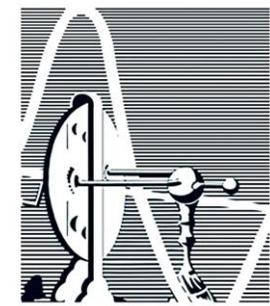




UFRJ



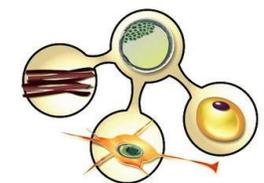
IBCCF

Instituto de Biofísica
Carlos Chagas Filho

Facing health challenges with science and technology

Antonio Carlos Campos de Carvalho

acarlos@biof.ufrj.br



INCT - Regenera

Instituto Nacional
de Ciência e Tecnologia
em Medicina Regenerativa

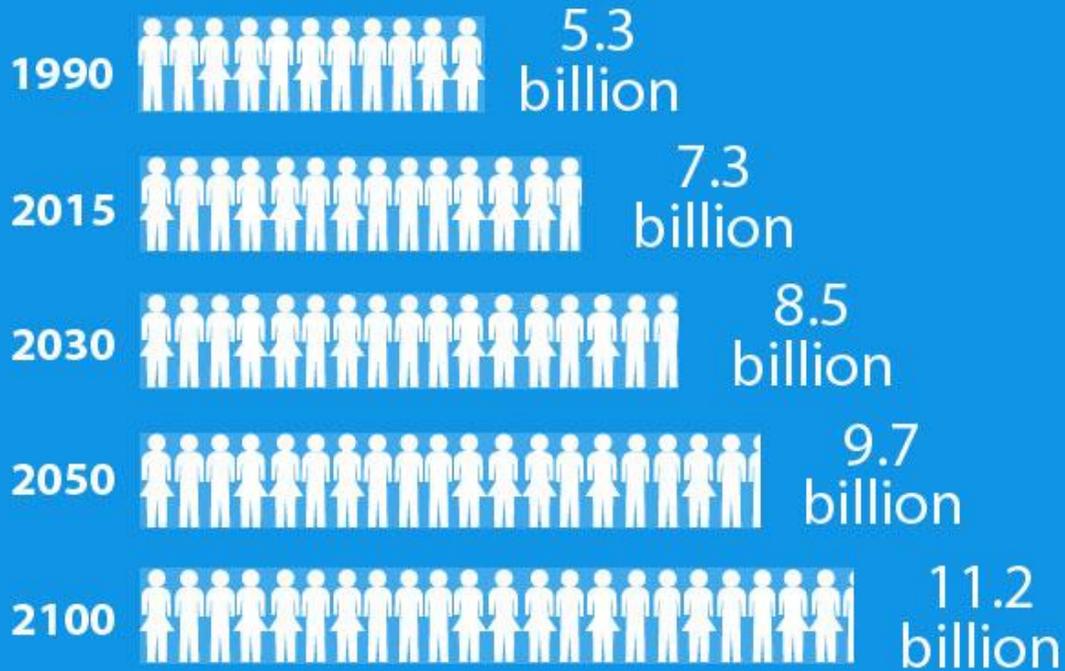


RNTC
Rede Nacional de Terapia Celular

STATING THE PROBLEM

World Population

Projected world population until 2100

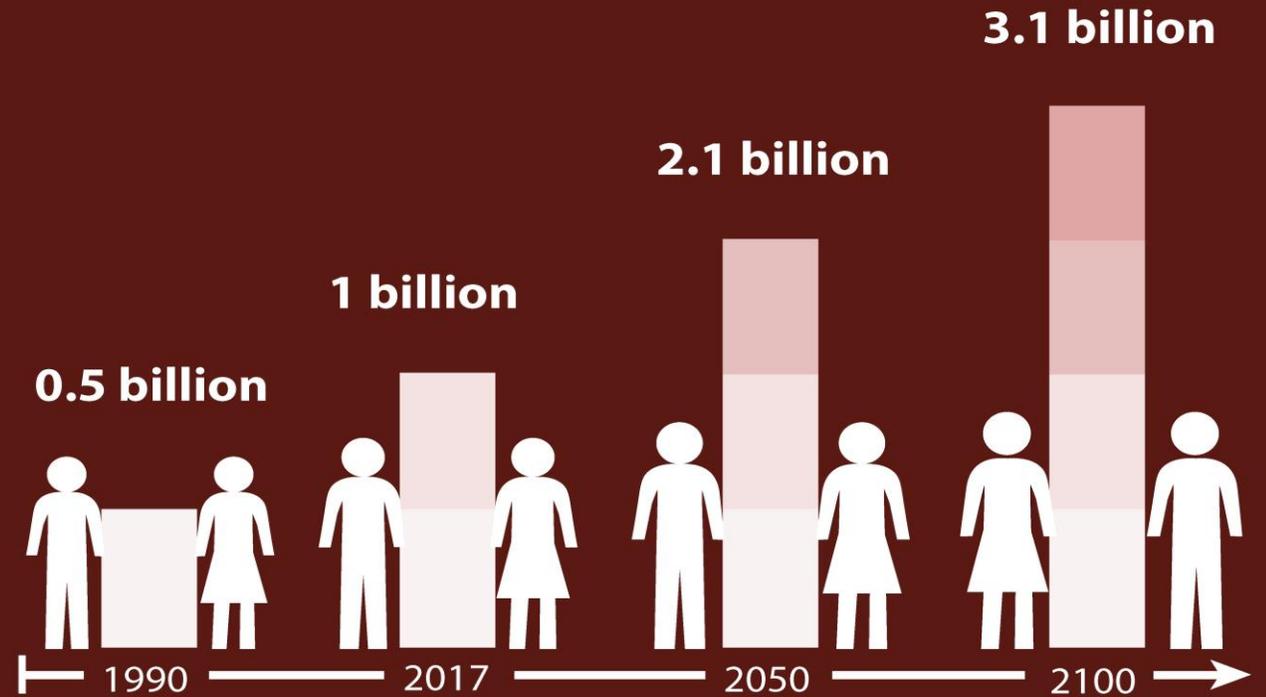


Source: United Nations Department of Economic and Social Affairs, Population Division, *World Population Prospects: The 2015 Revision*
Produced by: United Nations Department of Public Information



Ageing Population

Projected global population aged 60 years or over

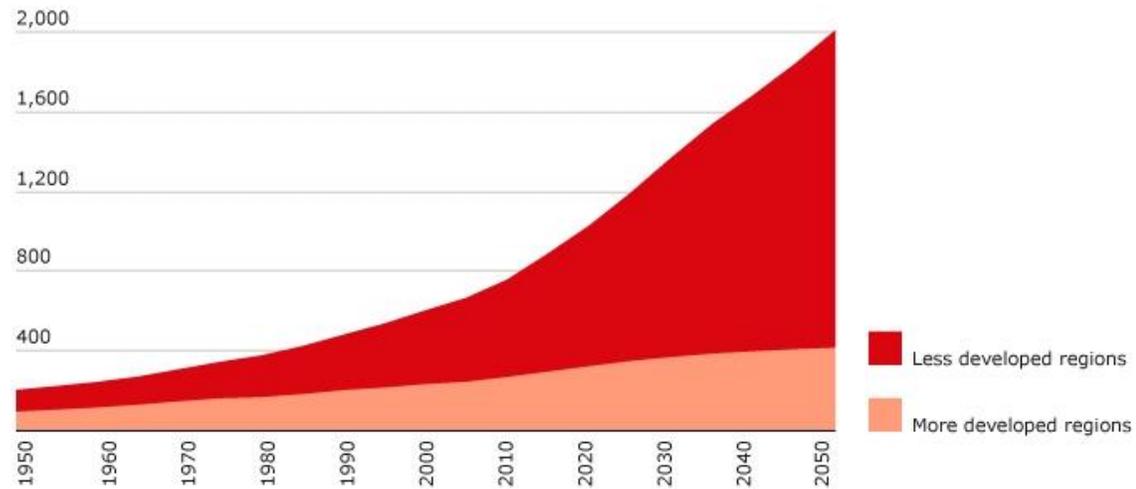


Source: United Nations Department of Economic and Social Affairs, Population Division, *World Population Prospects: The 2017 Revision*
Produced by: United Nations Department of Public Information



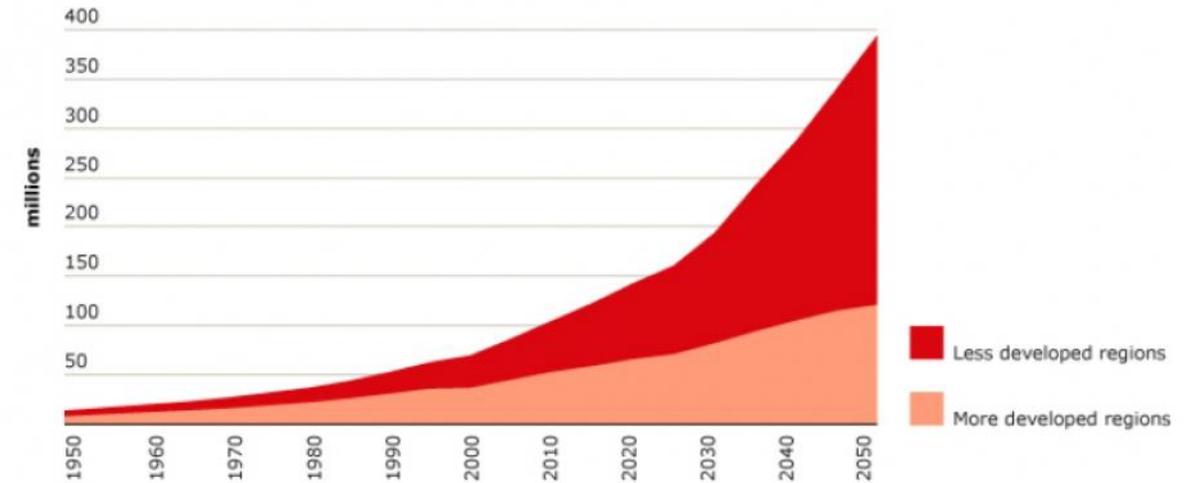
AGING RATE IS GREATER IN LESS DEVELOPED REGIONS

1. Population over 60 by region



Source: World Population Prospects: The 2004 Revision Population Database, UN Department of Economic and Social Affairs
<http://esa.un.org/unpp/index.asp?panel=2> (23 November 2006)

2. Population over 80 by region



Source: Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat, *World Population Prospects: The 2008 Revision*; <http://esa.un.org/unpp>, accessed 13 May 2010

AGING IN THE WORLD

Ageing and Health

#yearsahead

Populations are getting older



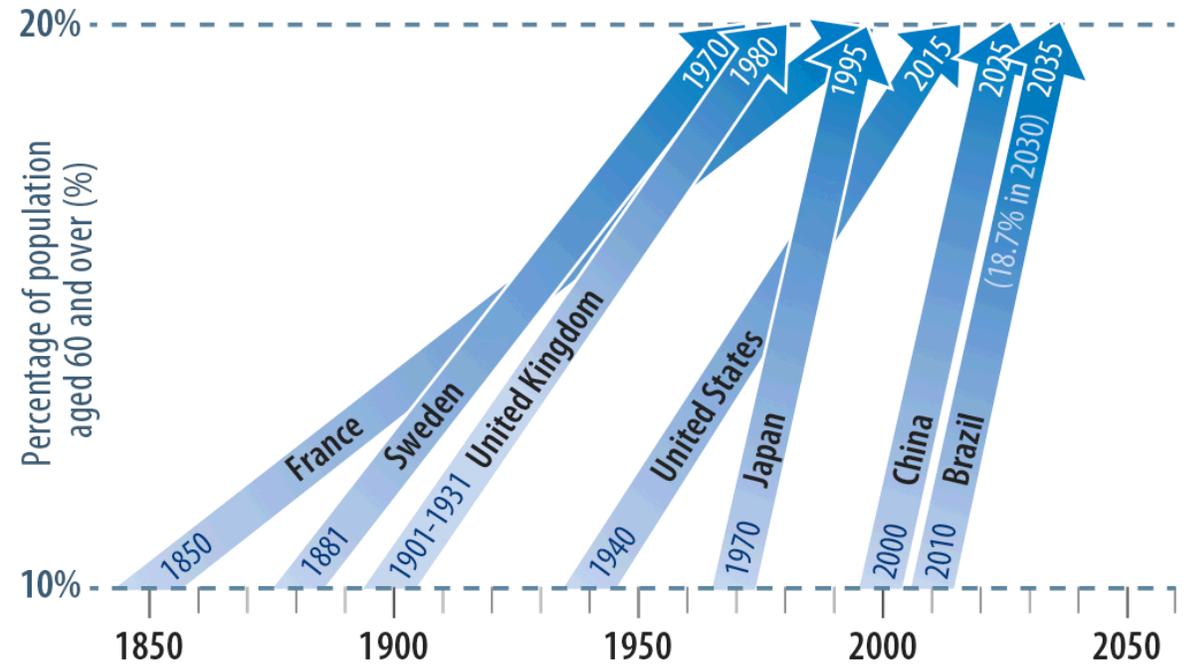
2015

Ageing and Health

#yearsahead

Speed of population ageing

Time for percentage of population **over age 60** to double



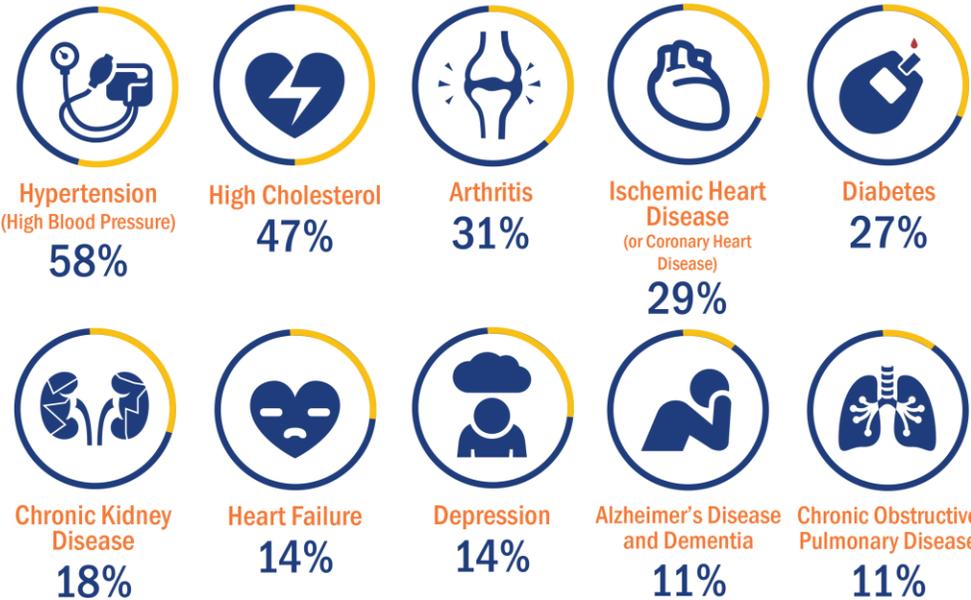
AGING AND CHRONIC DISEASES

10 Common Chronic Conditions for Adults 65+

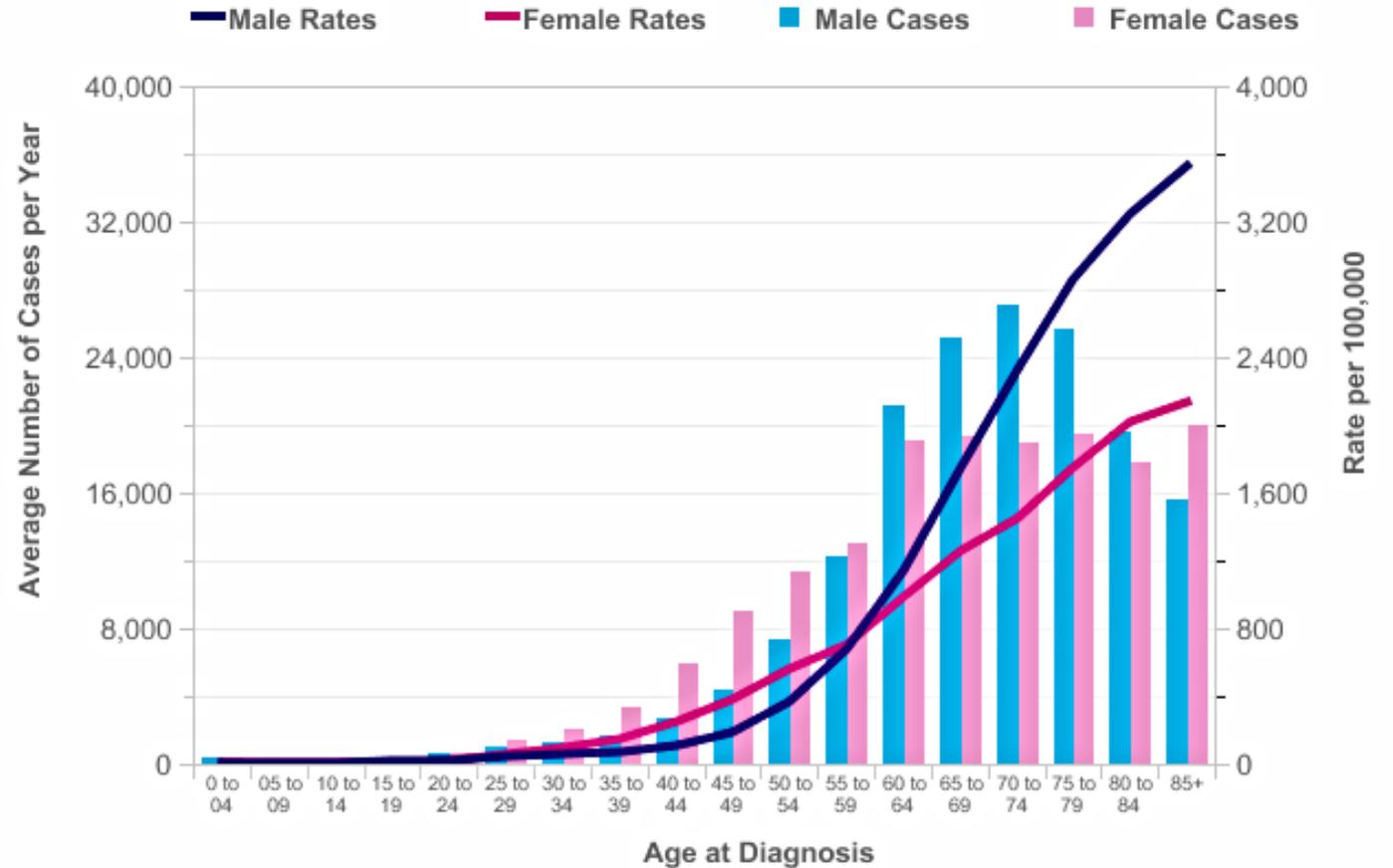
Quick Facts

80% have at least 1 chronic condition

68% have 2 or more chronic conditions



Source: Centers for Medicare & Medicaid Services, Chronic Conditions Prevalence State/County Table: All Fee-for-Service Beneficiaries, 2015



Distribution of **YLL** for ten main causes, by sex in Brazil

Order	Men	%	Women	%
1	Homicide & violence	11,3	Ischemic Heart dis.	10,9
2	Ischemic heart dis.	10,1	Stroke	10,7
3	Transit accident	7,2	Diabetes mellitus	6,3
4	Stroke	7,0	Lung infections	4,9
5	Lung infections	3,9	Breast cancer	3,5
6	Diabetes mellitus	3,3	Hypertension	3,2
7	Cirrhosis – alcohol & other	3,1	COPD	2,7
8	COPD	2,3	Transit accident	2,4
9	HIV/AIDS	2,2	Uterine cancer	2,3
10	Hypertension	2,1	Lung cancer	1,9

Distribution of YLD for ten main causes, by sex in Brazil

Order	Men	%	Women	%
1	Alcohol abuse & dep.	9,6	Depression	22,3
2	Depression	8,3	Bipolar disease	4,9
3	Bipolar disease	6,4	Alzheimer & other dementias	4,7
4	Diabetes mellitus	6,0	Diabetes mellitus	4,2
5	COPD	5,1	COPD	4,0
6	Asthma	3,6	Asthma	3,5
7	Ischemic heart dis.	3,1	Ischemic heart dis.	3,4
8	Alzheimer & other dementias	2,7	Osteoarthritis	2,6
9	Schizophrenia	2,2	Alcohol abuse & dep.	1,7
10	Epilepsy	2,1	Anemia by iron deficiency	1,7

WHY DO WE NEED MORE SCIENCE AND TECHNOLOGY IN THE HEALTH SECTOR?

IMPRECISION MEDICINE

For every person they do help (blue), the ten highest-grossing drugs in the United States fail to improve the conditions of between 3 and 24 people (red).

1. ABILIFY (aripiprazole)
Schizophrenia



2. NEXIUM (esomeprazole)
Heartburn



3. HUMIRA (adalimumab)
Arthritis



4. CRESTOR (rosuvastatin)
High cholesterol



5. CYMBALTA (duloxetine)
Depression



6. ADVAIR DISKUS (fluticasone propionate)
Asthma



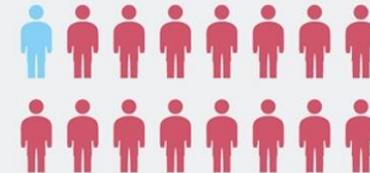
7. ENBREL (etanercept)
Psoriasis



8. REMICADE (infliximab)
Crohn's disease



9. COPAXONE (glatiramer acetate)
Multiple sclerosis



10. NEULASTA (pegfilgrastim)
Neutropenia



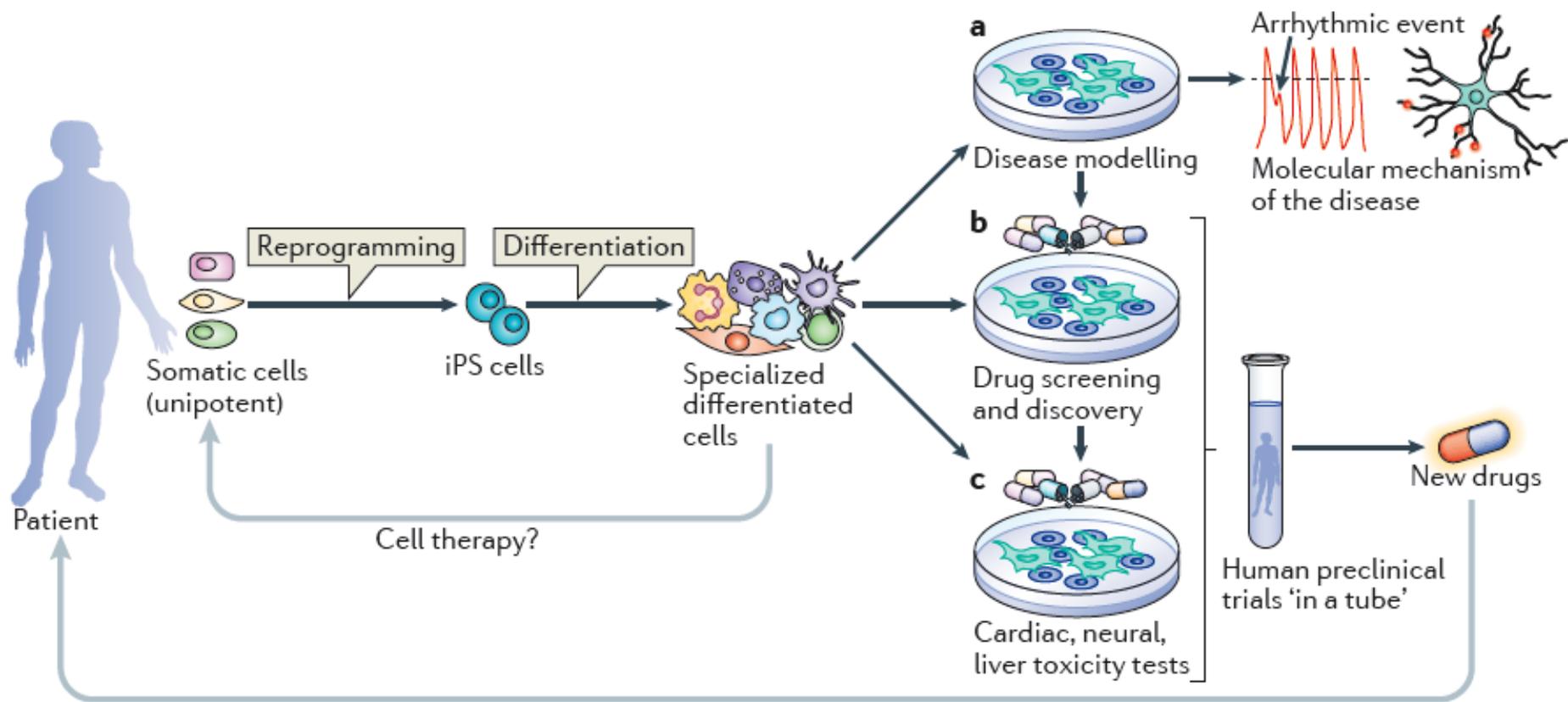
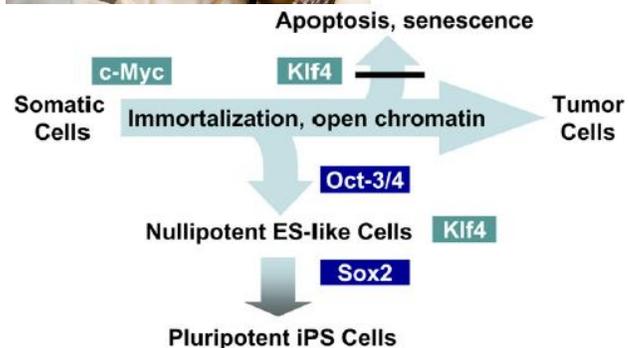
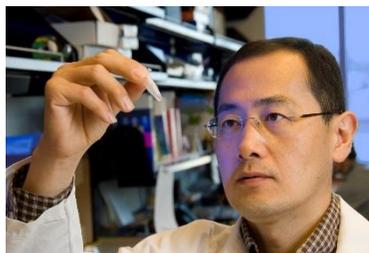
Based on published number needed to treat (NNT) figures. For a full list of references, see Supplementary Information at go.nature.com/4dr78f.

HOW CAN WE IMPROVE THIS SCENARIO?

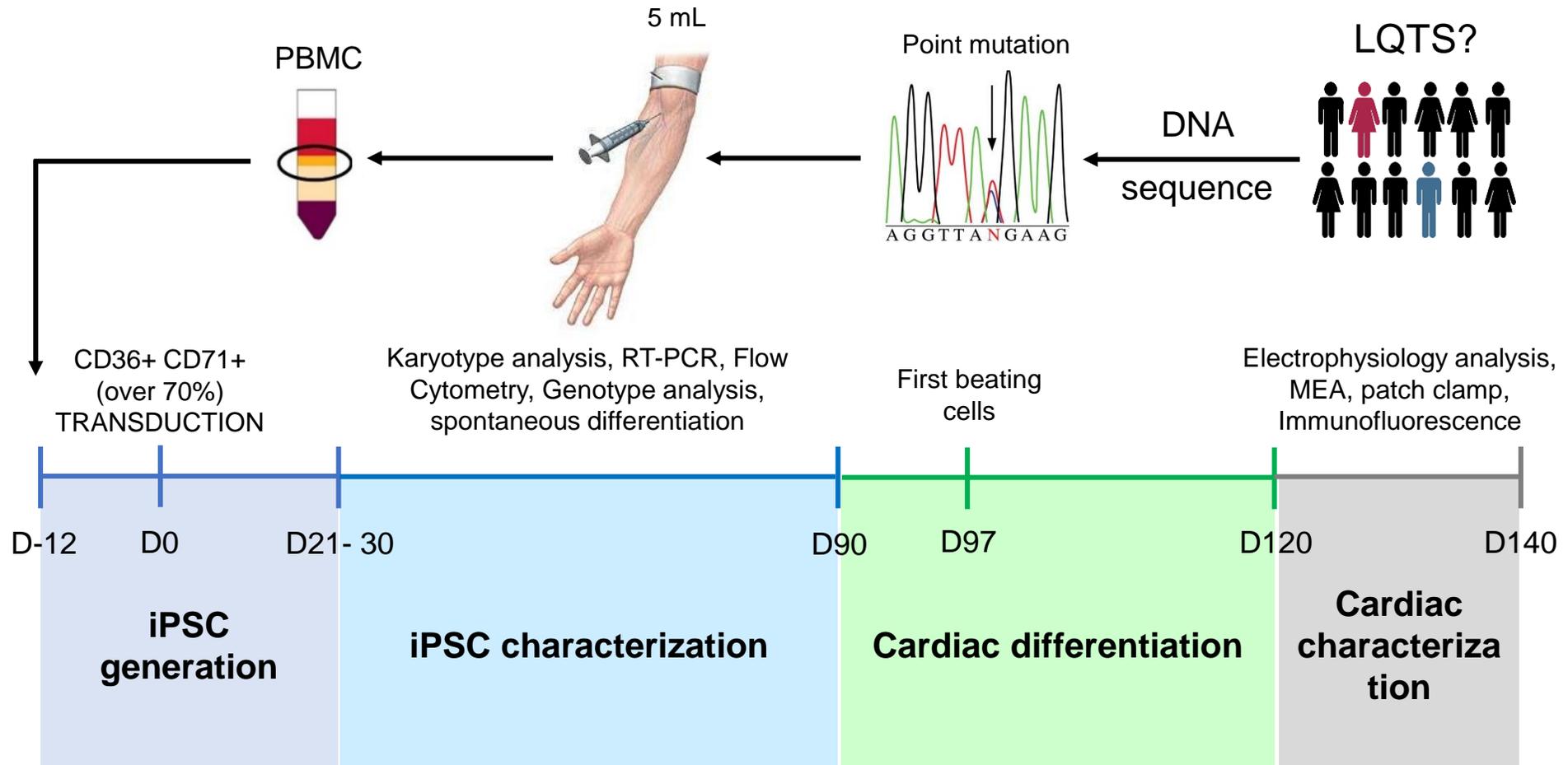
- **WE NEED BETTER DISEASE MODELS**
- **WE NEED TO IMPROVE DRUG SCREENING**
- **WE NEED AFFORDABLE PERSONALISED MEDICINE**
- **WE NEED NEW THERAPIES FOR INCURABLE DISEASES**

IS THIS ACHIEVABLE?

INDUCIBLE PLURIPOTENT STEM CELLS - iPS

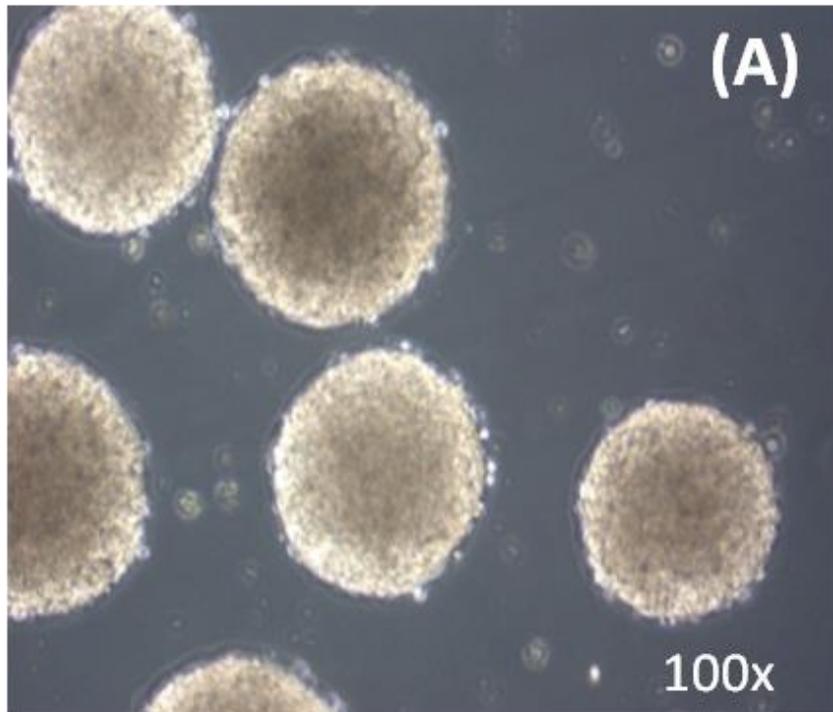


USING iPS FOR DISEASE MODELLING

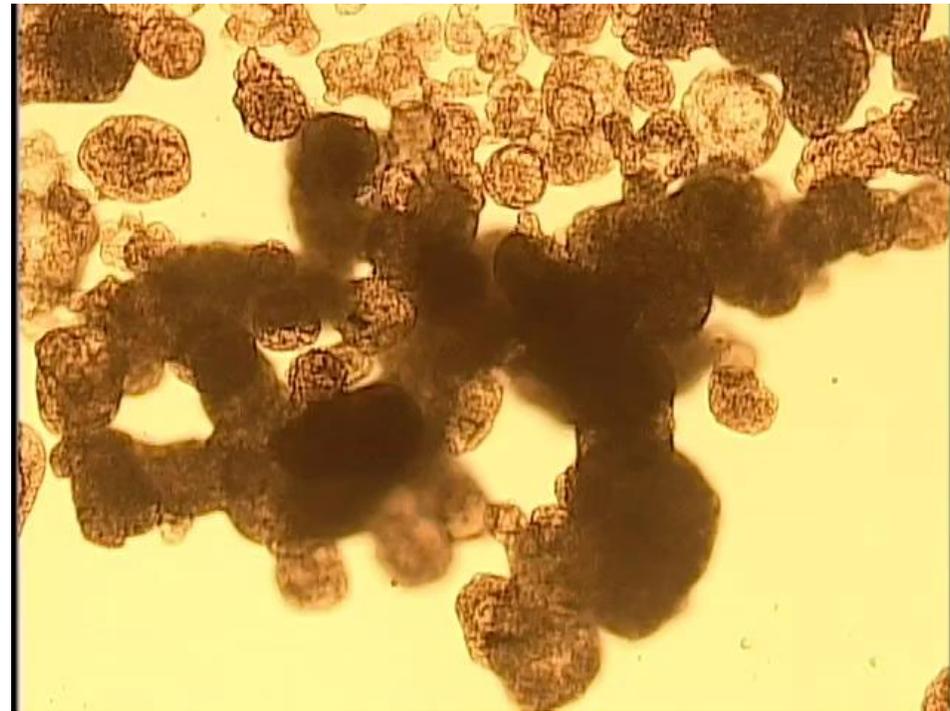


Embryoid Bodies (EB)

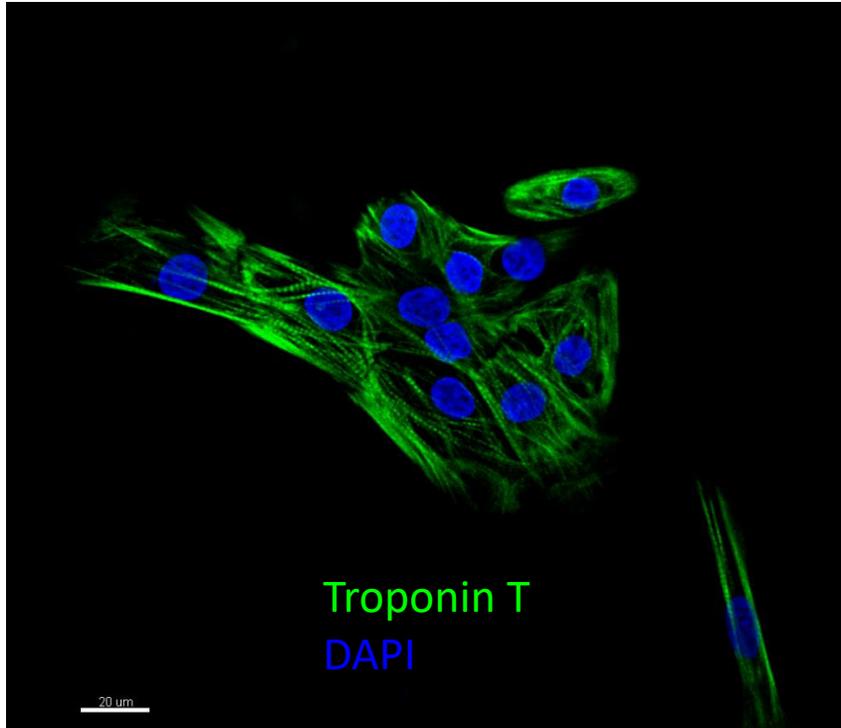
EB 2 days in suspension



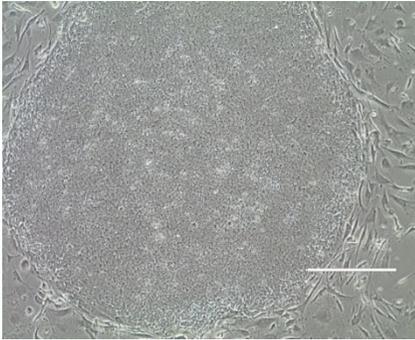
EB post differentiation



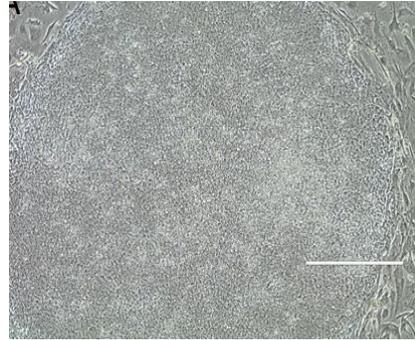
iPS DERIVED CARDIOMYOCYTES



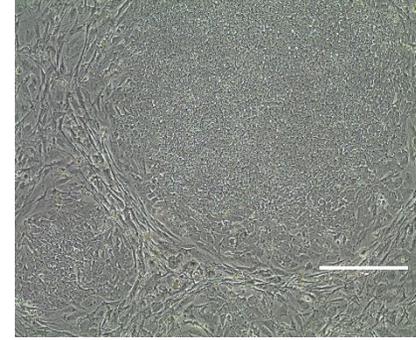
CONTROL (iBM1.2)



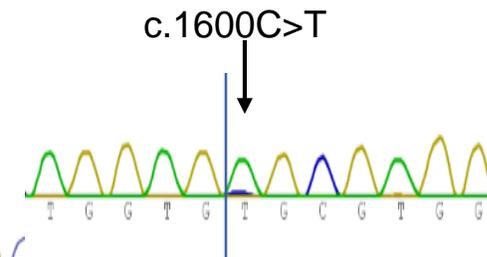
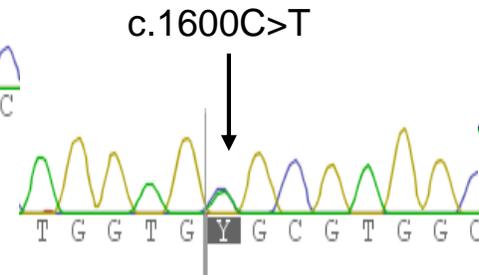
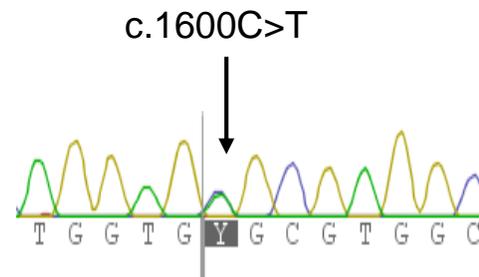
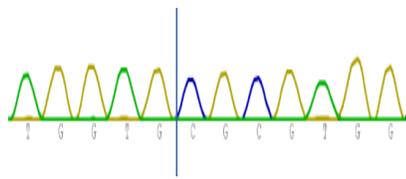
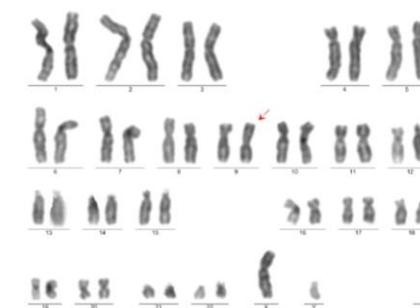
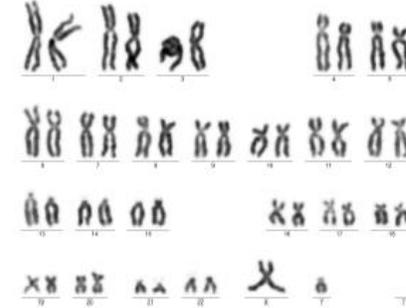
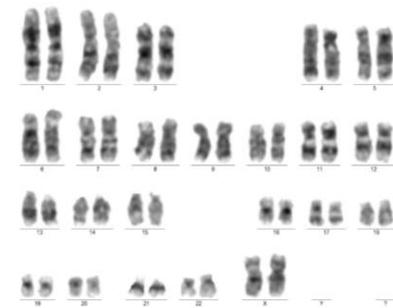
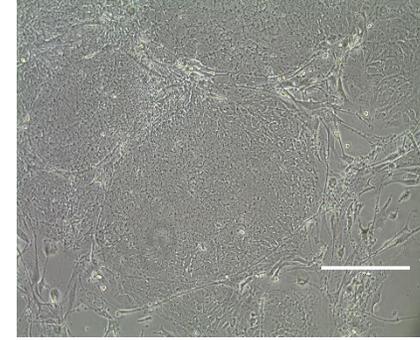
PAC1 CI9



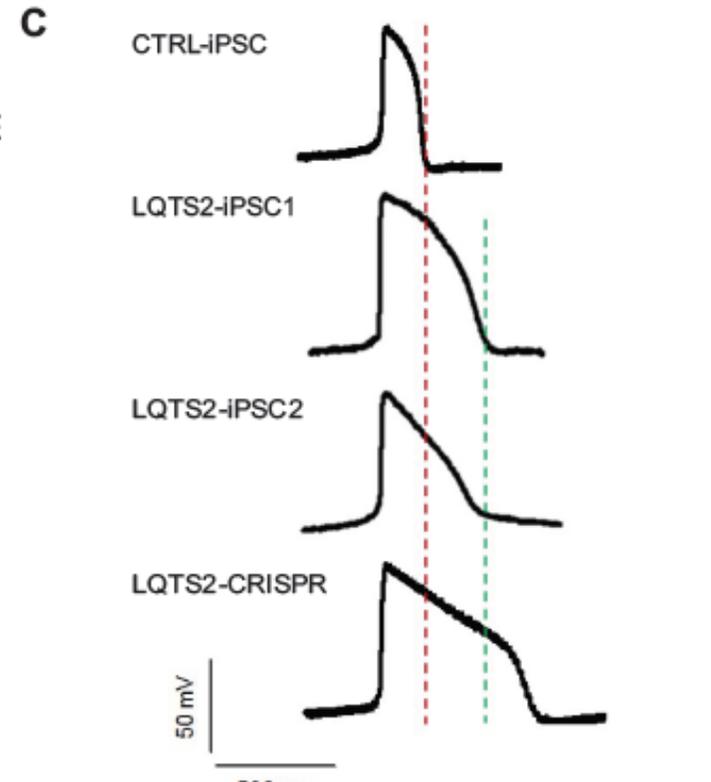
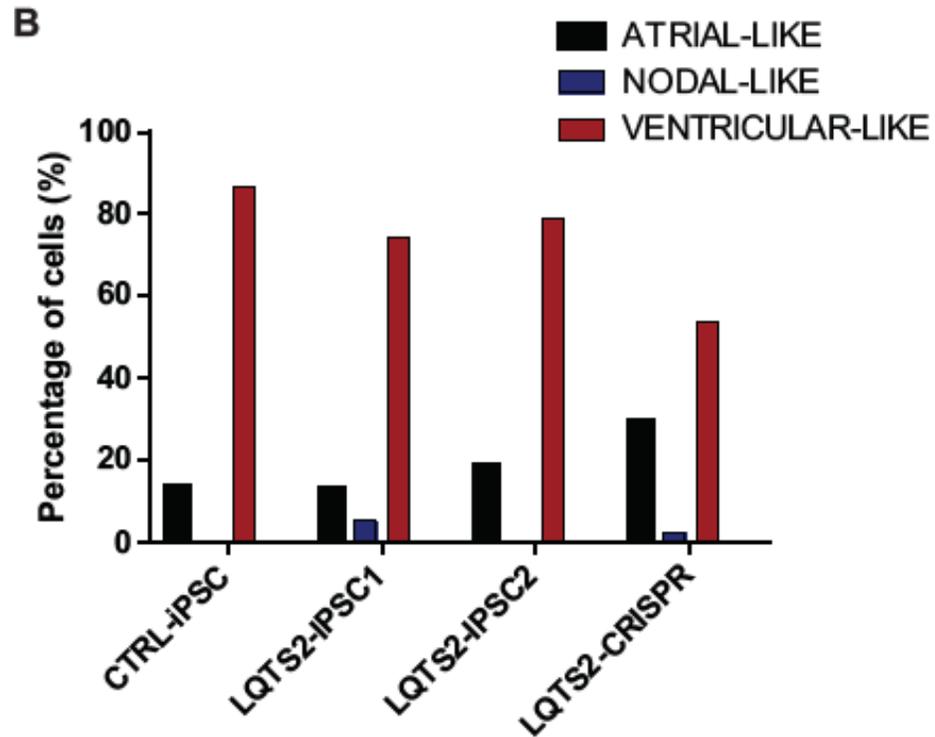
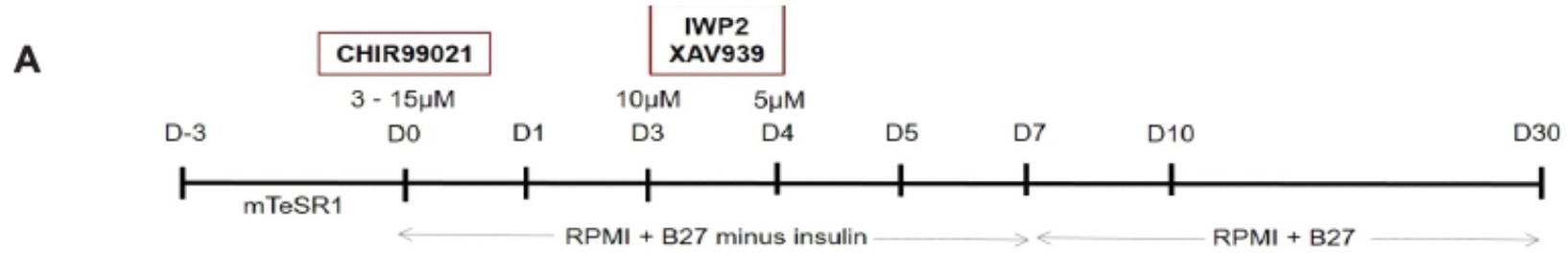
PAC2 CI11



iBM_CRISPR_CI12

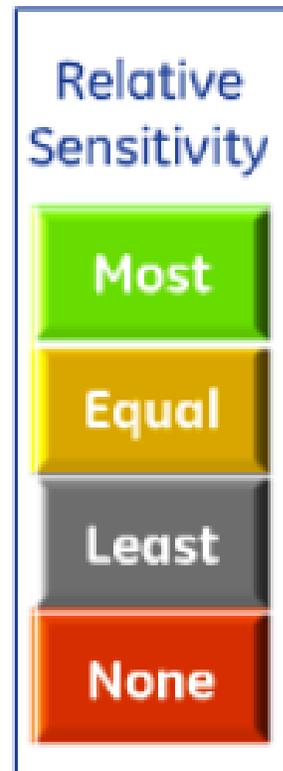


ACTION POTENTIAL DURATION AFTER DIFFERENTIATION



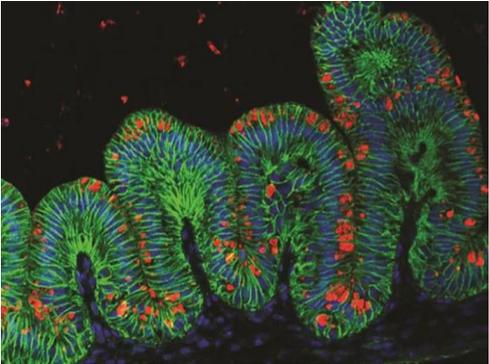
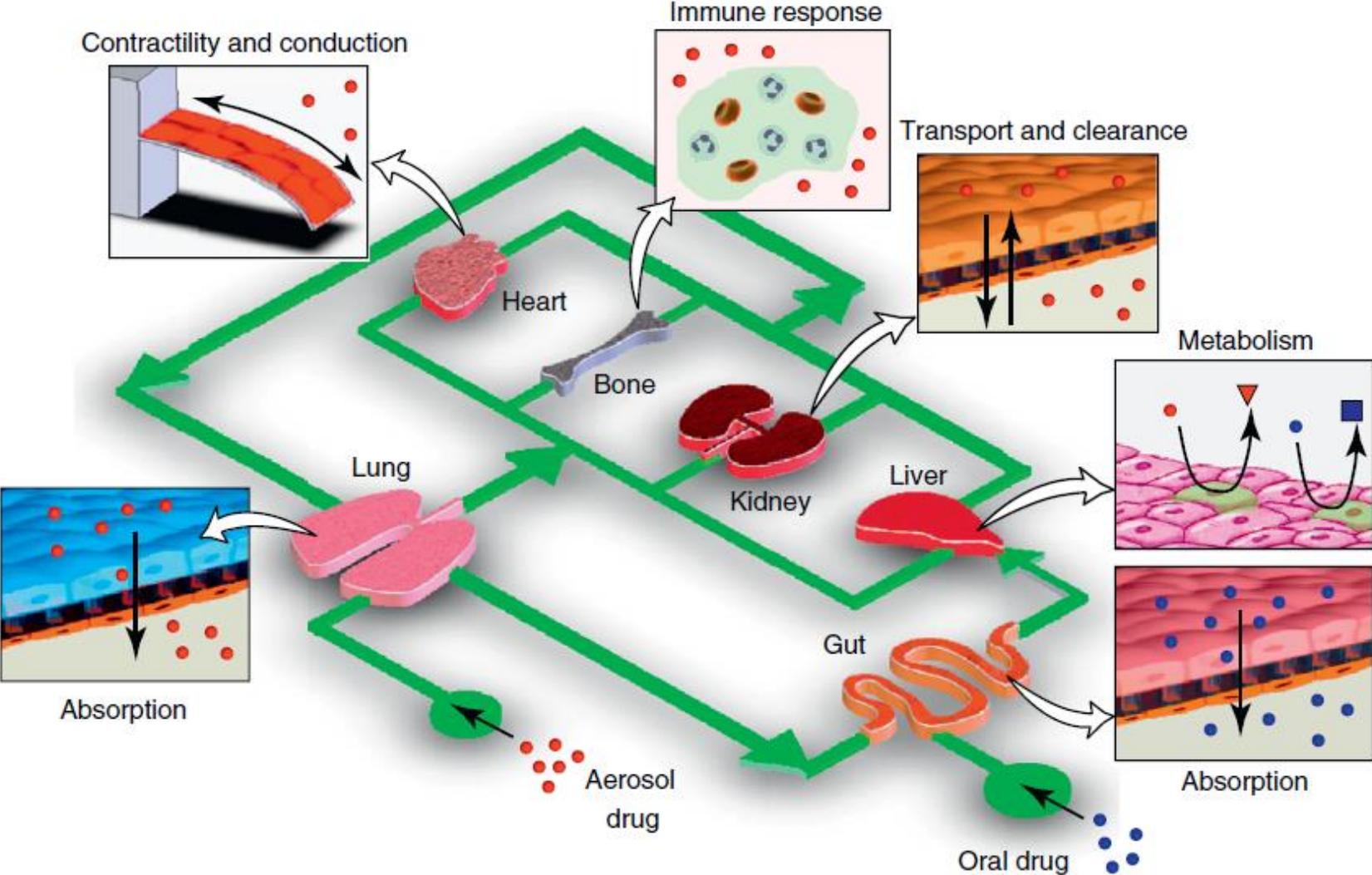
BETTER DRUG SCREENING

Compound	RABBIT Purkinje Fibre	CANINE Purkinje Fibre	HUMAN hESC-VM
Terfenadine	1.0 μ M ⊕	False ⊖	0.03 μ M ⊕
Quinidine	1.0 μ M ⊕	1.0 μ M ⊕	0.3 μ M ⊕
Cisapride	0.1 μ M ⊕	0.1 μ M ⊕	0.01 μ M ⊕
Sotalol	10 μ M ⊕	100 μ M ⊕	10 μ M ⊕
Chromanol 293B	False ⊖	False ⊖	300 μ M ⊕
E-4031	N/A	0.1 μ M ⊕	0.1 μ M ⊕
Nifedipine	N/A	>10 μ M ⊕	0.03 μ M ⊕



⊕ Change in APD₉₀ >10%

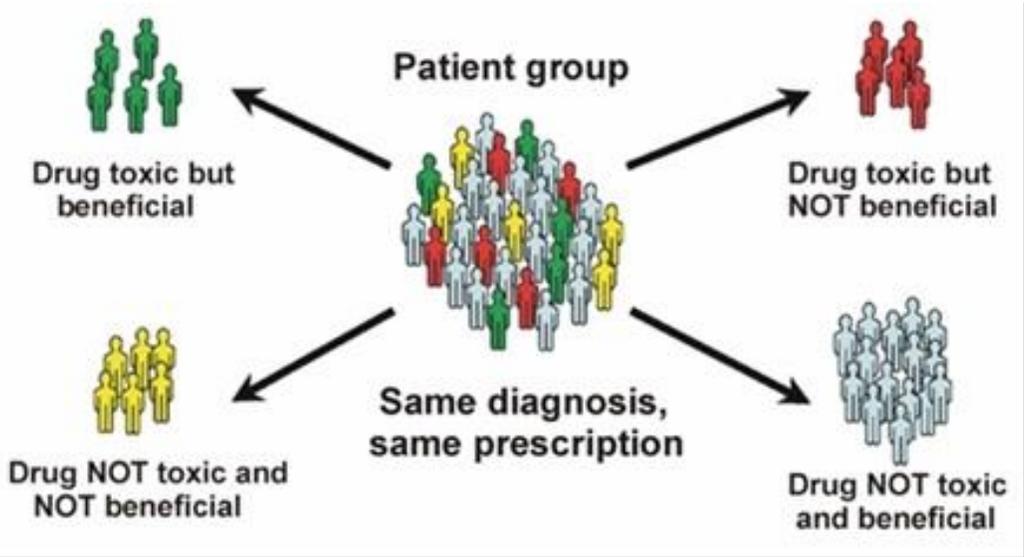
BETTER DRUG SCREENING



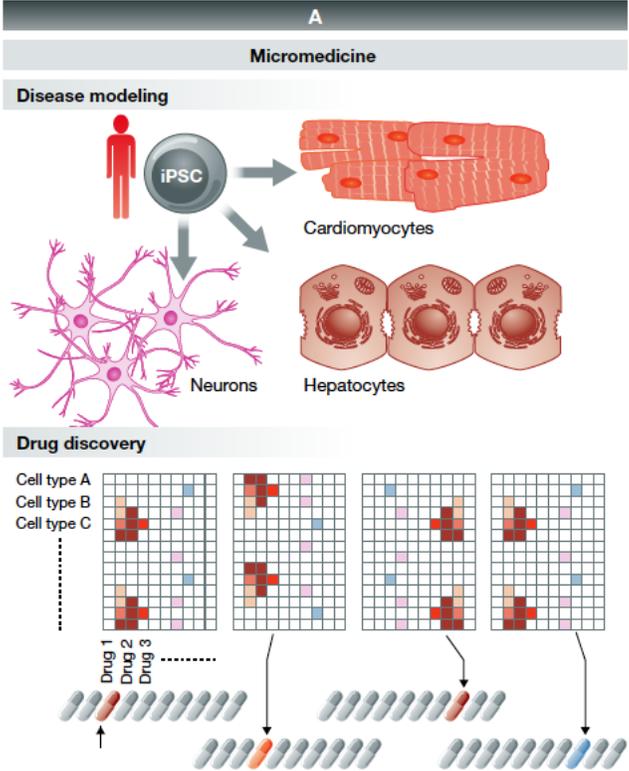
INTESTINAL ORGANOID

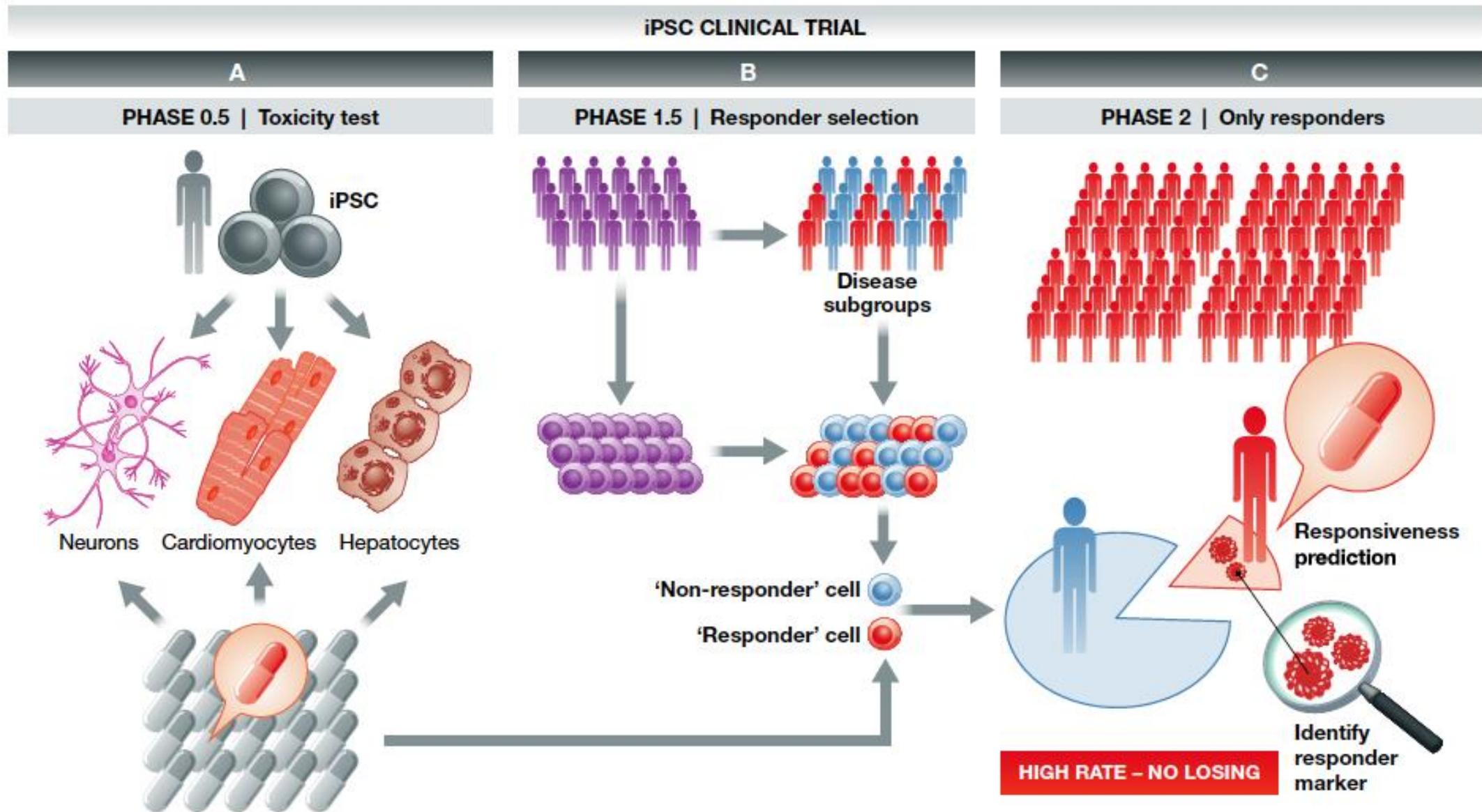
PERSONALISED MEDICINE

THE OLD MODEL



THE NEW MODEL





CELL THERAPIES FOR INCURABLE DISEASES

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Autologous Induced Stem-Cell-Derived Retinal Cells for Macular Degeneration

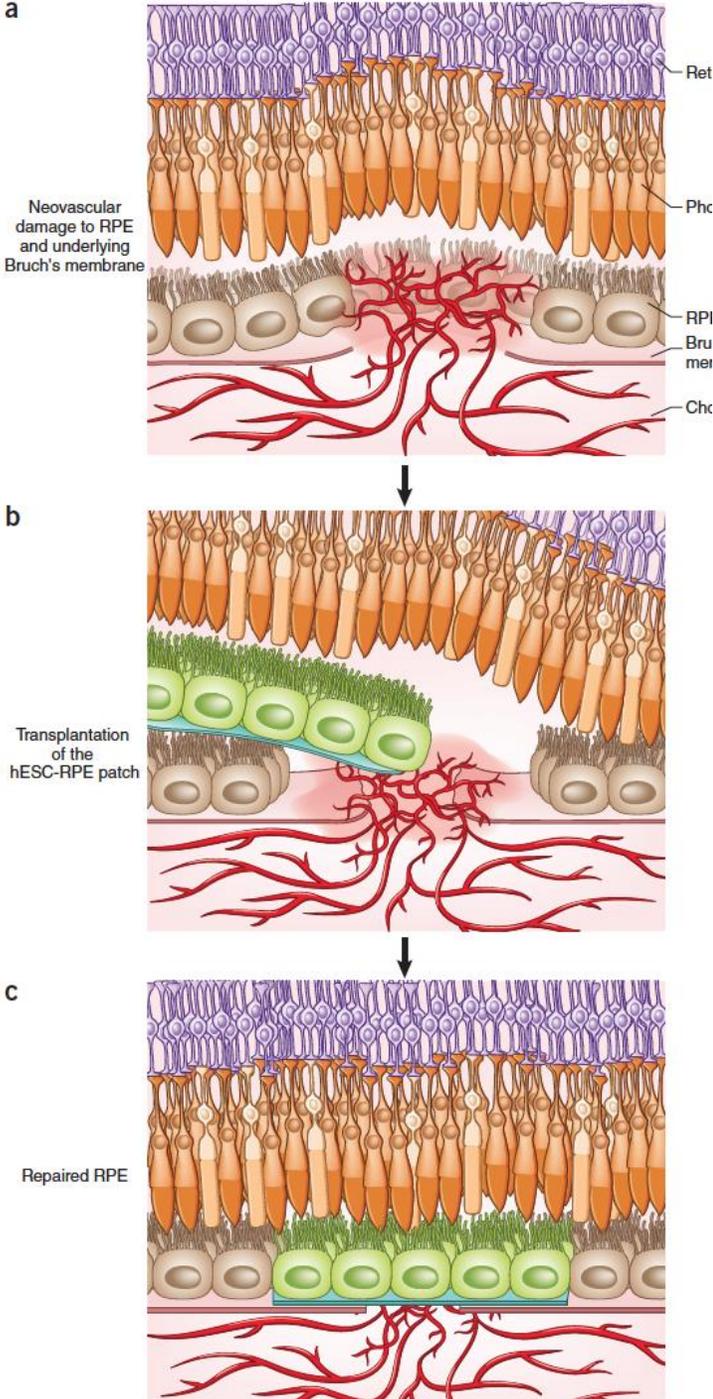
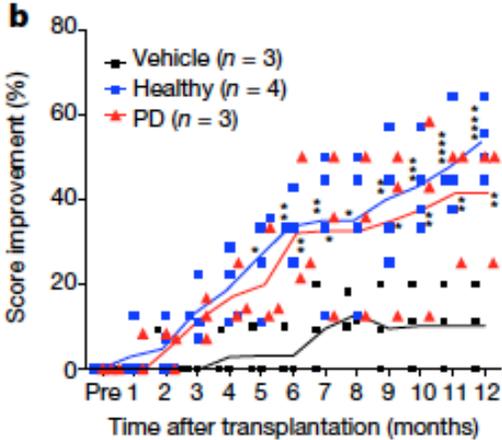
n engl j med 376;11 nejm.org March 16, 2017

Human iPS cell-derived dopaminergic neurons function in a primate Parkinson's disease model

Tetsuhiro Kikuchi¹, Asuka Morizane¹, Daisuke Doi¹, Hiroaki Magotani¹, Hiroataka Onoe², Takuya Hayashi², Hiroshi Mizuma², Sayuki Takara², Ryosuke Takahashi³, Haruhisa Inoue⁴, Satoshi Morita⁵, Michio Yamamoto⁵, Keisuke Okita⁶, Masato Nakagawa⁶, Malin Parmar⁷ & Jun Takahashi^{1,8}

592 | NATURE | VOL 548 | 31 AUGUST 2017

Clinical trial to start in 2019 in Japan



GENE THERAPIES FOR INCURABLE DISEASES

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Gene Therapy in a Patient with Sickle Cell Disease

N ENGL J MED 376:9 NEJM.ORG MARCH 2, 2017

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

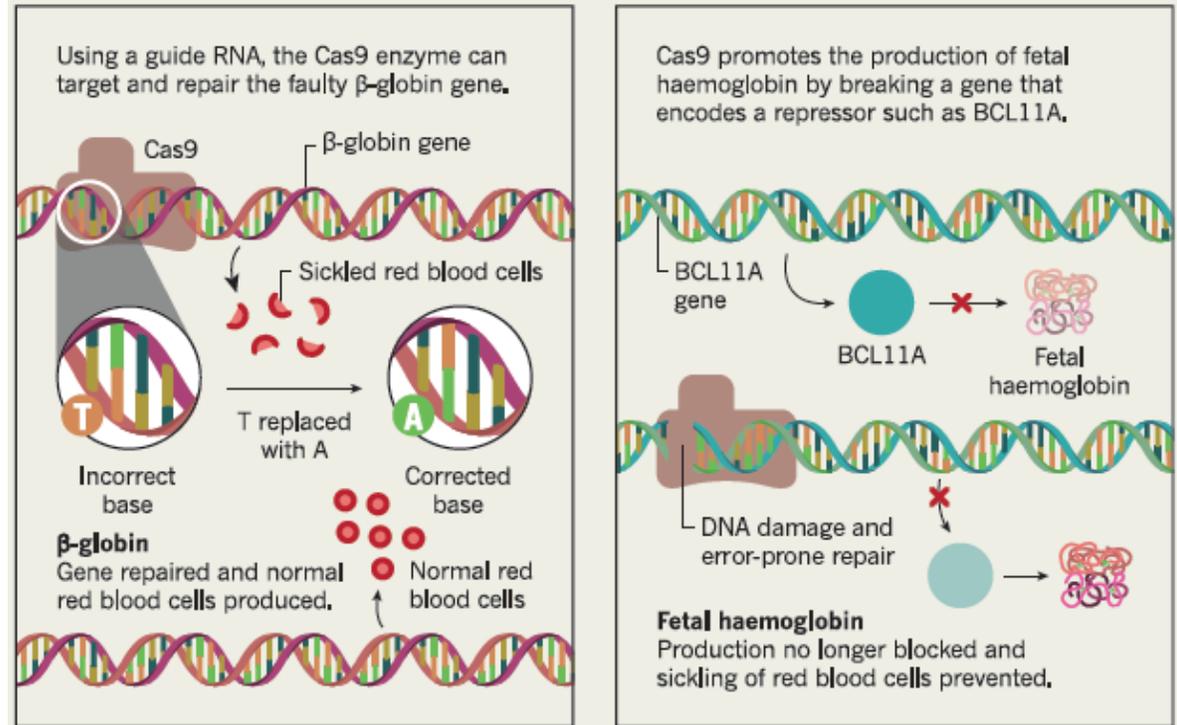
APRIL 19, 2018

VOL. 378 NO. 16

Gene Therapy in Patients with Transfusion-Dependent β -Thalassemia

GENE EDITING WITH CRISPR

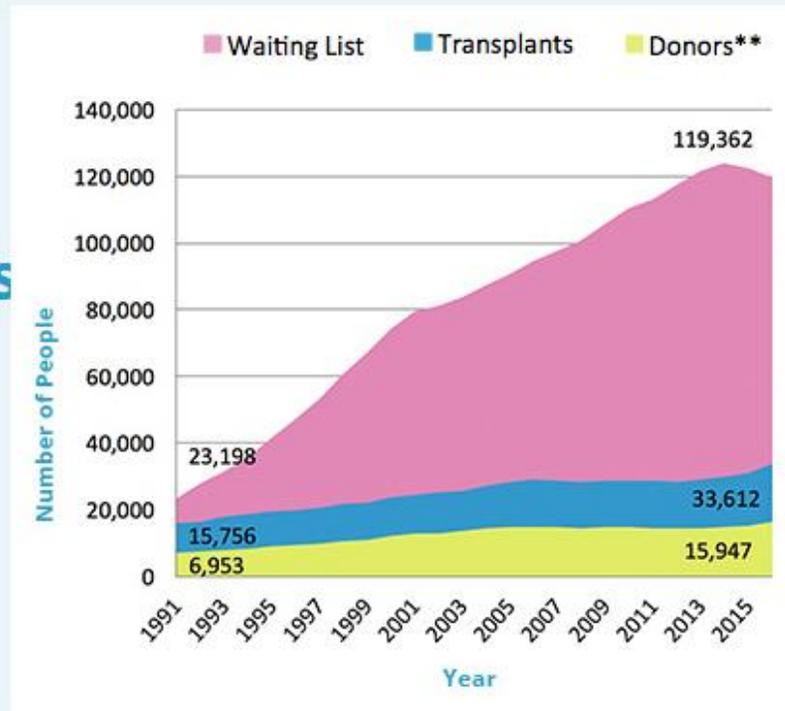
CRISPR-Cas9 gene editing is helping to tackle sickle-cell disease in two ways.



HOW TO DEAL WITH THE SHORTAGE OF ORGAN TRANSPLANTS

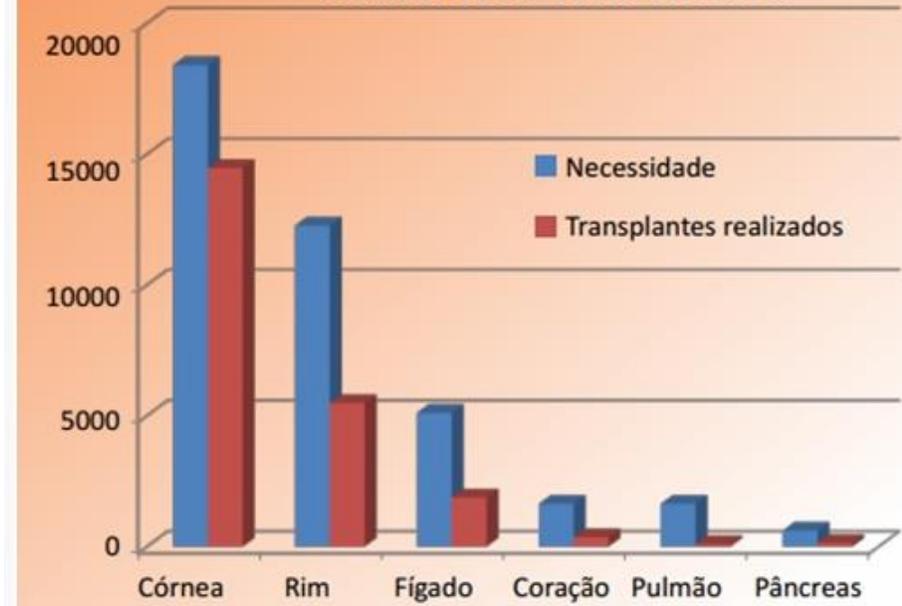
the organ shortage continues

Each year, the number of people on the waiting list continues to be much larger than both the number of donors and transplants, which grow slowly.



Data from optn.transplant.hrsa.gov and OPTN/SRTR Annual Report. OPTN has current, in-depth statistics. [Click to view.](#)

Necessidade Estimada e número de transplantes realizados no Brasil em 2016



*Fonte: Associação Brasileira de Transplante de Órgãos

HEART TRANSPLANTS IN BRAZIL

Em ritmo de crescimento

Total de transplantes de coração realizados no Brasil, por ano



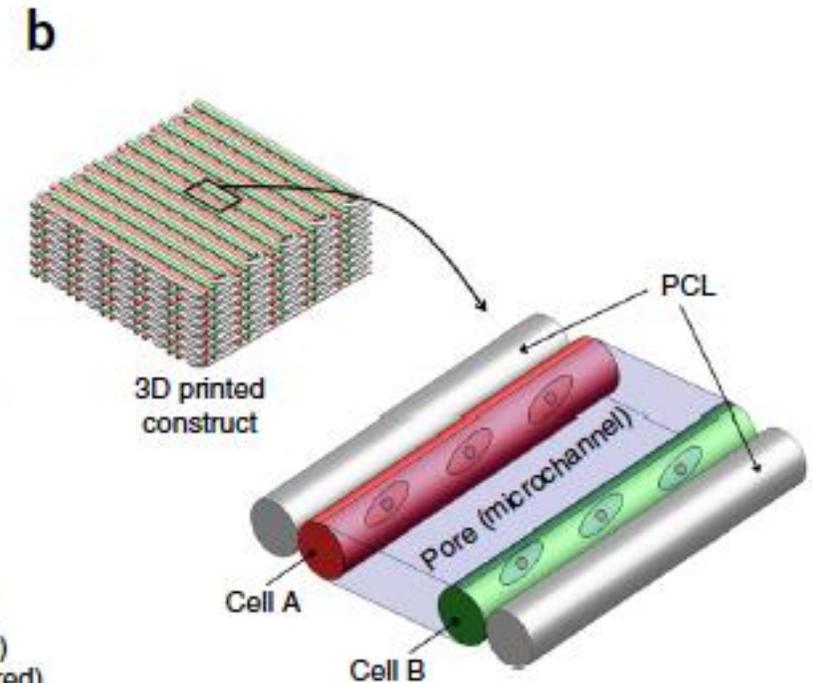
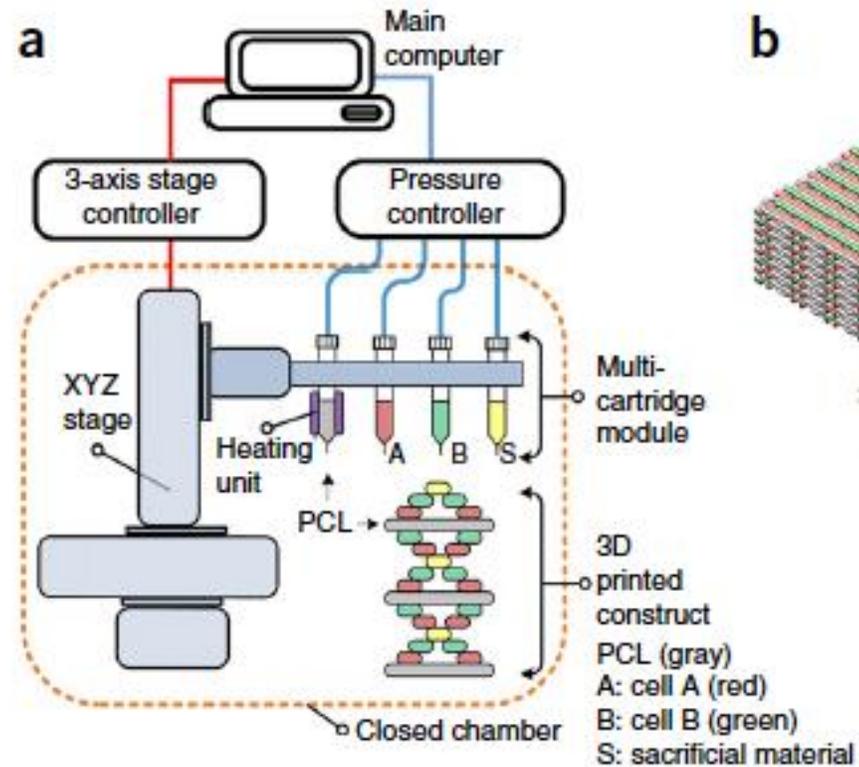
* Primeiro ano dos registros anuais de transplantes da ABTO

FONTE ABTO

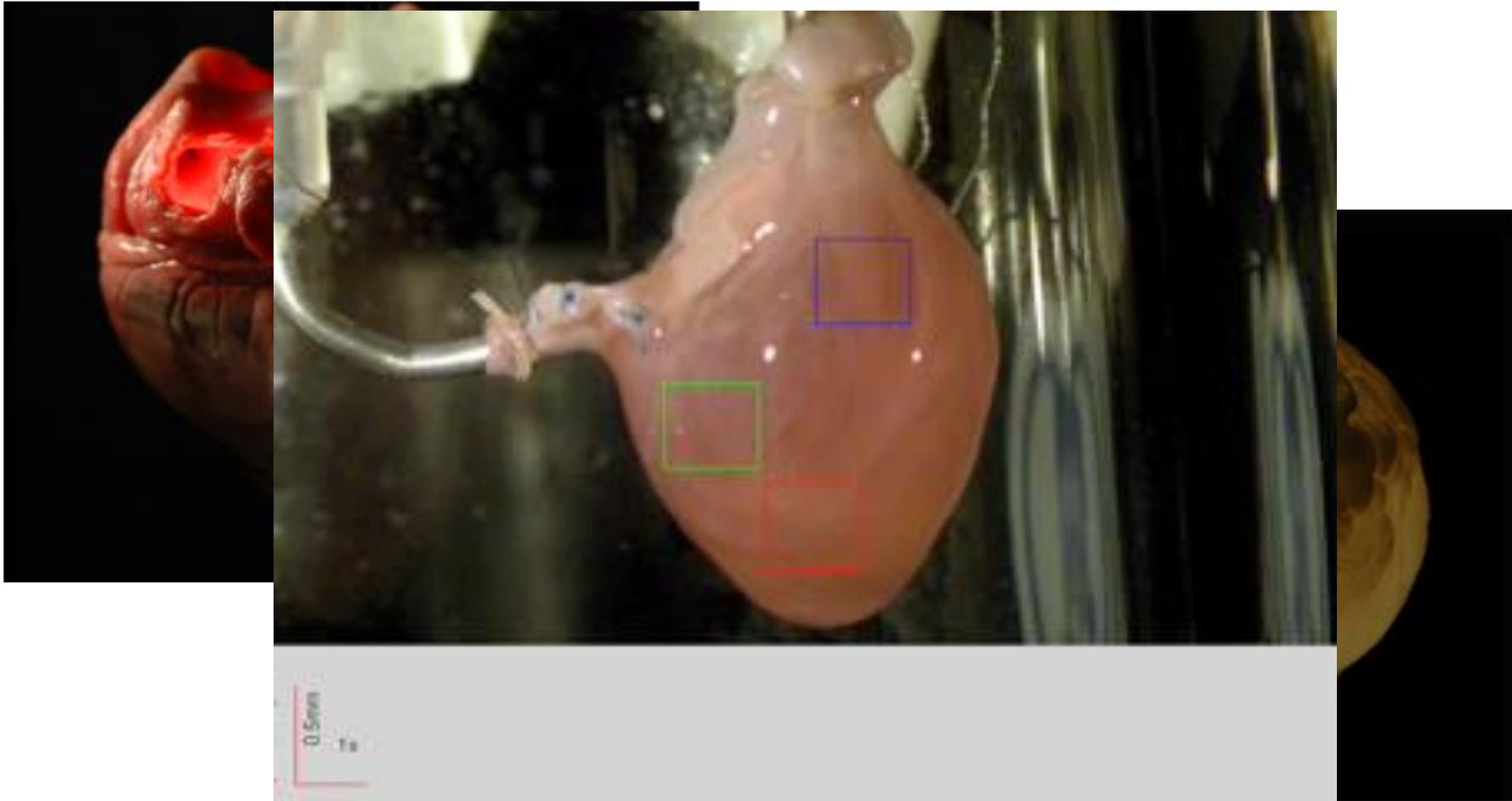


BIOENGINEERING ORGANS AND TISSUES

3D PRINTING



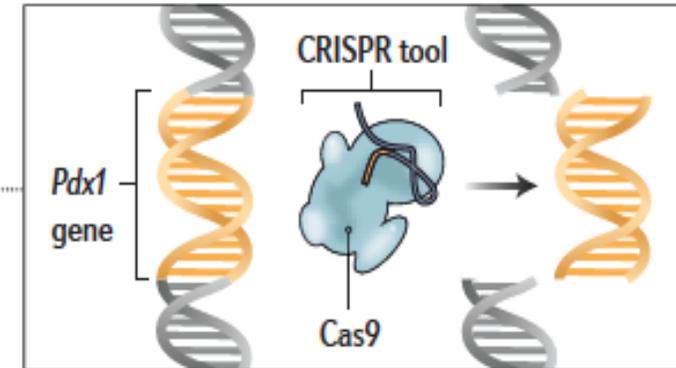
BIOENGINEERING ORGANS AND TISSUES



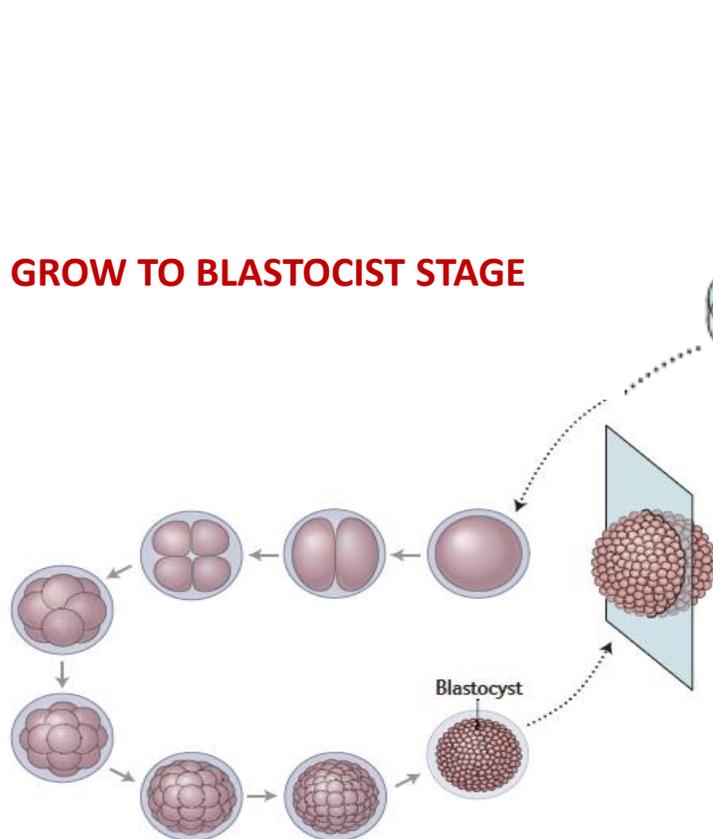
USING BIOREACTOR-ANIMALS AS A SOURCE

1. GENE EDIT THE EMBRYO

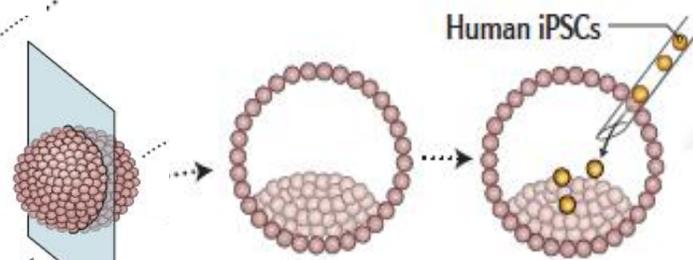
Delete Pdx1



2. GROW TO BLASTOCYST STAGE



3. INJECT HUMAN iPS

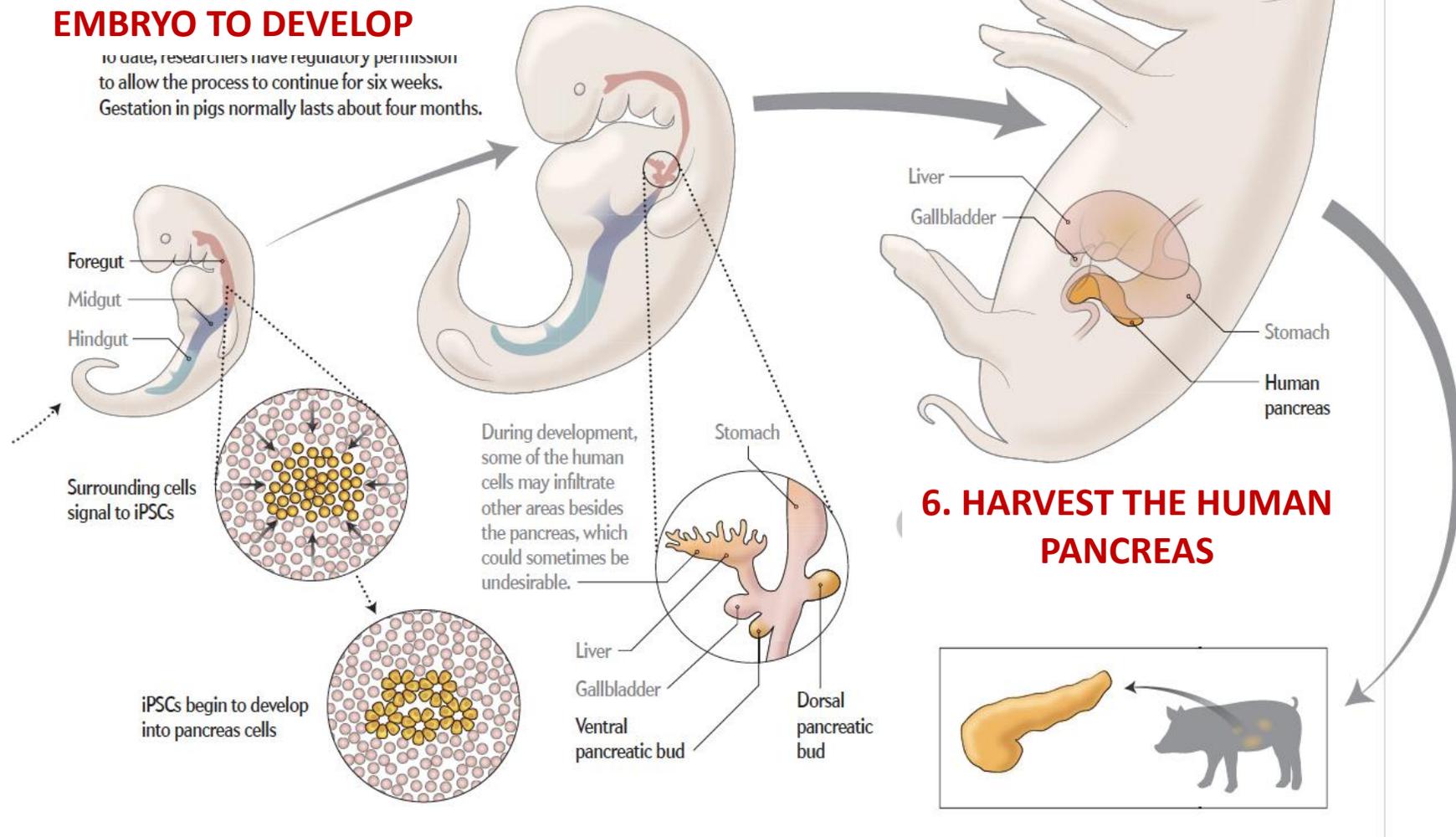


4. IMPLANT THE CHIMERIC EMBRYO



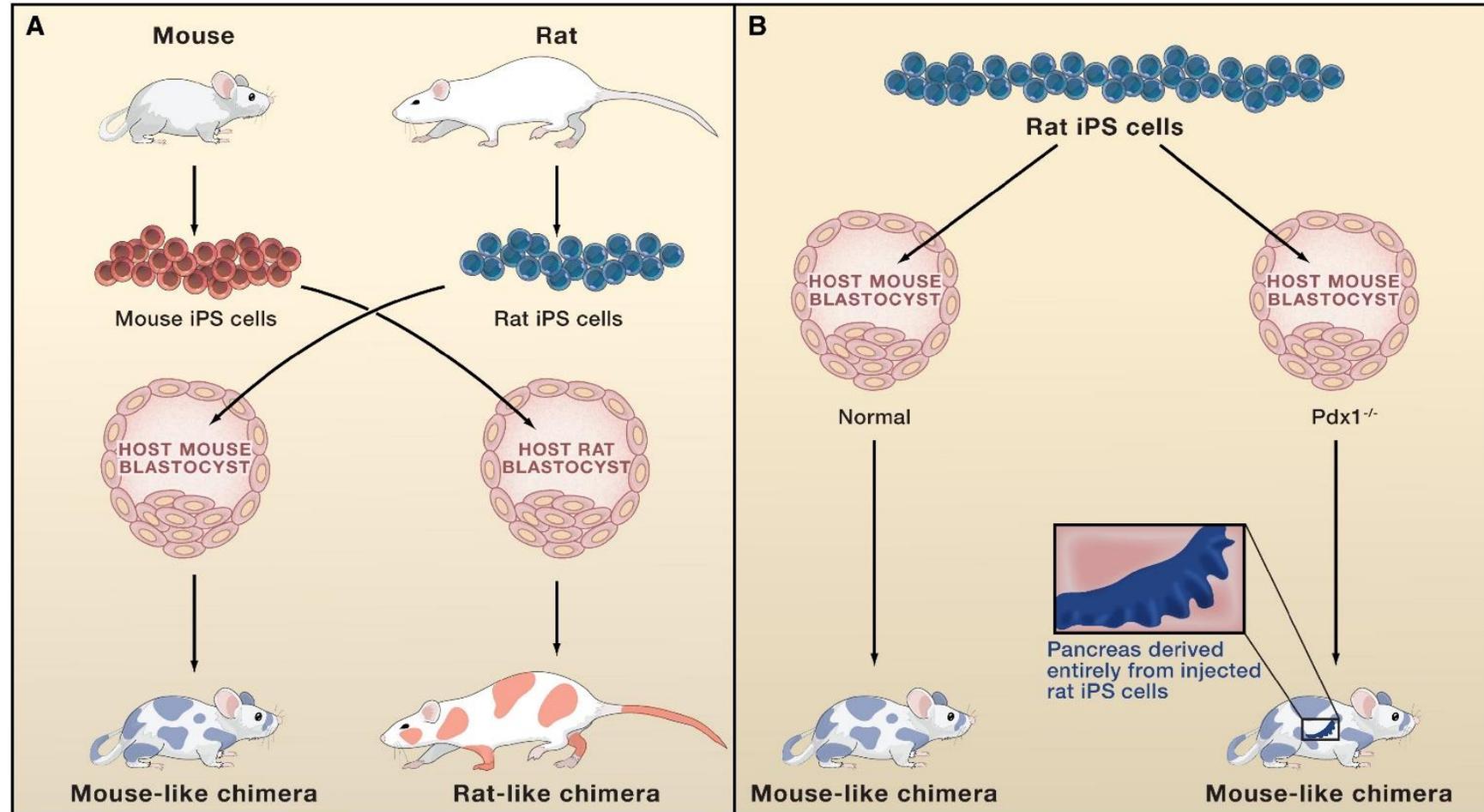
5. ALLOW CHIMERIC EMBRYO TO DEVELOP

To date, researchers have regulatory permission to allow the process to continue for six weeks. Gestation in pigs normally lasts about four months.



Generation of Rat Pancreas in Mouse by Interspecific Blastocyst Injection of Pluripotent Stem Cells

Toshihiro Kobayashi,^{1,2} Tomoyuki Yamaguchi,^{1,2} Sanae Hamanaka,^{1,2} Megumi Kato-Itoh,^{2,3} Yuji Yamazaki,^{1,2} Makoto Ibata,² Hideyuki Sato,^{1,2} Youn-Su Lee,^{1,2} Jo-ichi Usui,^{1,6} A.S. Knisely,⁵ Masumi Hirabayashi,^{3,4} and Hiromitsu Nakauchi^{1,2,*}





Dilza



Fernanda



Taís



Gustavo



Adriana



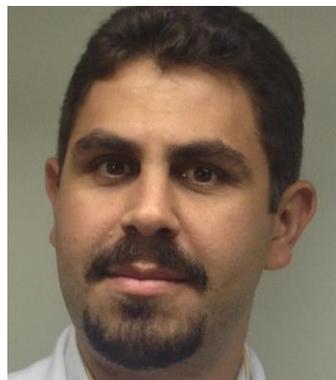
Emiliano



Regina



Fernando



Glauber



Jorge

