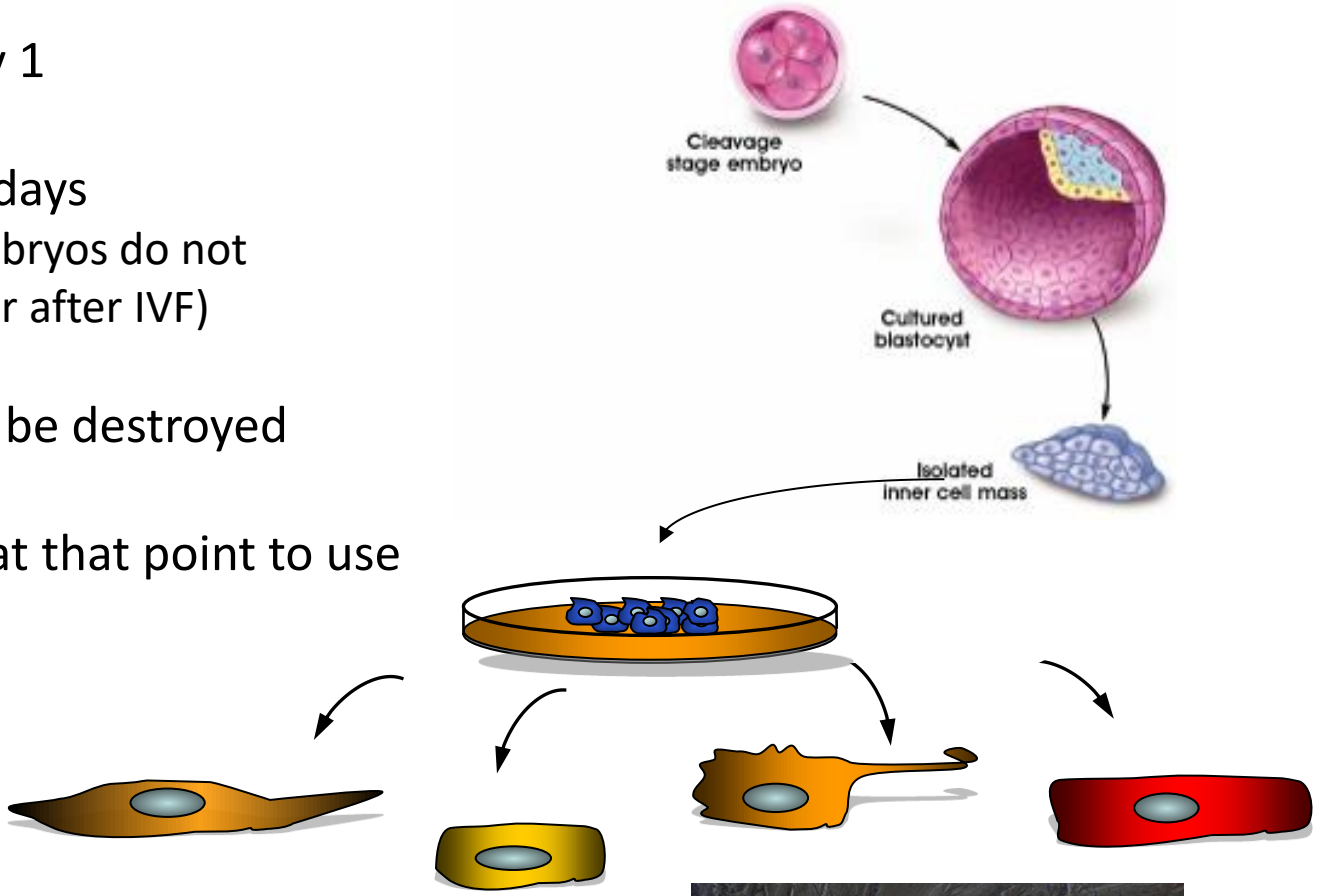
Permission requested at that point to use for research

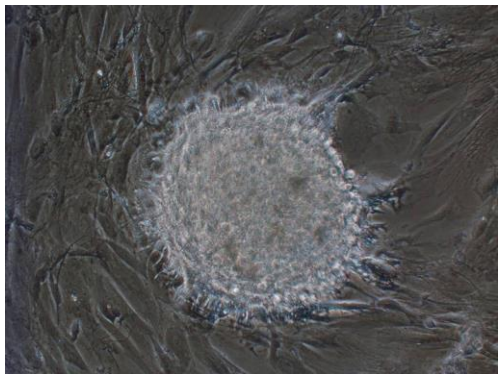
Cell line made

Held in Stem Cell Bank

Distributed free to researchers

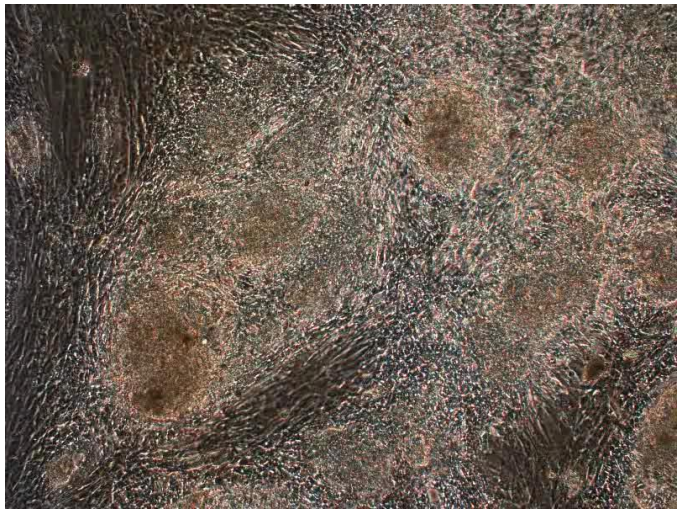
Can become any cell type in the body

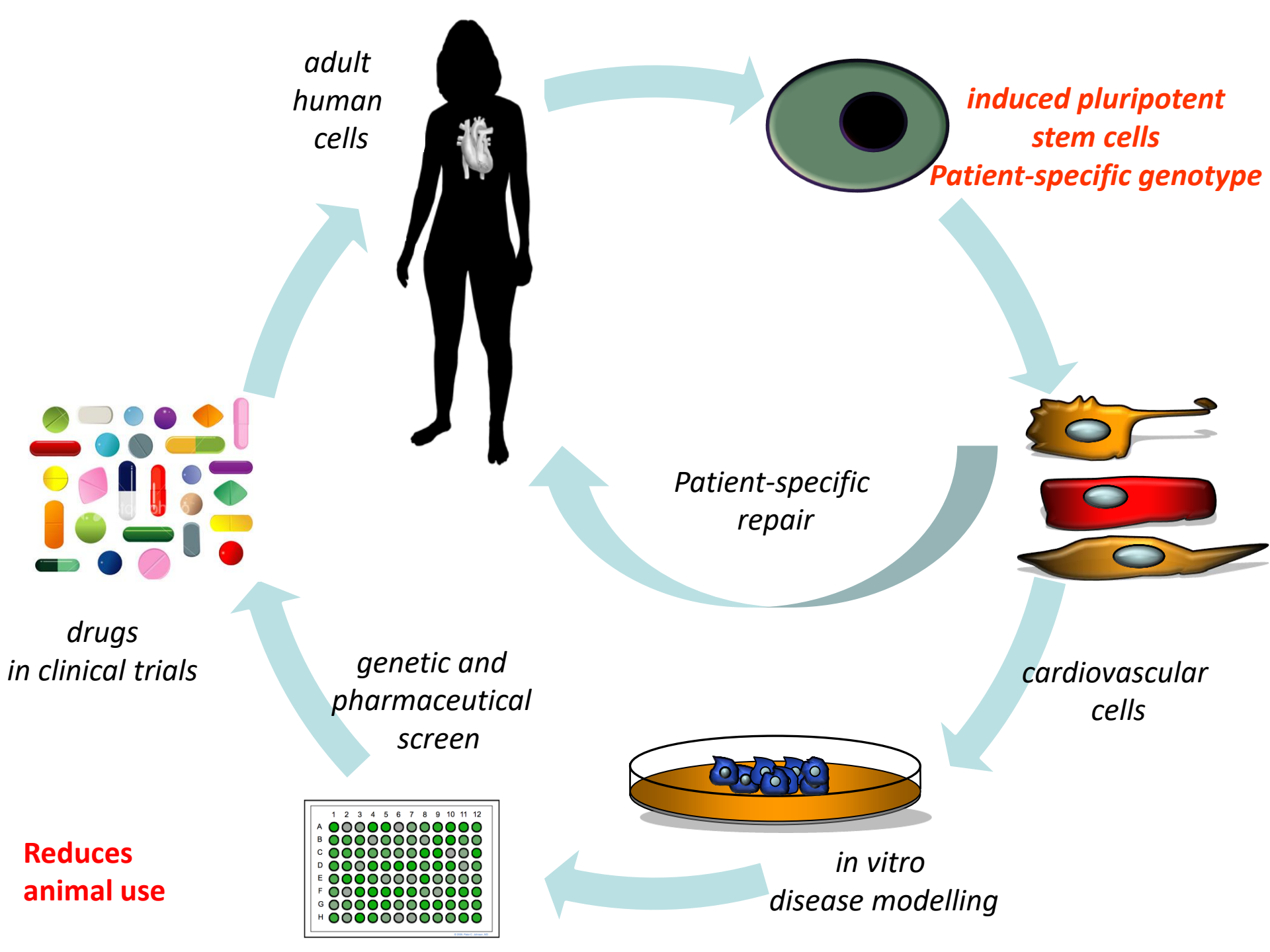




Human induced pluripotent stem cells -2008
Nobel Prize 2012

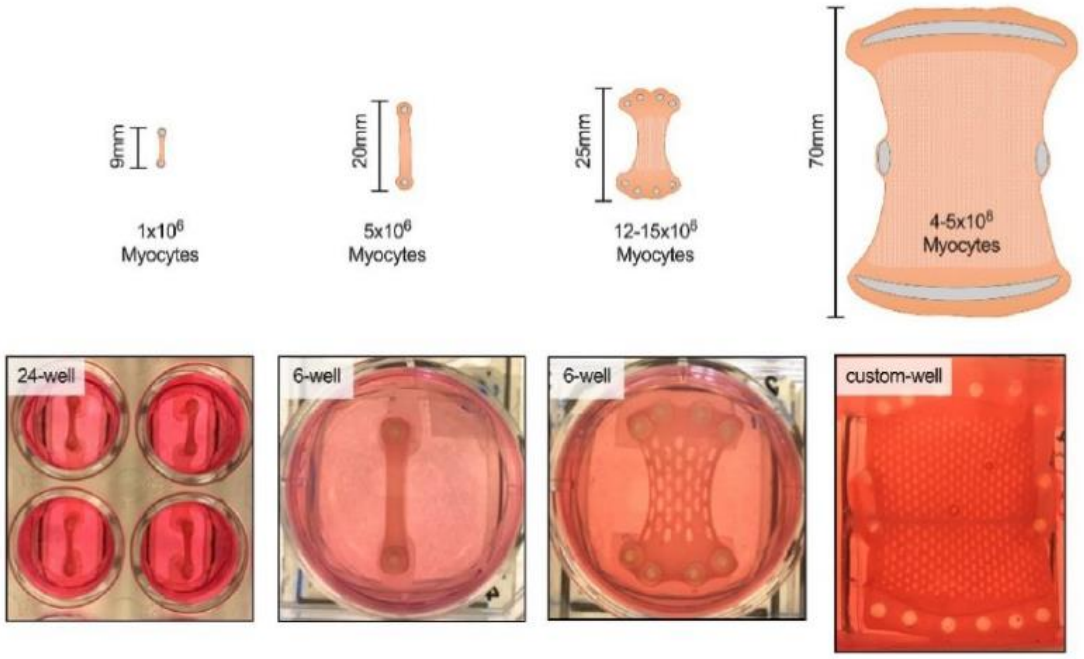
- Skin fibroblasts are treated with retroviruses carrying “stemness” factors discovered in embryonic stem cells
- They form embryonic-like stem cells which differentiate into many cell types (including cardiomyocytes):-
- Person-specific stem cells with matched immune systems

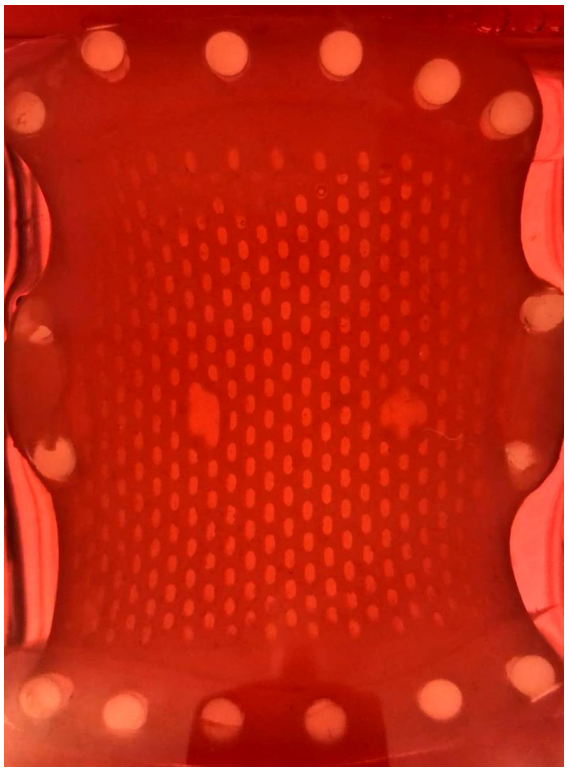



adult
human
cells
induced pluripotent
stem cells
Patient-specific genotype
Patient-specific
repair
cardiovascular
cells
in vitro
disease modelling
genetic and
pharmaceutical
screen
drugs
in clinical trials
Reduces
animal use

Generation of human scale engineered heart tissue patches

Small EHT | Stripe-EHT | Patch-EHT | Human scale- EHT



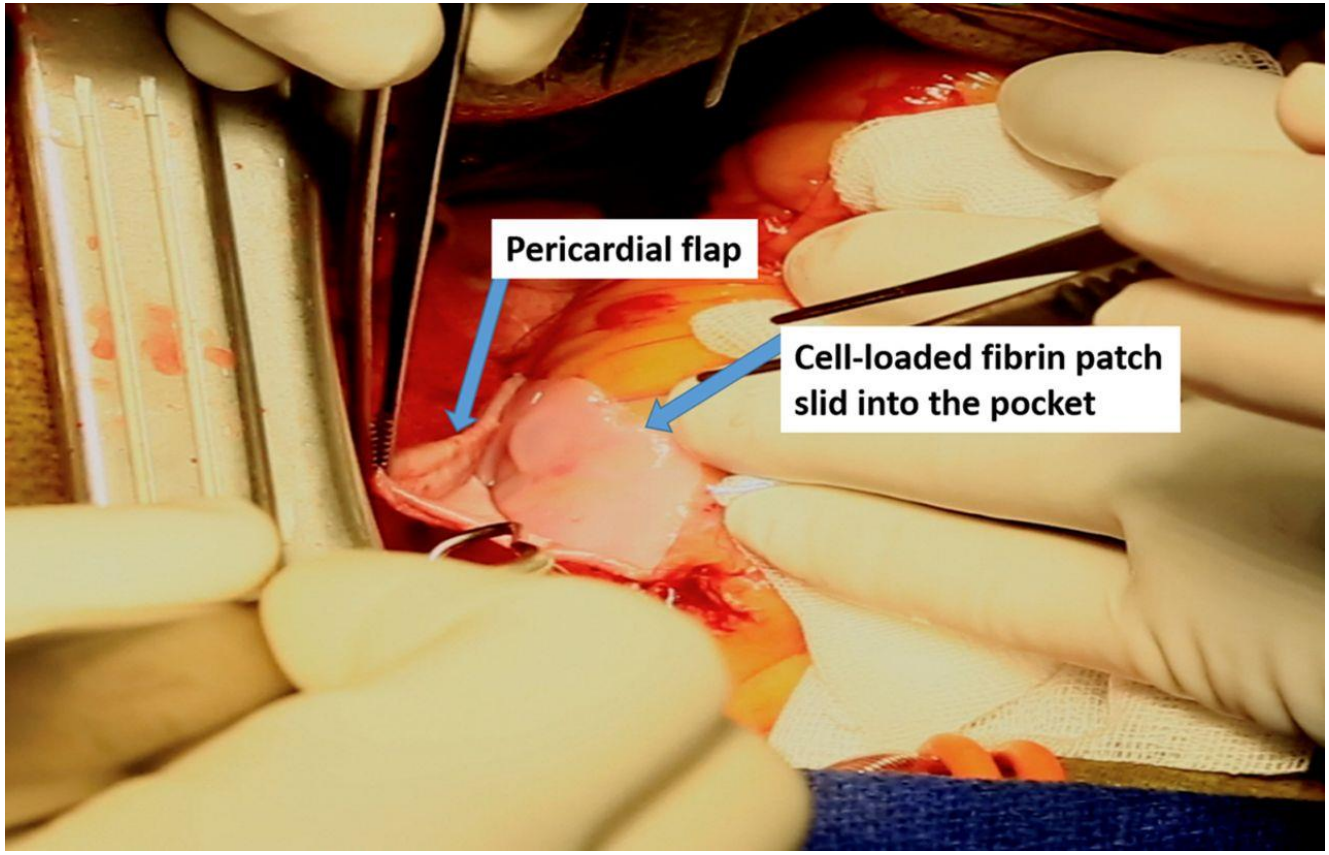


Spontaneous beating human scale-EHT

Weinberger and Eschenhagen

Human embryonic stem cell-derived cardiac progenitors for severe heart failure treatment: first clinical case report.

Intraoperative view of the progenitor cell-loaded fibrin patch that has been slid into the pocket between an autologous pericardial flap and the epicardial surface of the infarct area.



Menasche et al

European Heart Journal

Japan approves first trials of stem cell-based heart treatment

iPS procedure raises hopes for alternative to donations and artificial organs

Nikkei staff writers
MAY 16, 2018 15:16 JST

Osaka University professor Yoshiki Sawa outlines his plans for treating heart failure in 2017. (Photo by Hiromasa Matsuura)

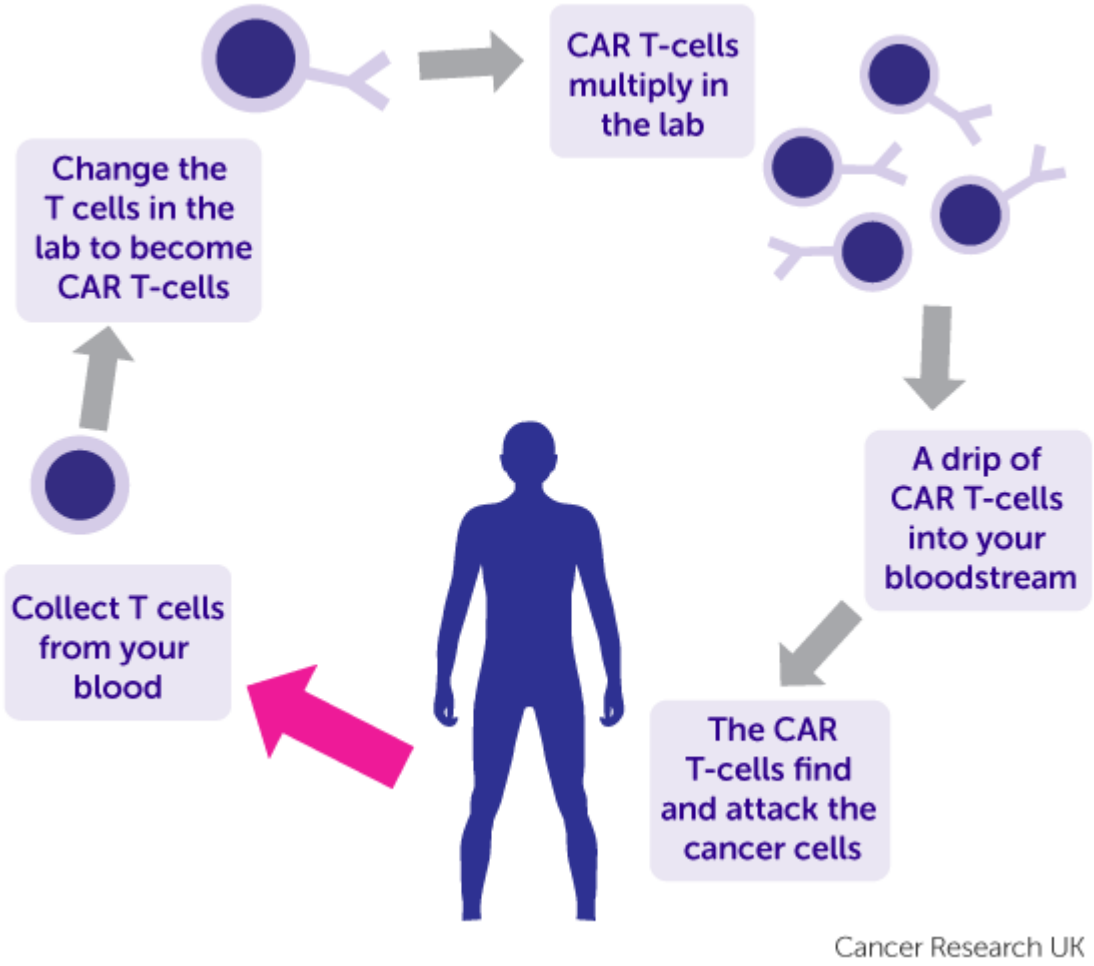
…iPS cells .. at the Center for iPS Cell Research and Application at Kyoto University, where Nobel laureate Shinya Yamanaka serves as director. The created cells, in the form of 0.1 millimeter-thick sheets, will be layered onto the surface of the patient's heart

Doctors hope for blindness cure after restoring patients' sight

Treatment for common cause of blindness could be available within five years, scientists say

Moorfield – retinal cells from pluripotent stem cells

CAR T-cells – gene+cell therapy



Thank you for listening

Any Questions?