UFRJ

IBCCF
Instituto de Biofísica
Carlos Chagas Filho

Facing health challenges with science and technology

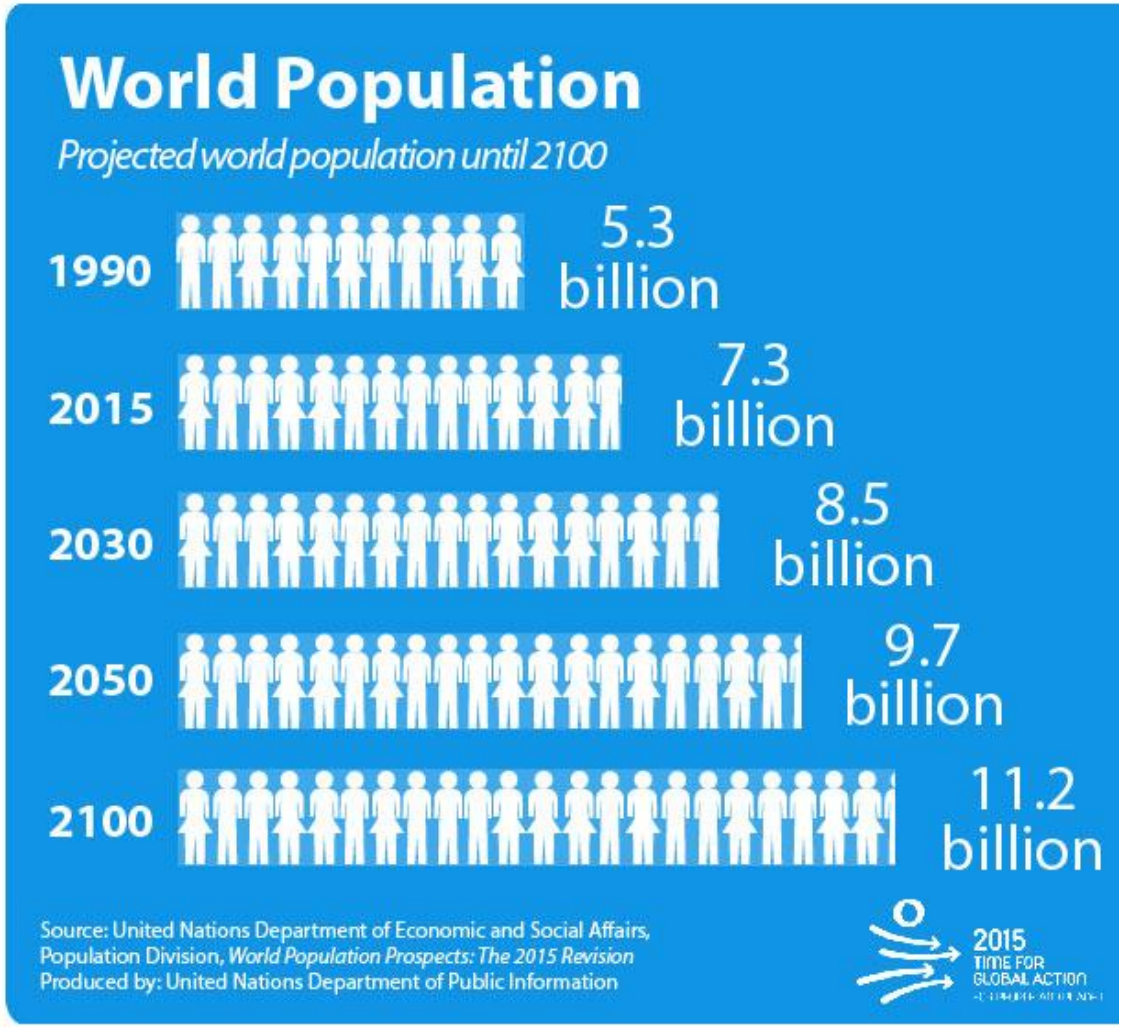
Antonio Carlos Campos de Carvalho

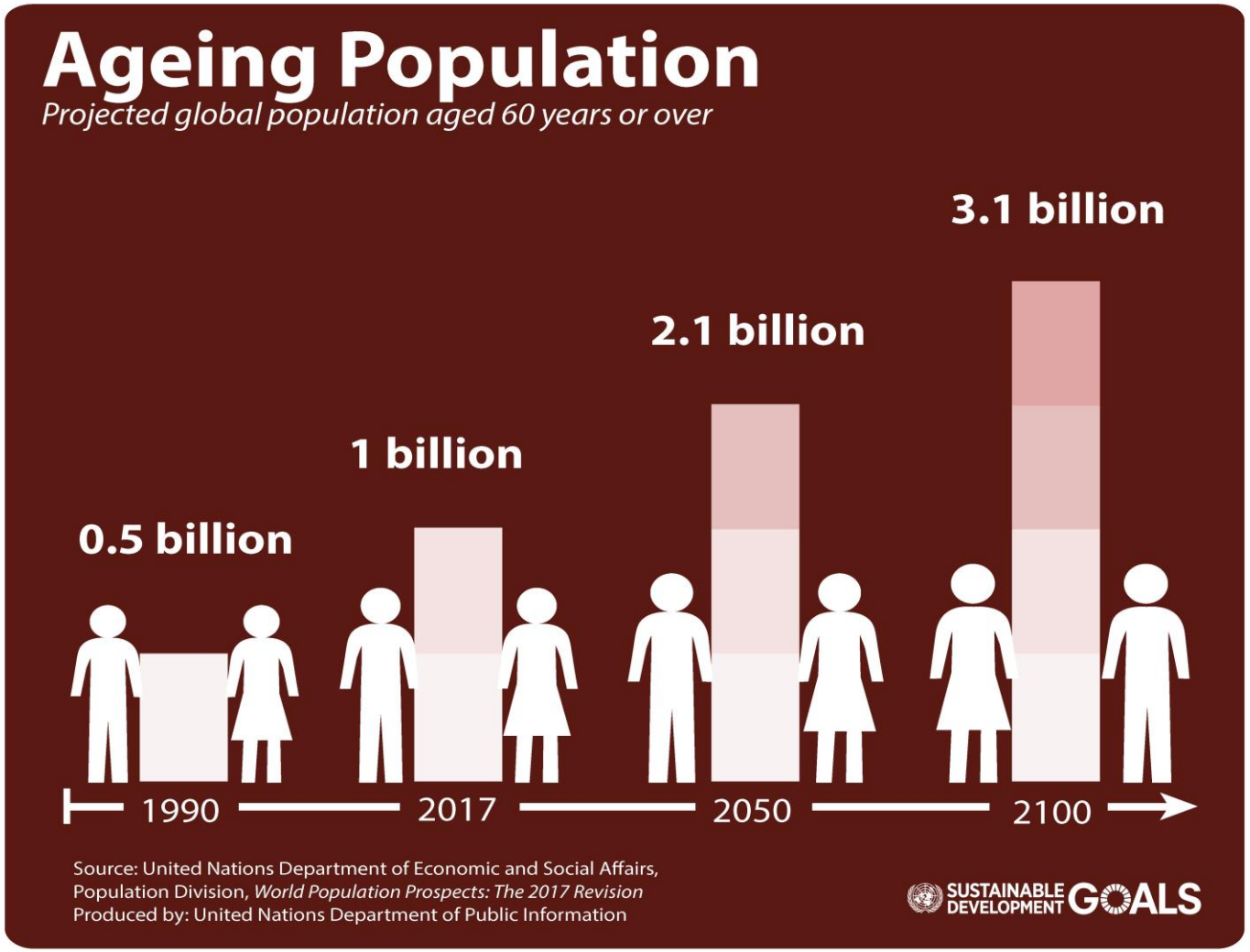
acarlos@biof.ufrj.br

INCT - Regenera
Instituto Nacional
de Ciência e Tecnologia
em Medicina Regenerativa

RNTC
Rede Nacional de Terapia Celular

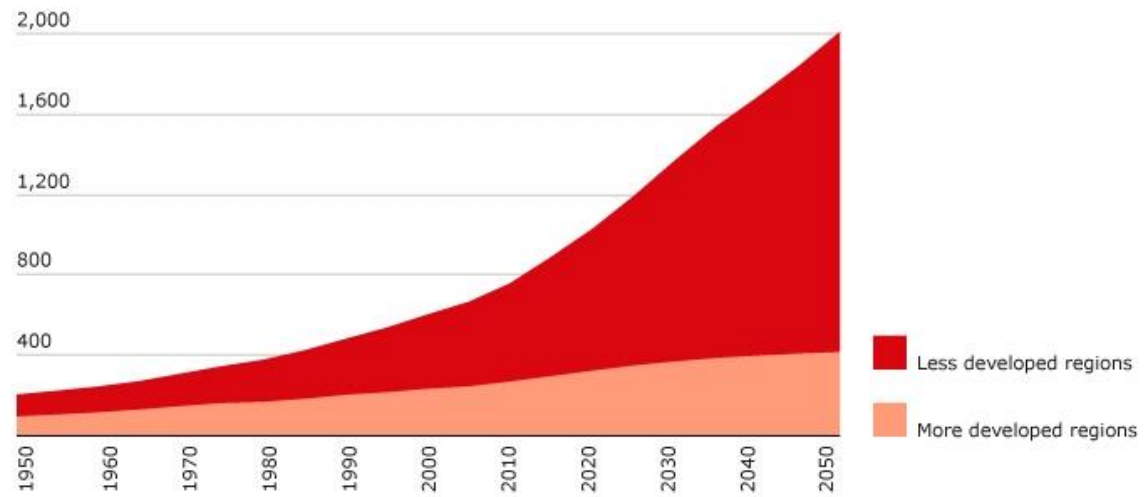
STATING THE PROBLEM





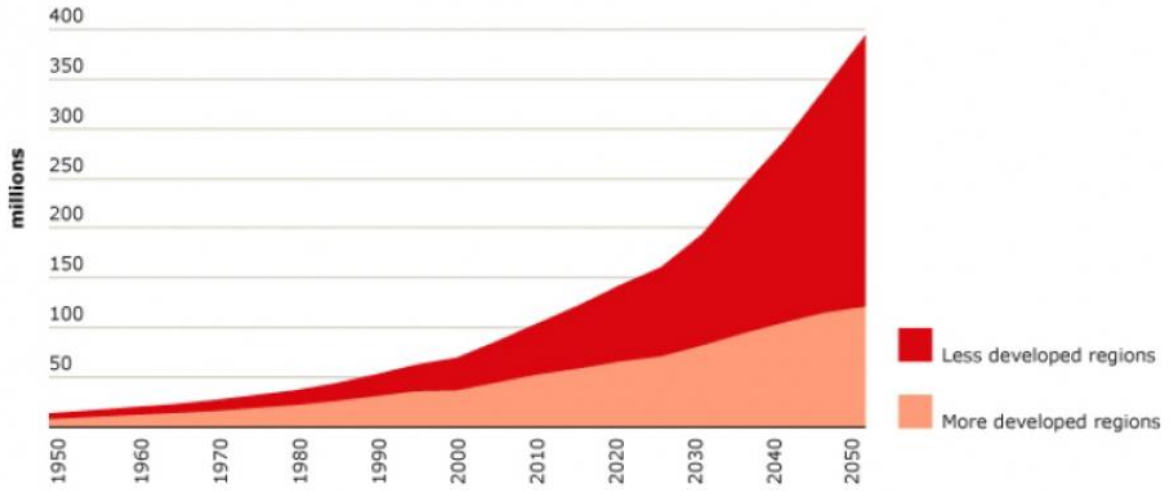
AGING RATE IS GREATER IN LESS DEVELPED REGIONS

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

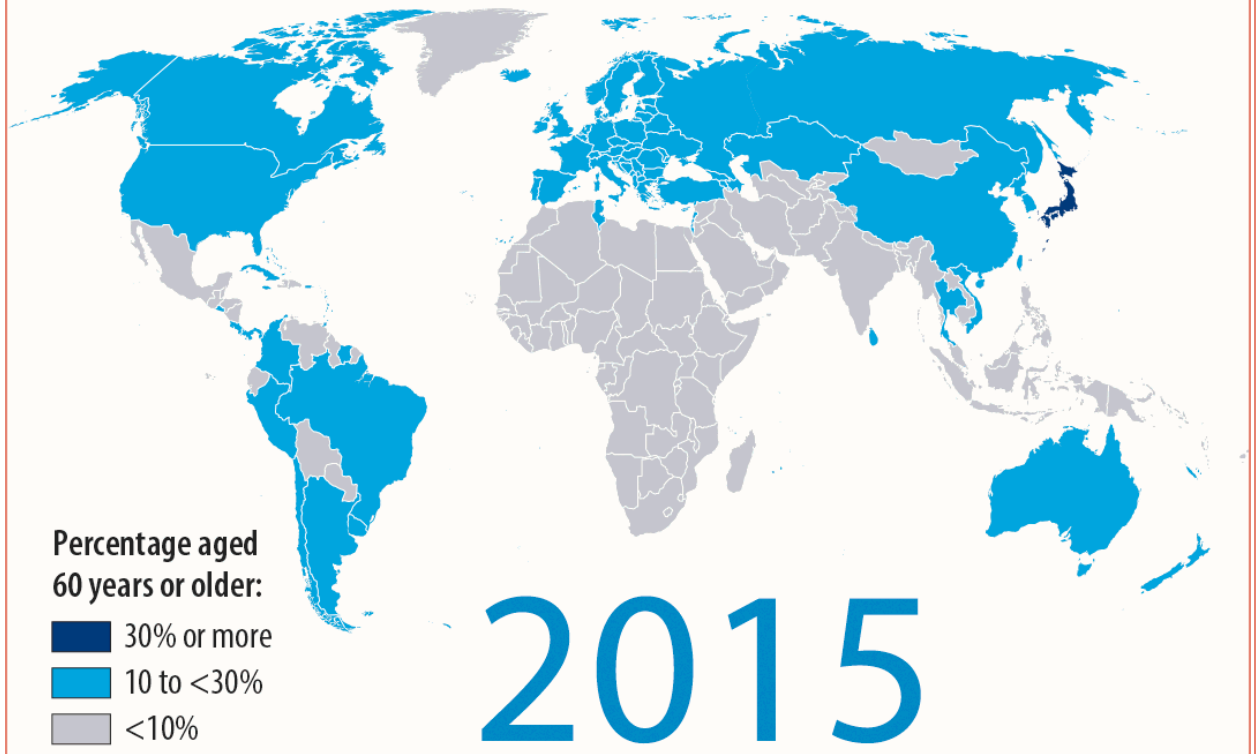


Source: Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat, *World Population Prospects: The 2008 Revision;* http://esa.un.org/unpp, accessed 13 May 2010

AGING IN THE WORLD

Ageing and Health #yearsahead

Populations are getting older

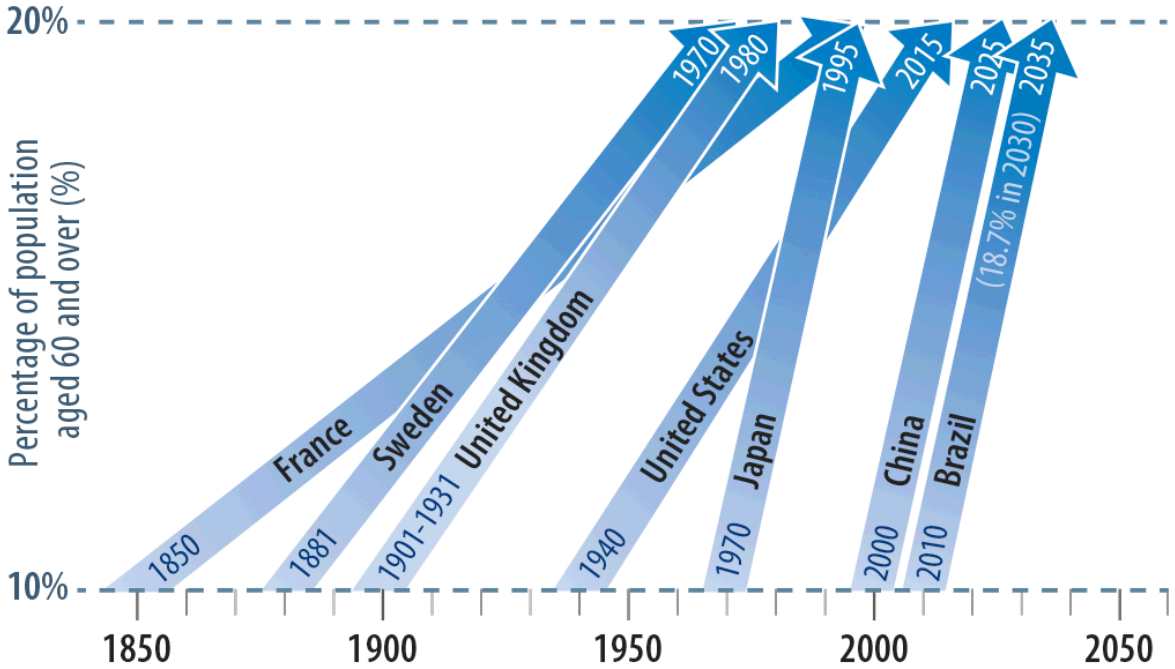


World Health Organization

Ageing and Health #yearsahead

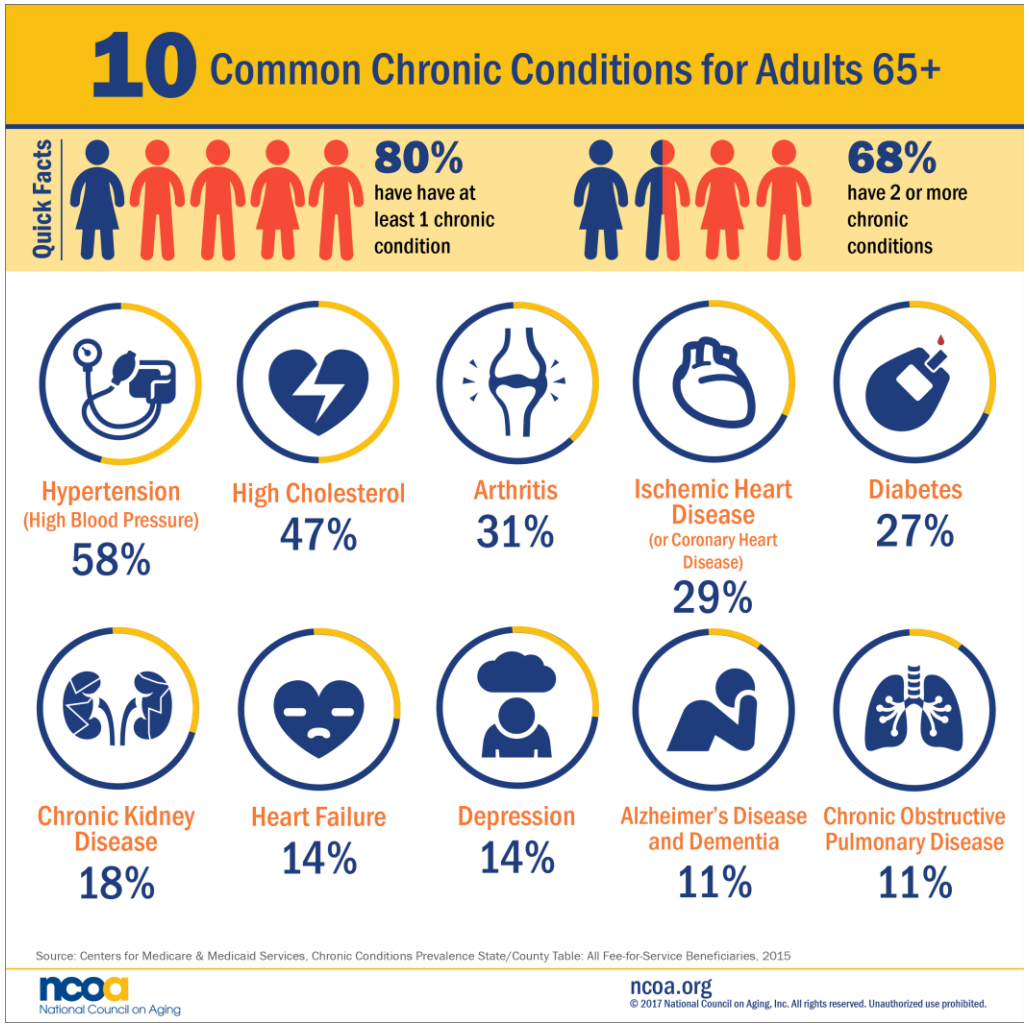
Speed of population ageing

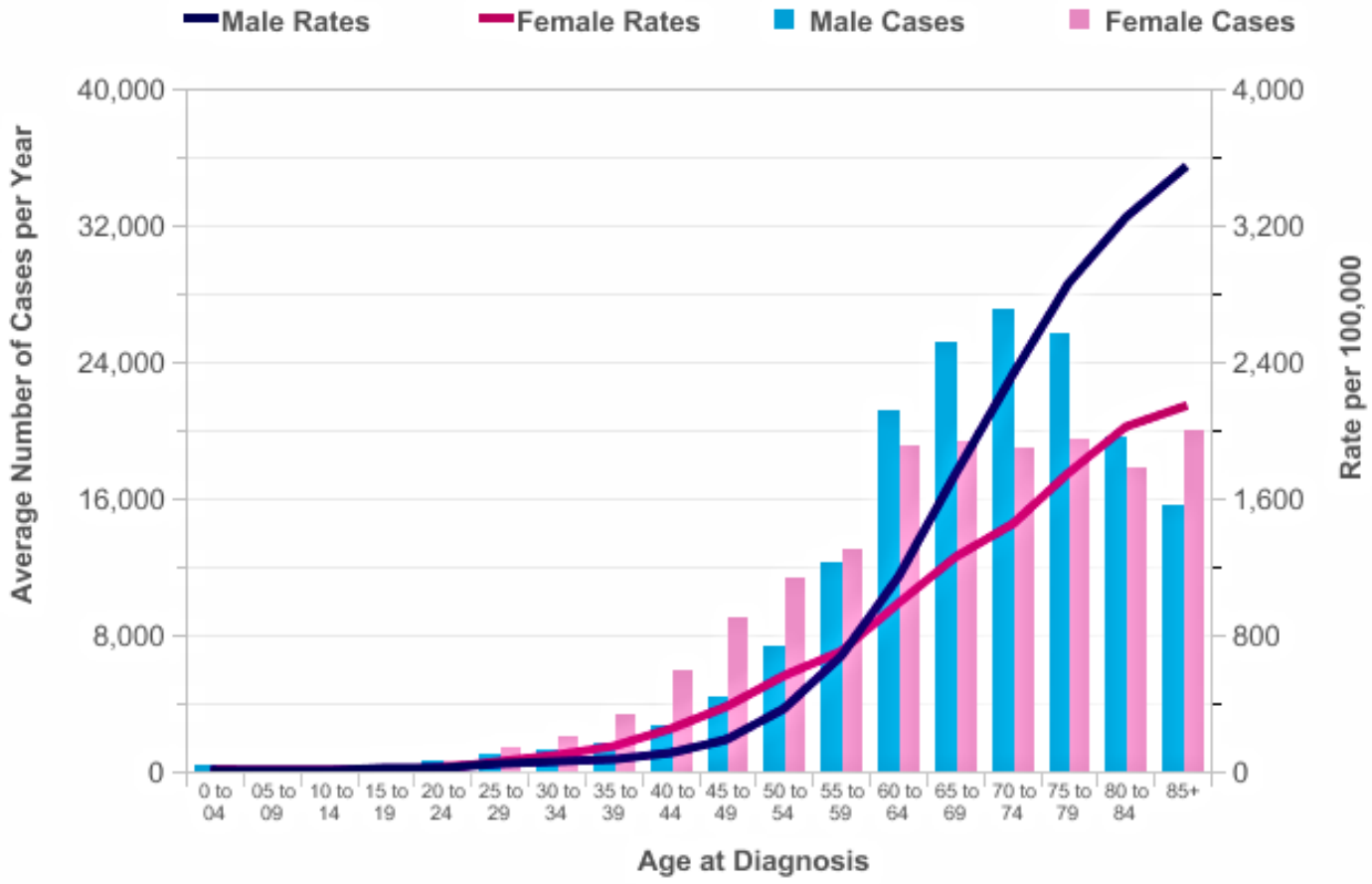
Time for percentage of population **over age 60** to double



World Health Organization

AGING AND CHRONIC DISEASES





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

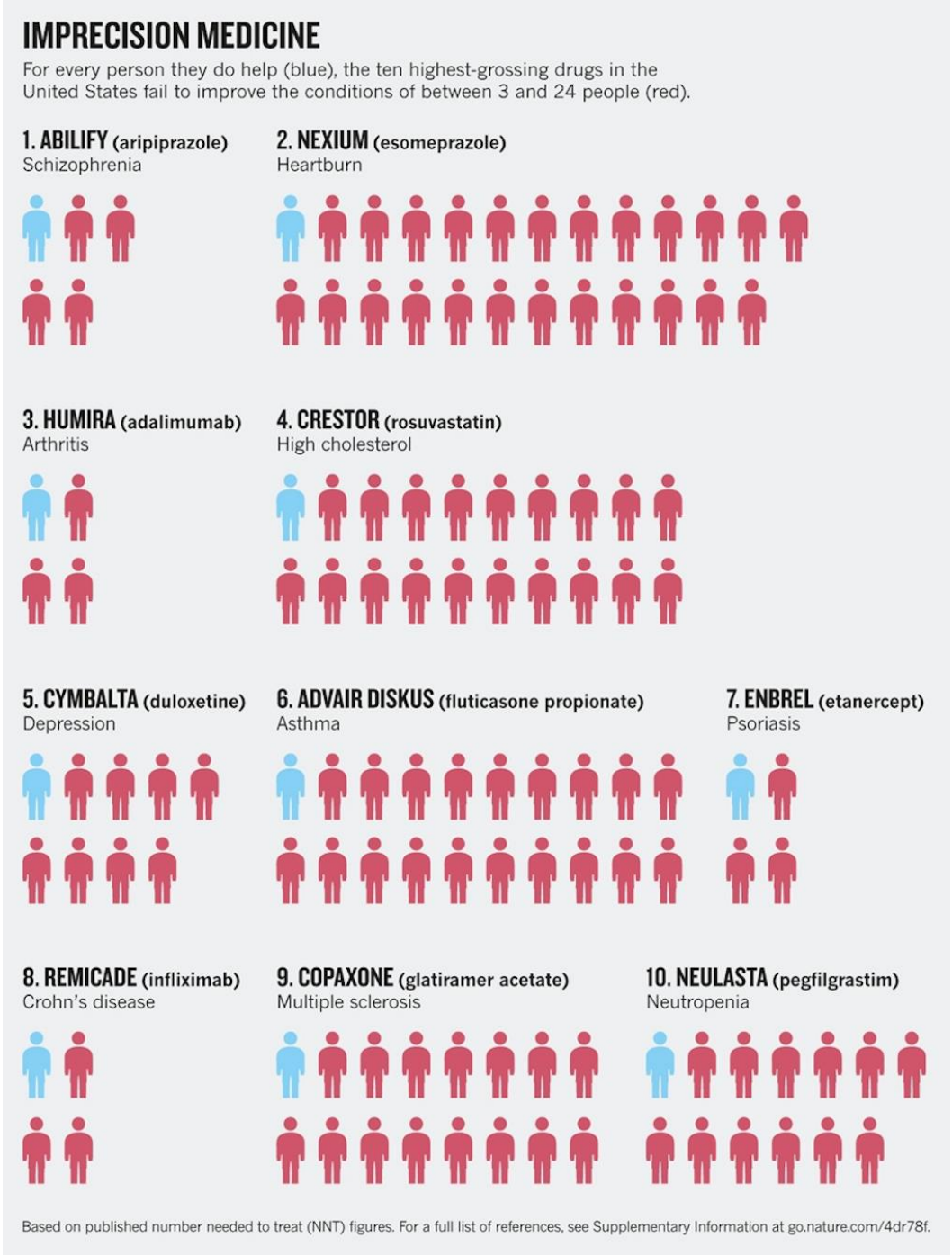
CARGA de DOENÇA

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

CARGA de DOENÇA

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

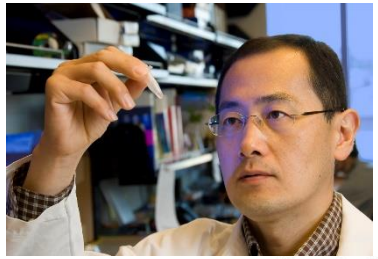


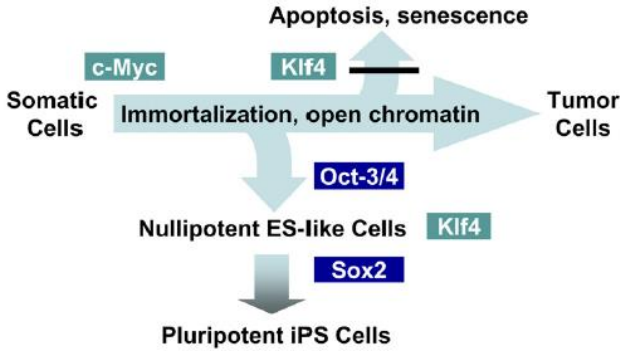
HOW CAN WE IMPROVE THIS SCENARIO?

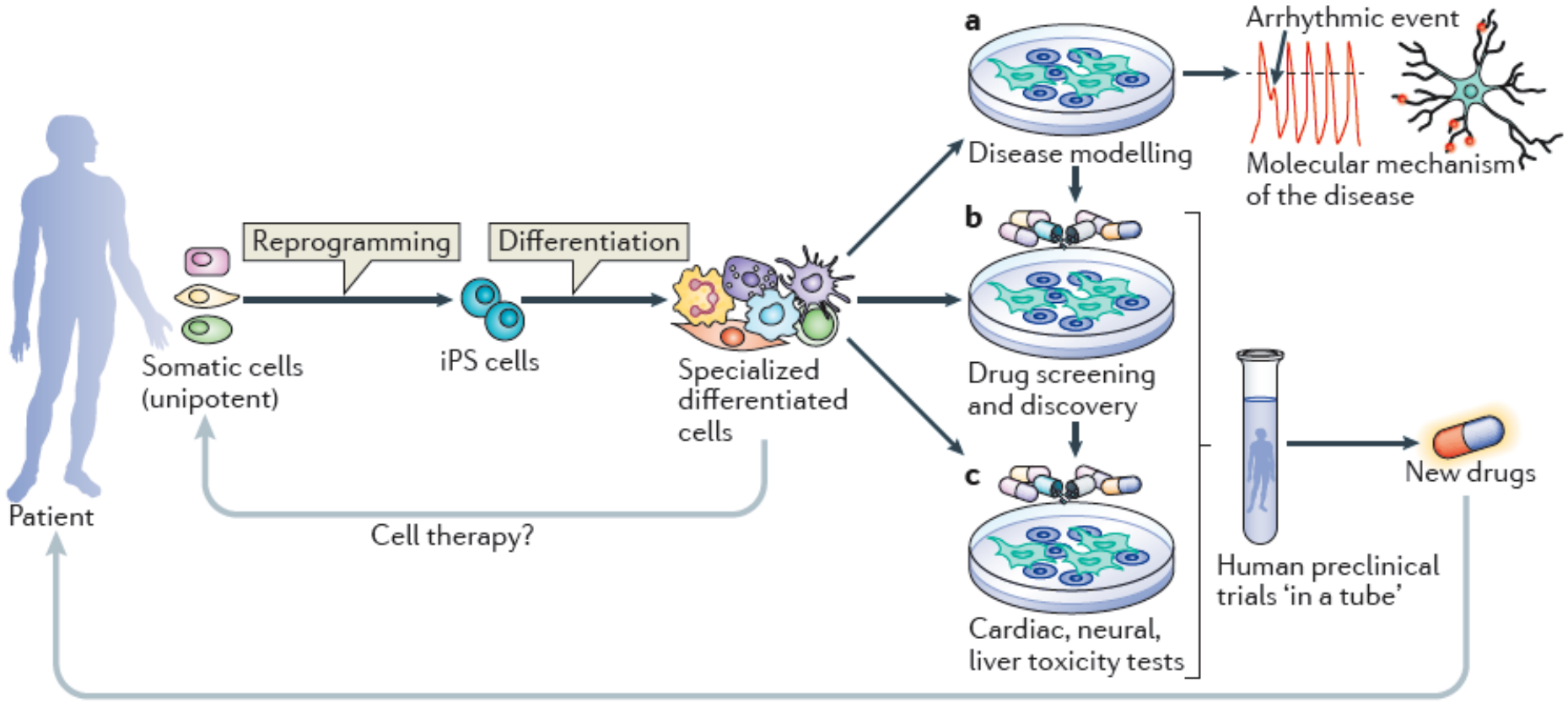
- **WE NEED BETTER DISEASE MODELS**
- **WE NEED TO IMPROVE DRUG SCREENING**
- **WE NEED AFFORDABLE PERSONALISED MEDICINE**
- **WE NEED NEW THERAPIES FOR INCURABLE DISEASES**

IS THIS ACHIEVABLE?

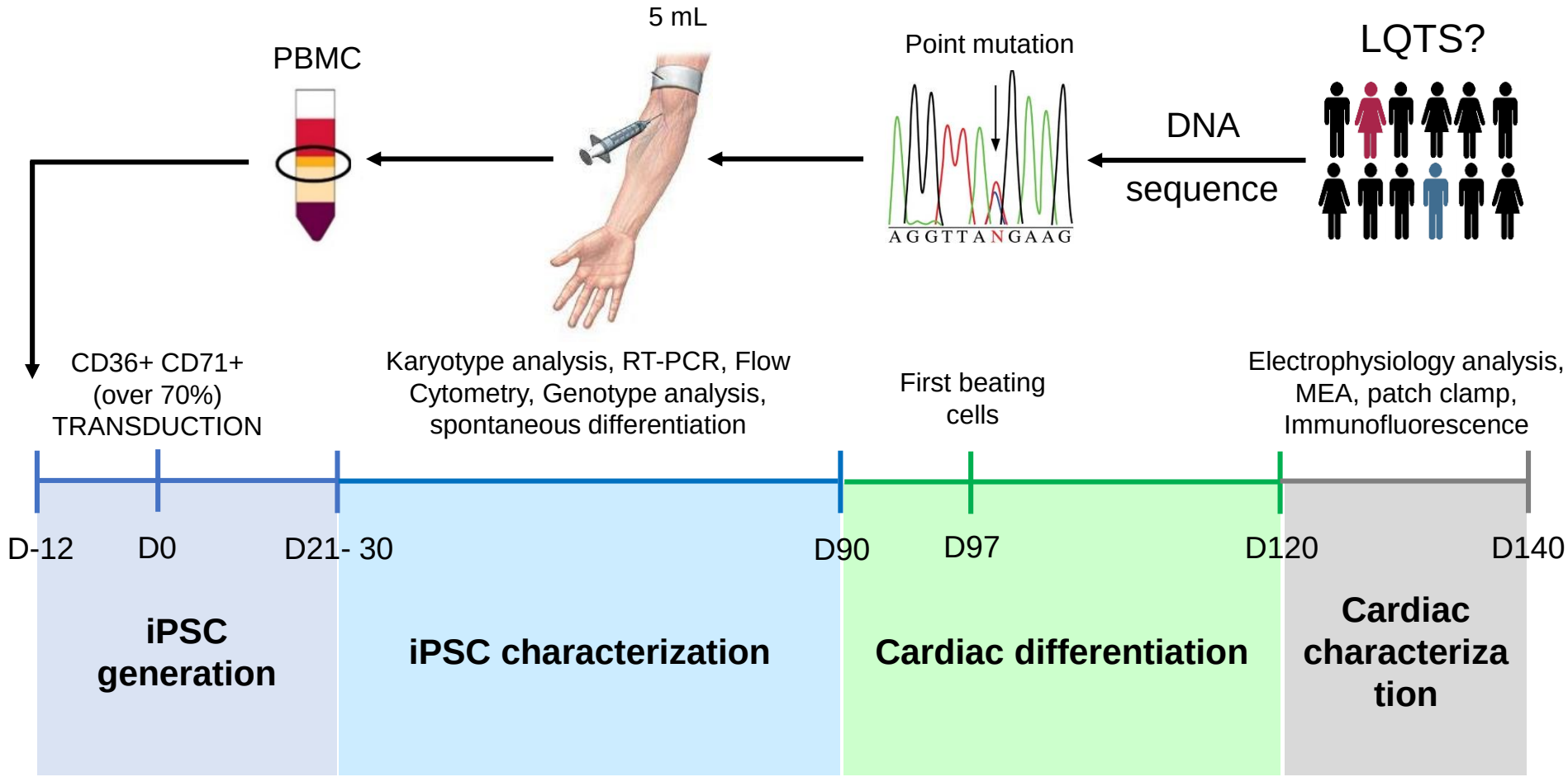
INDUCIBLE PLURIPOTENT STEM CELLS - iPS





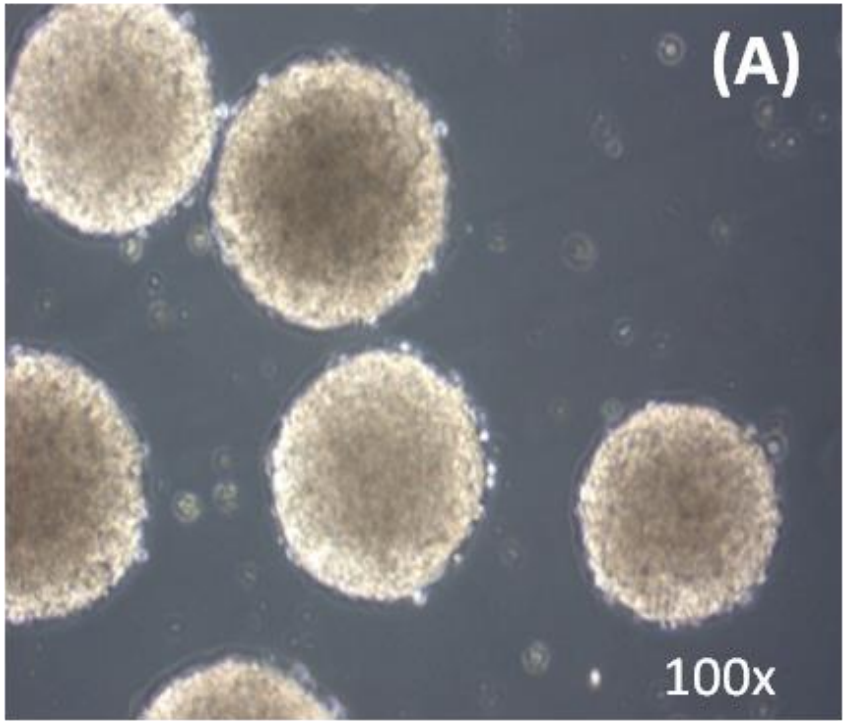


USING iPS FOR DISEASE MODELLING

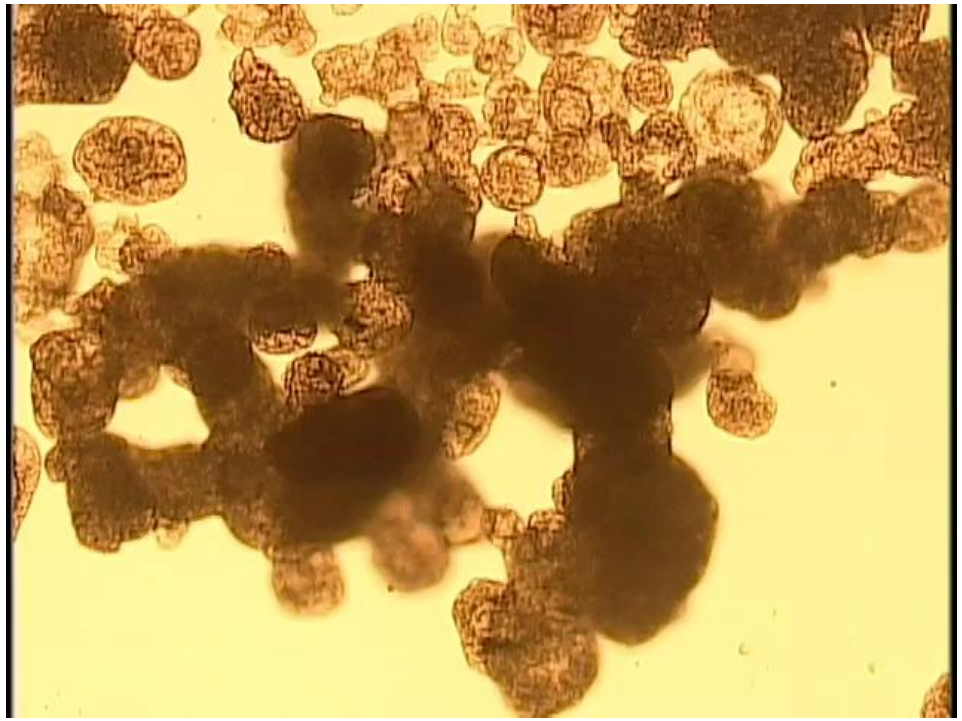


Embryoid Bodies (EB)

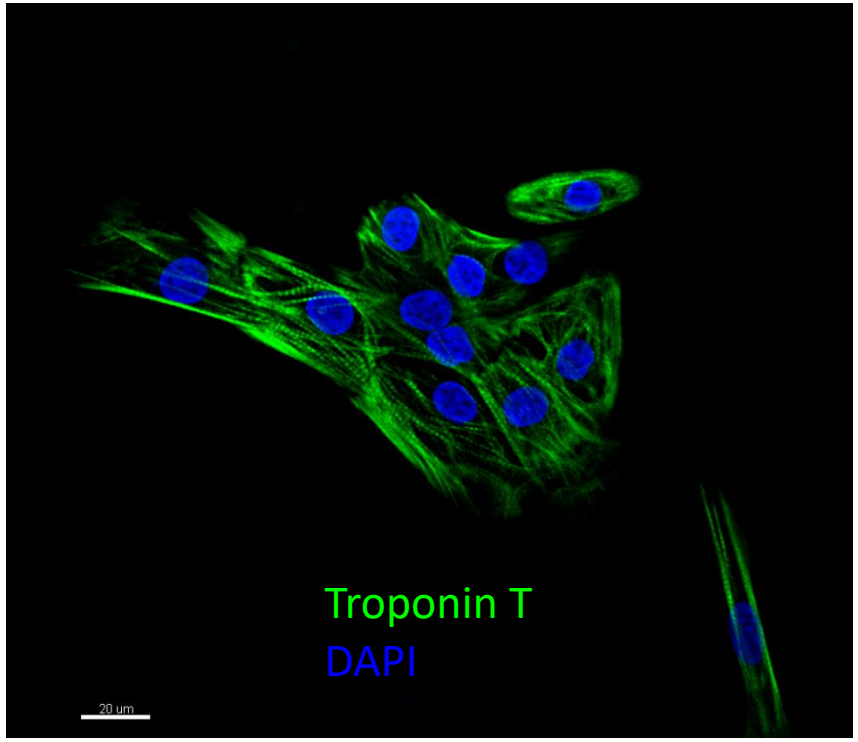
EB 2 days in suspension

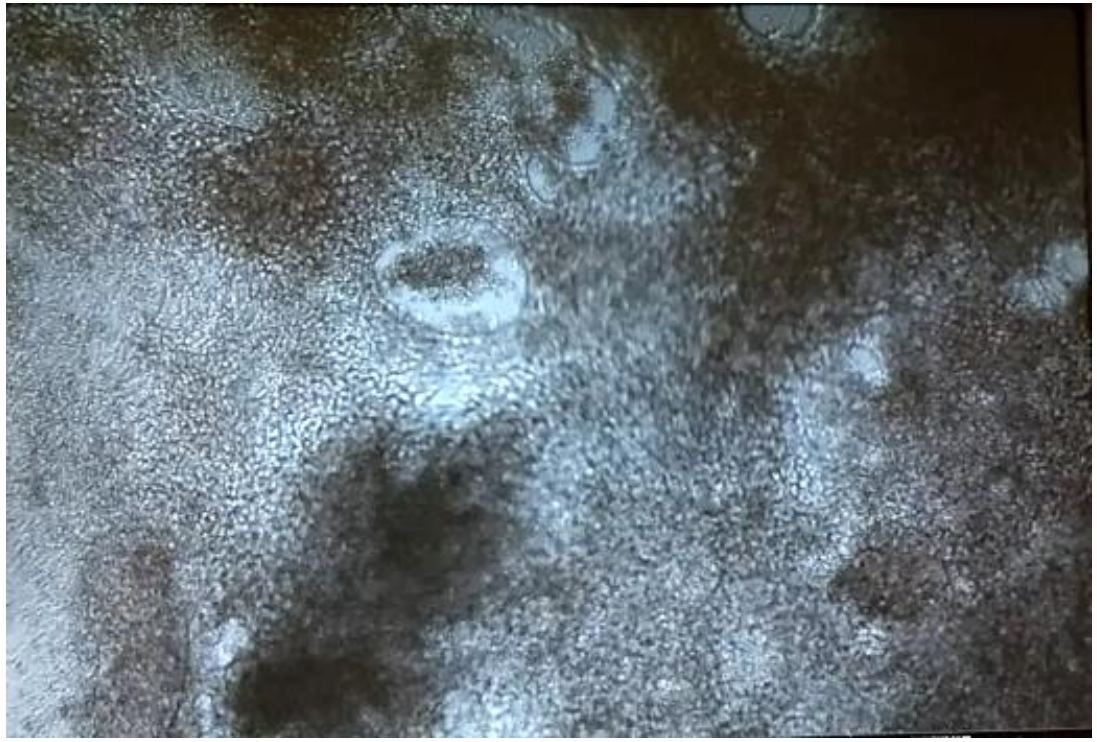


EB post differentiation

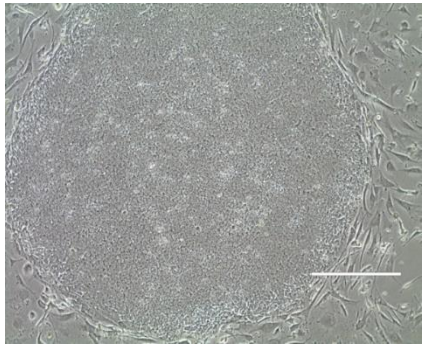


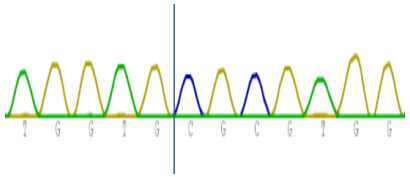
iPS DERIVED CARDIOMYOCYTES



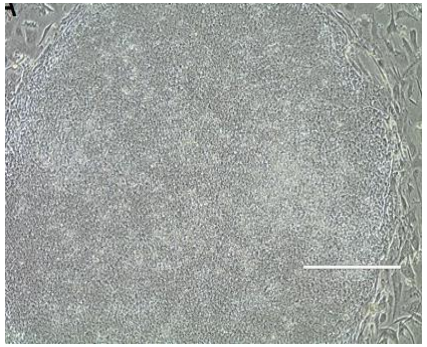


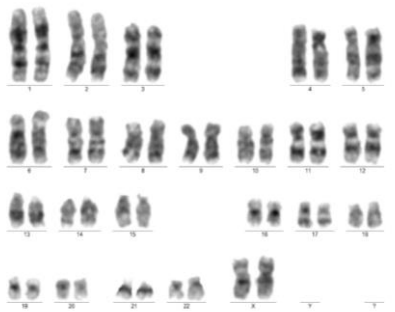
CONTROL (iBM1.2)

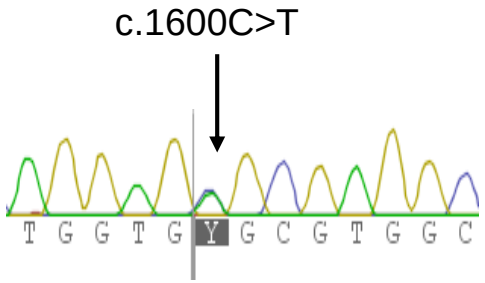




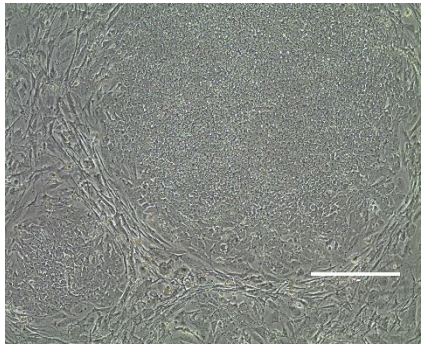
PAC1 Cl9

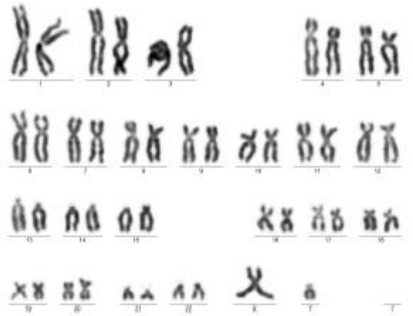


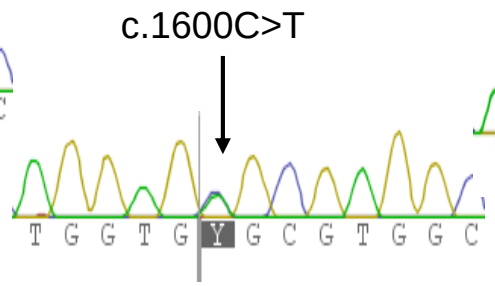




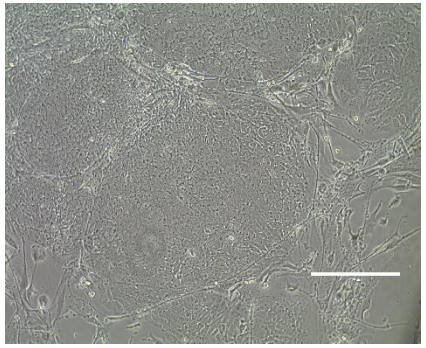
PAC2 Cl11

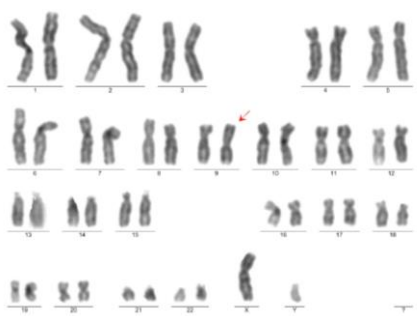


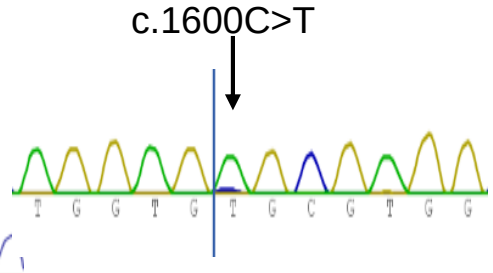




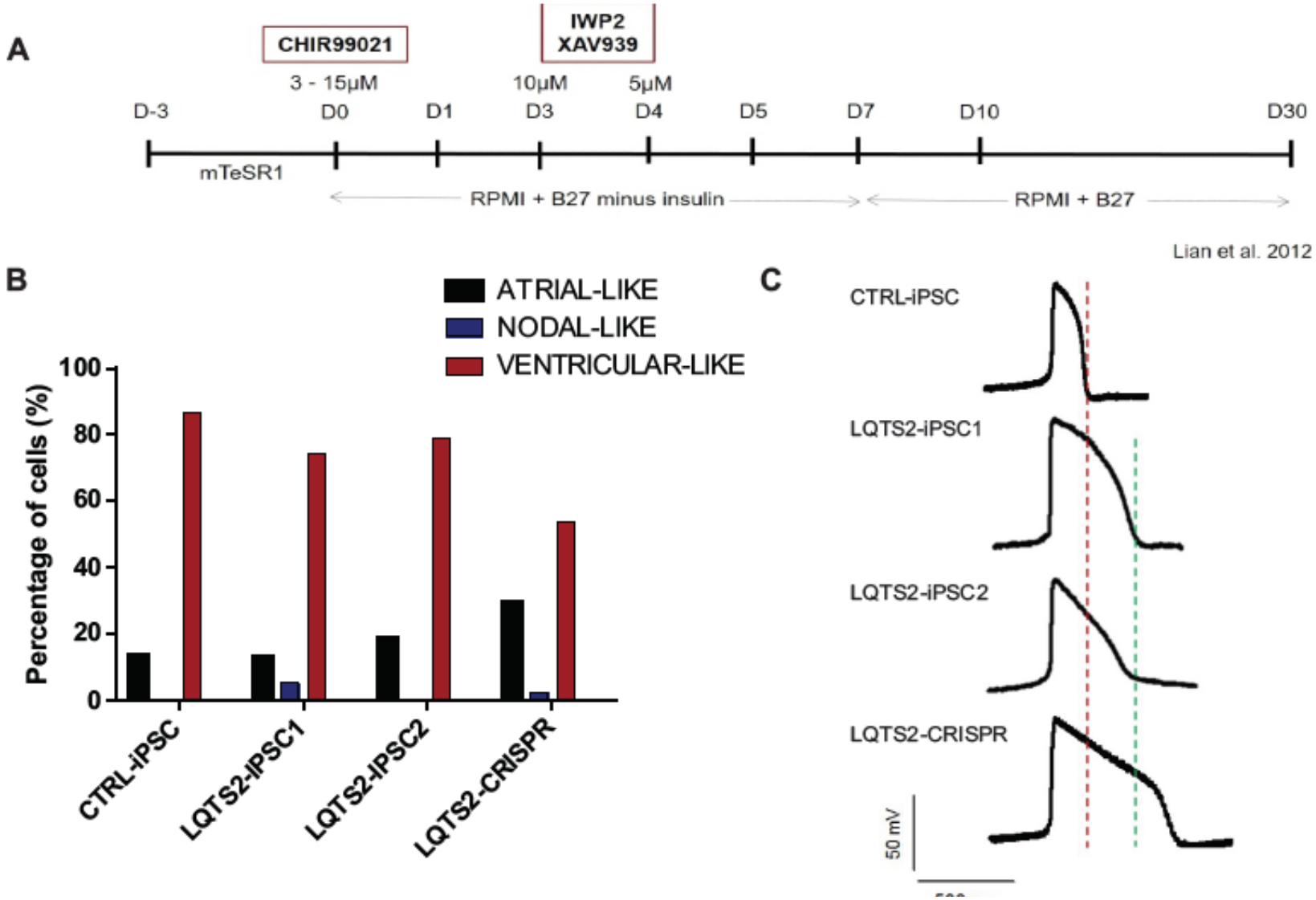
iBM_CRISPR_Cl12







ACTION POTENTIAL DURATION AFTER DIFFERENTITATION



BETTER DRUG SCREENING

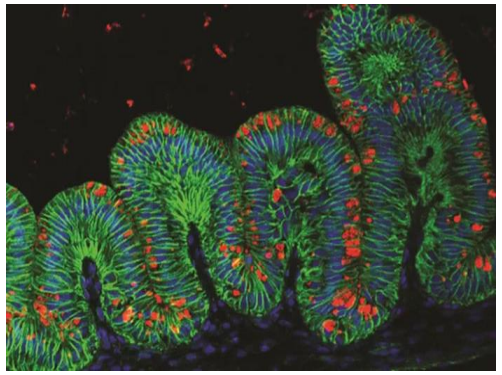
Compound	RABBIT Purkinje Fibre	CANINE Purkinje Fibre	HUMAN hESC-VM
Terfenadine	1.0μM ⊕	False ⊖	0.03μM ⊕
Quinidine	1.0μM ⊕	1.0μM ⊕	0.3μM ⊕
Cisapride	0.1μM ⊕	0.1μM ⊕	0.01μM ⊕
Sotalol	10μM ⊕	100μM ⊕	10μM ⊕
Chromanol 293B	False ⊖	False ⊖	300μM ⊕
E-4031	N/A	0.1μM ⊕	0.1μM ⊕
Nifedipine	N/A	>10μM ⊕	0.03μM ⊕

Relative Sensitivity

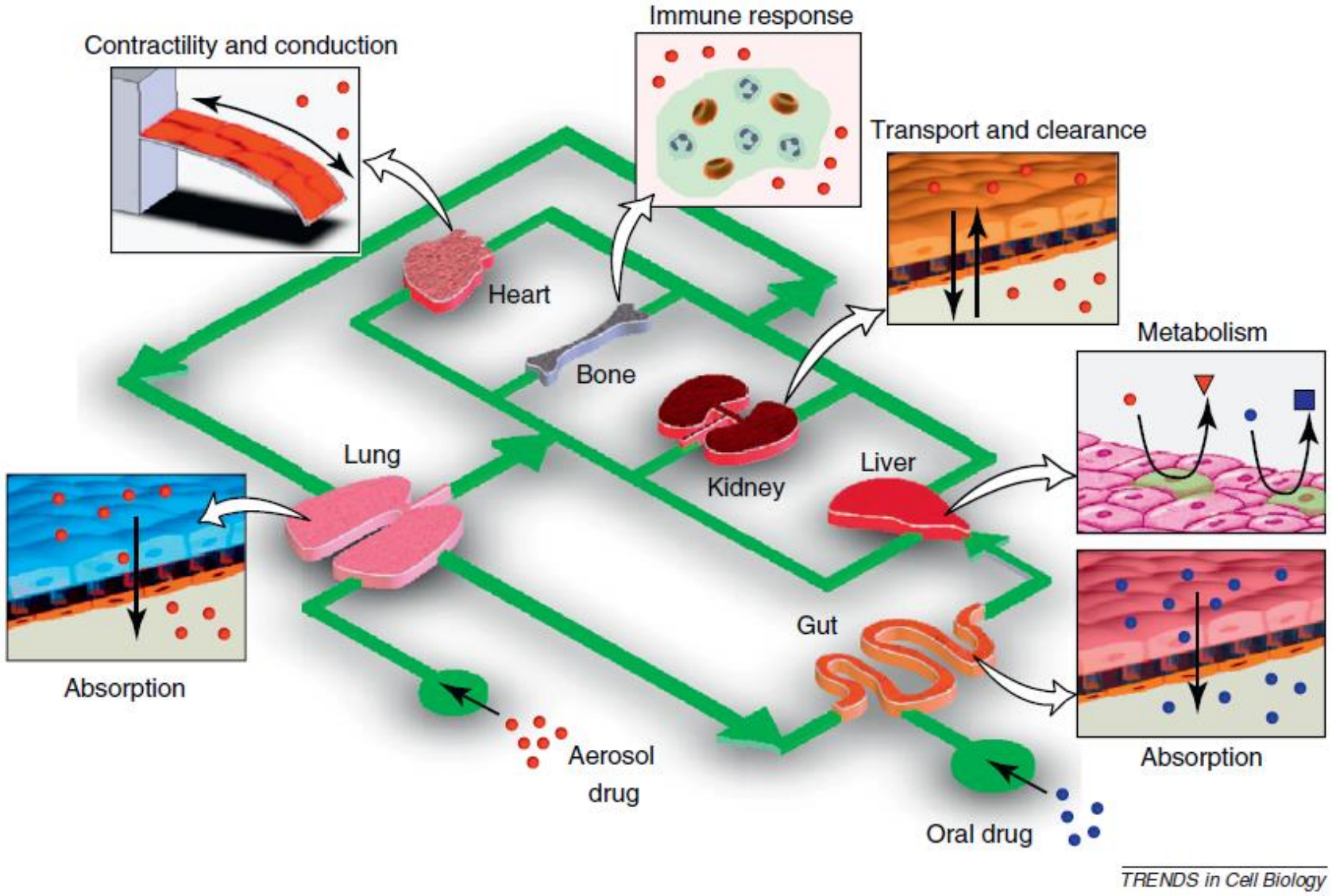
- Most
- Equal
- Least
- None

⊕ Change in APD_{90} >10%

BETTER DRUG SCREENING

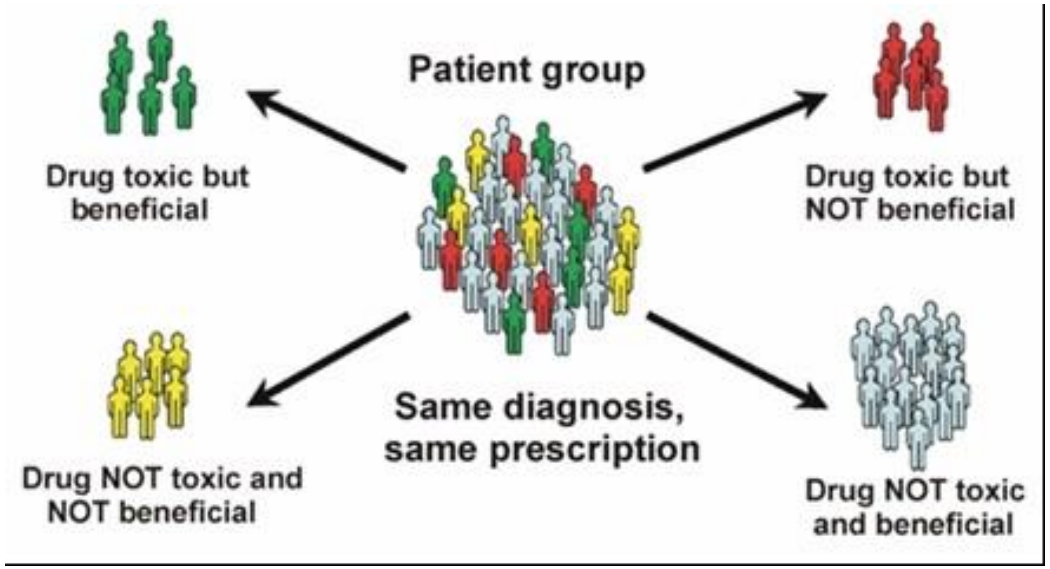


INTESTINAL ORGANOID

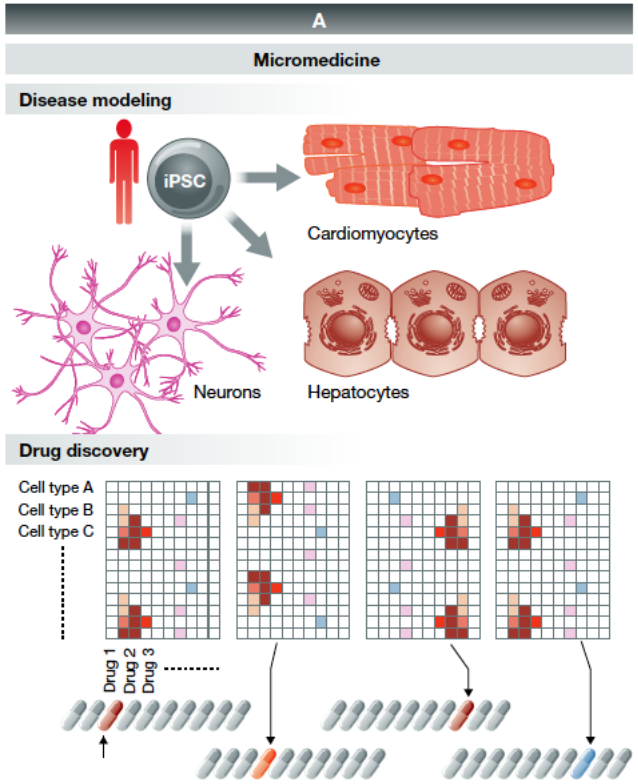


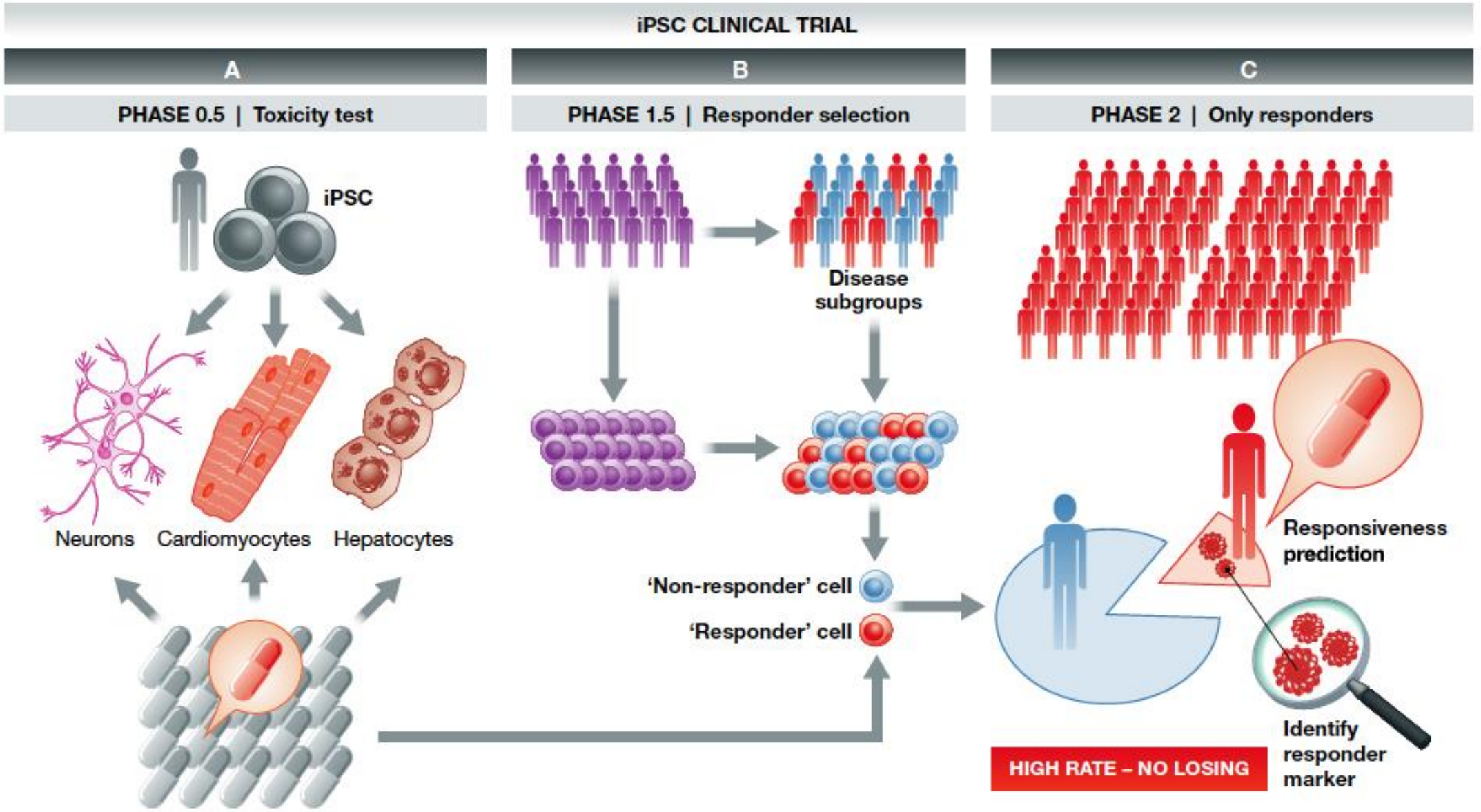
PERSONALISED MEDICINE

THE OLD MODEL



THE NEW MODEL





Haruhisa Inoue et al. EMBO J. 2014;33:409-417

THE EMBO JOURNAL

CELL THERAPIES FOR INCURABLE DISEASES

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

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

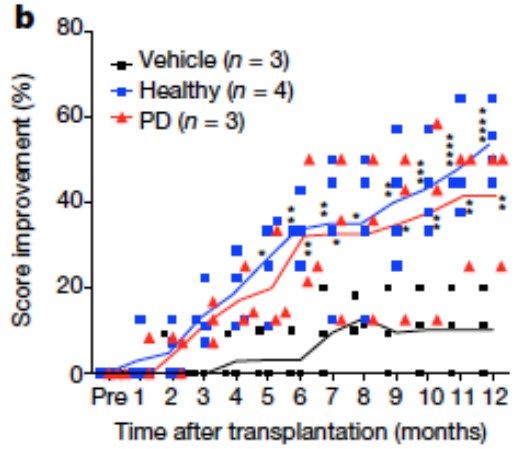
n engl j med 376;11 nejm.org March 16, 2017

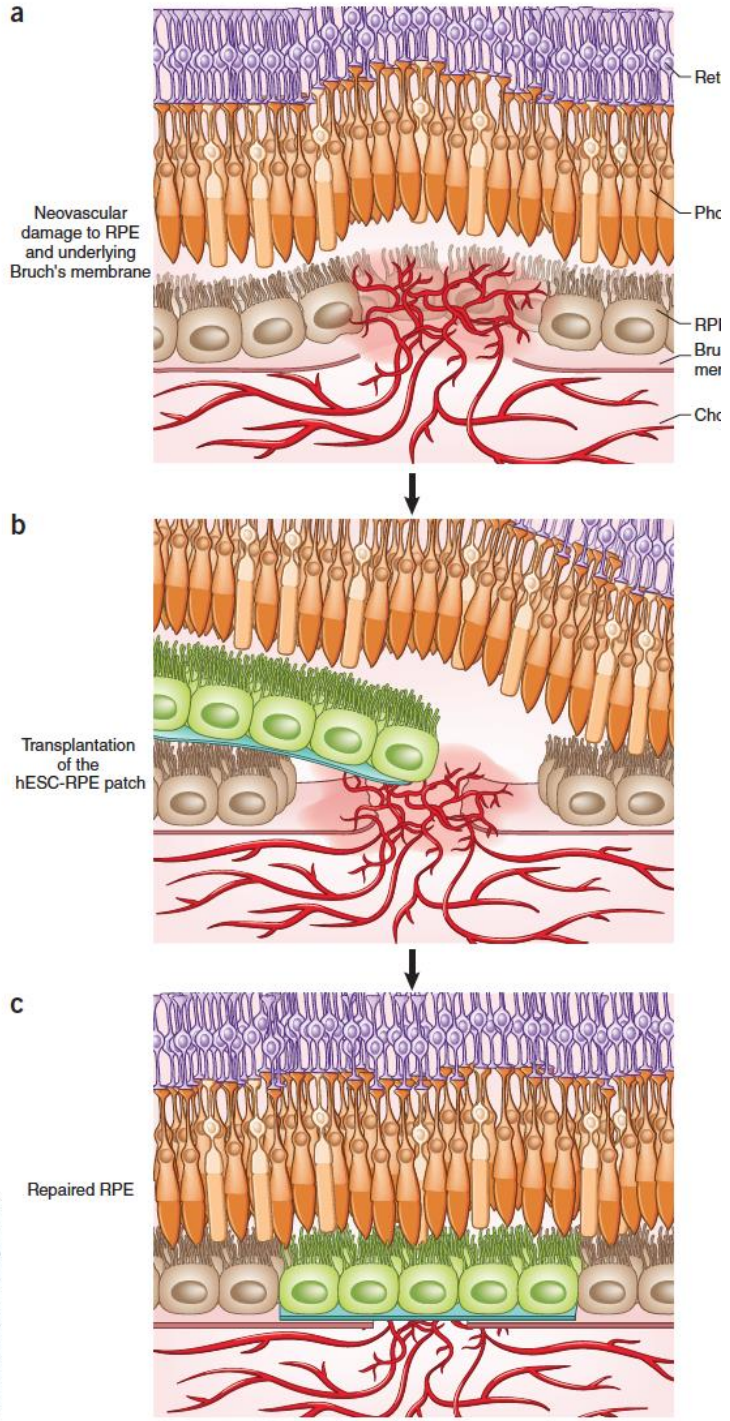
Human iPS cell-derived dopaminergic neurons function in a primate Parkinson's disease model

Tetsuhiro Kikuchi[1], Asuka Morizane[1], Daisuke Doi[1], Hiroaki Magotani[1], Hirotaka Onoe[2], Takuya Hayashi[2], Hiroshi Mizuma[2], Sayuki Takara[2], Ryosuke Takahashi[3], Haruhisa Inoue[4], Satoshi Morita[5], Michio Yamamoto[5], Keisuke Okita[6], Masato Nakagawa[6], Malin Parmar[7] & 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

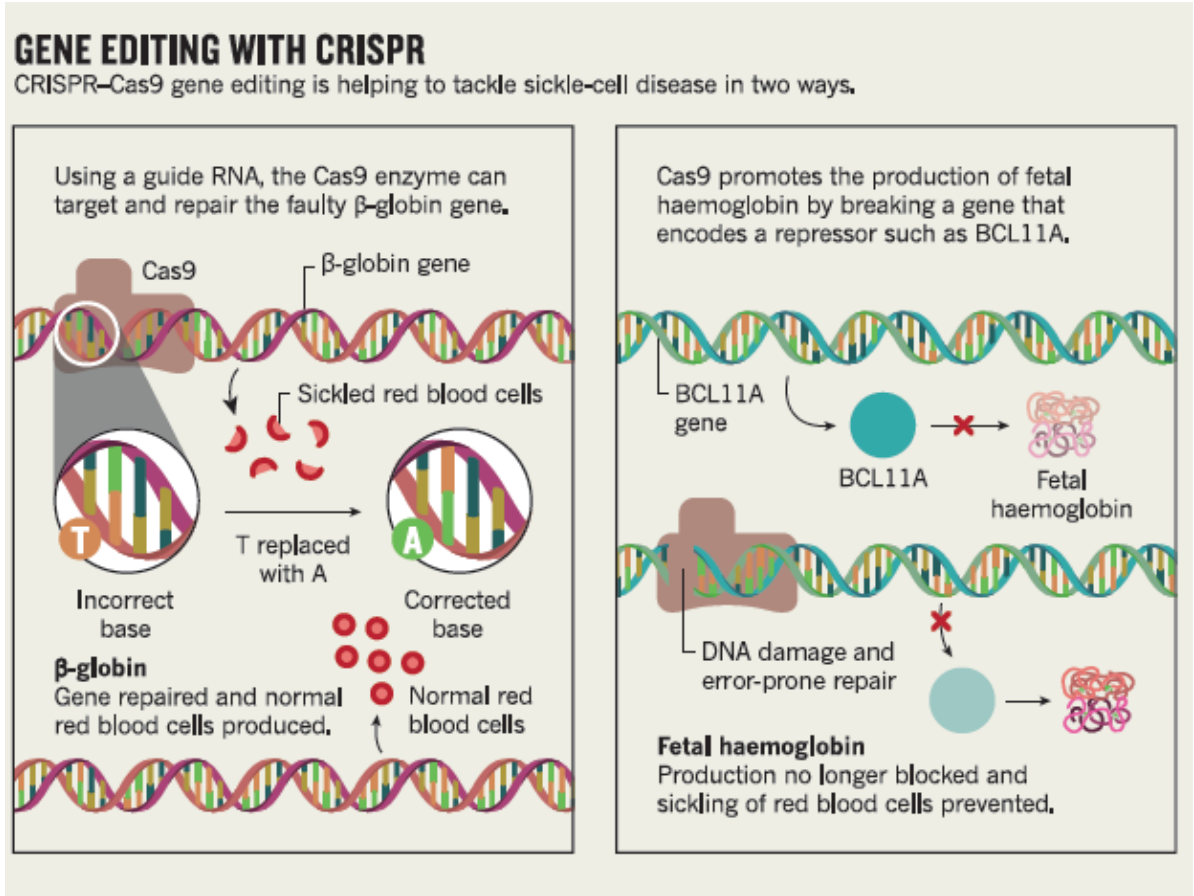
Gene Therapy in a Patient with Sickle Cell Disease

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

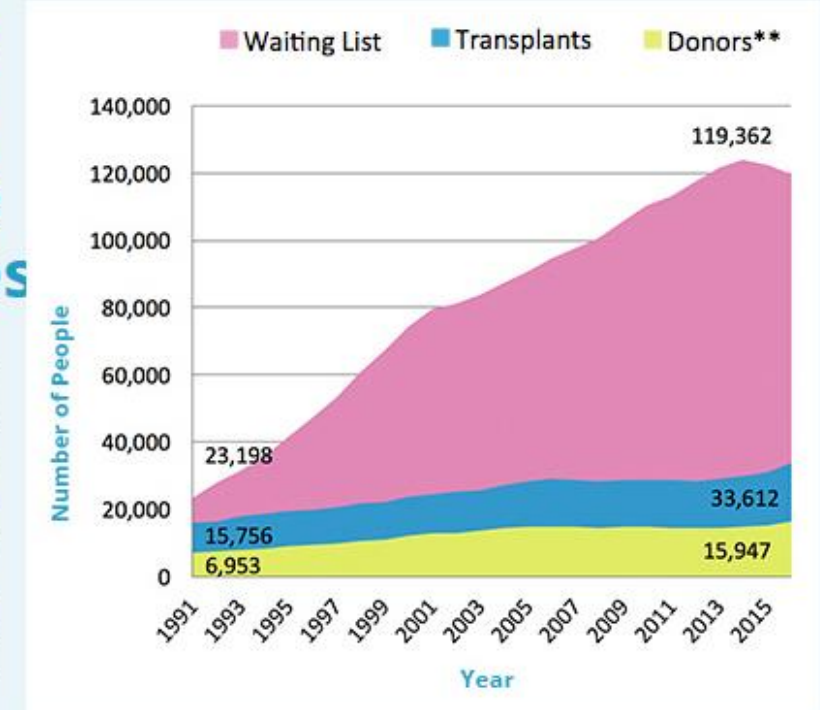
Gene Therapy in Patients with Transfusion-Dependent β-Thalassemia



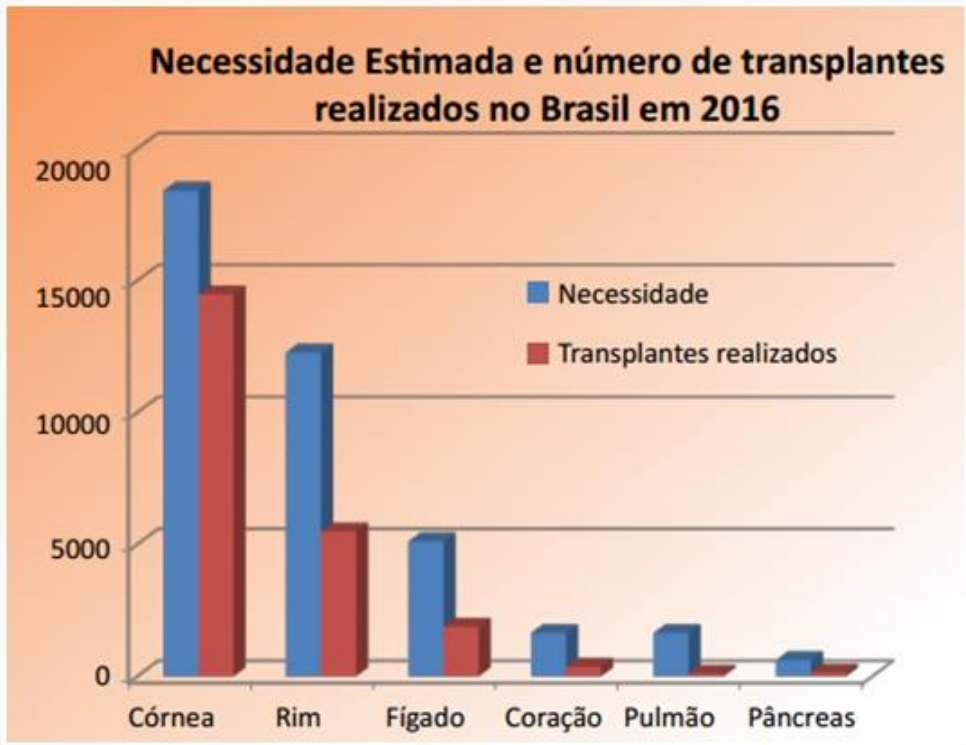
HOW TO DEAL WITH THE SHORTAGE OF ORGAN TRANSPLANTS

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.

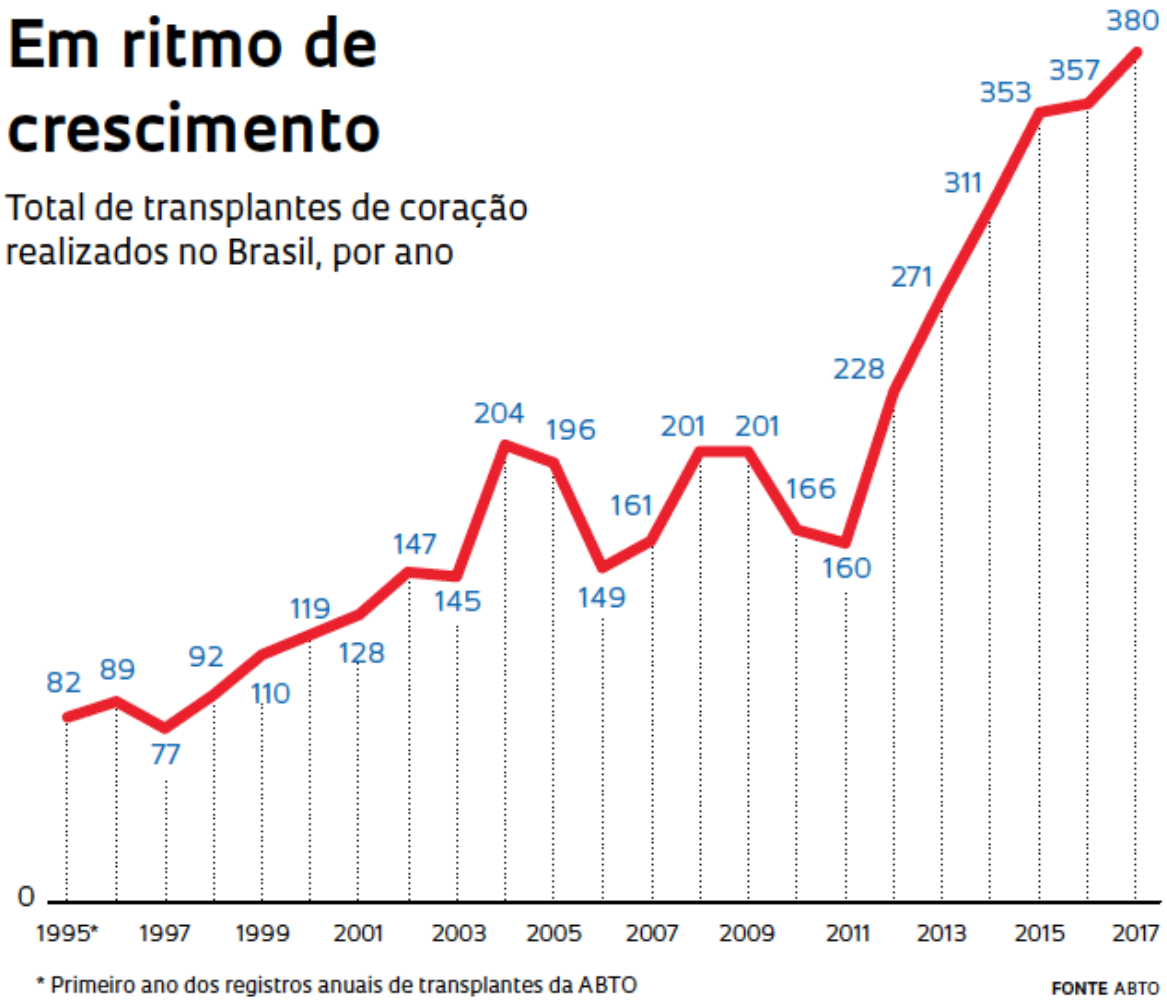


Data from optn.transplant.hrsa.gov and OPTN/SRTR Annual Report. OPTN has current, in-depth statistics. Click to view.



*Fonte: Associação Brasileira de Transplante de Órgãos

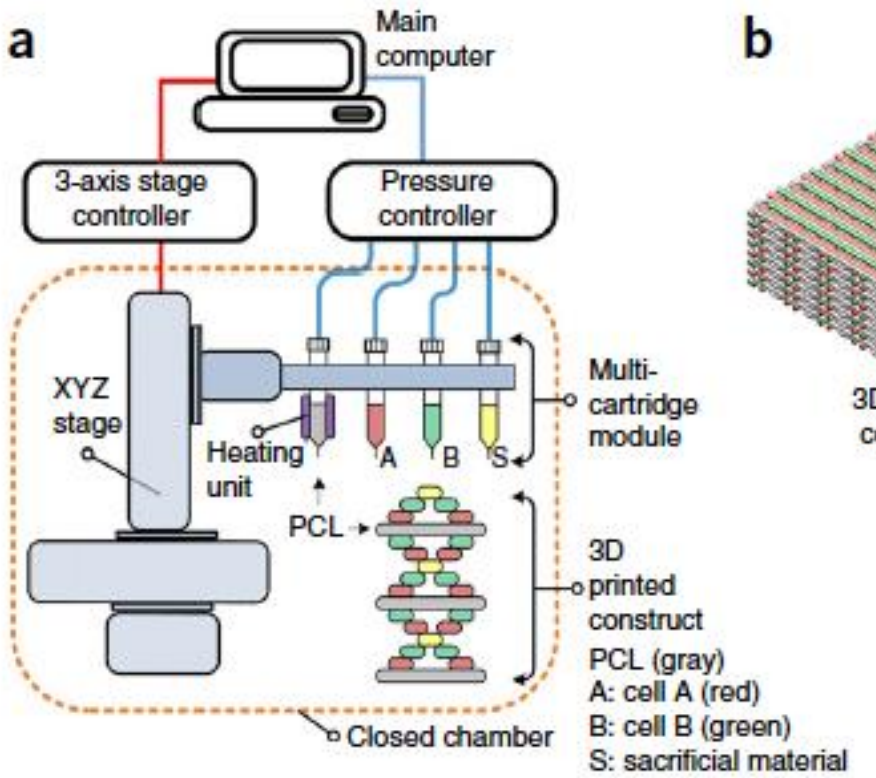
HEART TRANSPLANTS IN BRAZIL

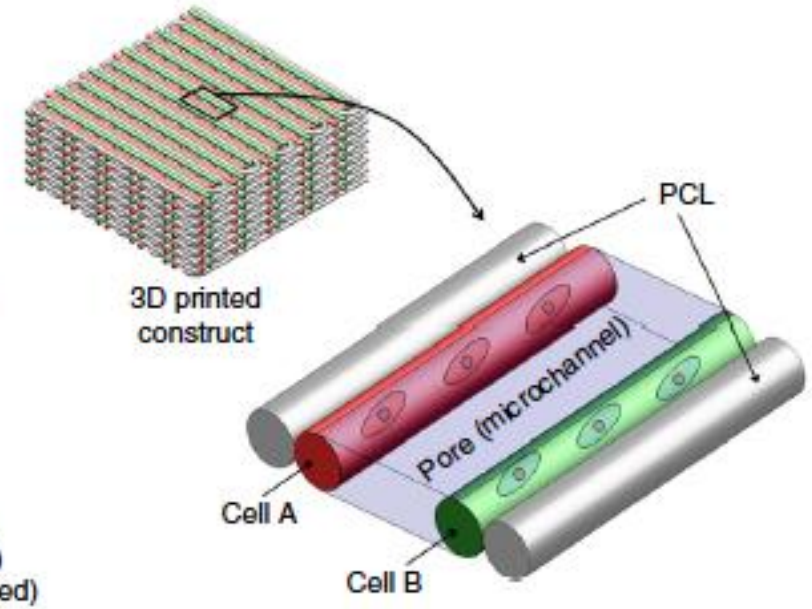


DEMAND IS 1600

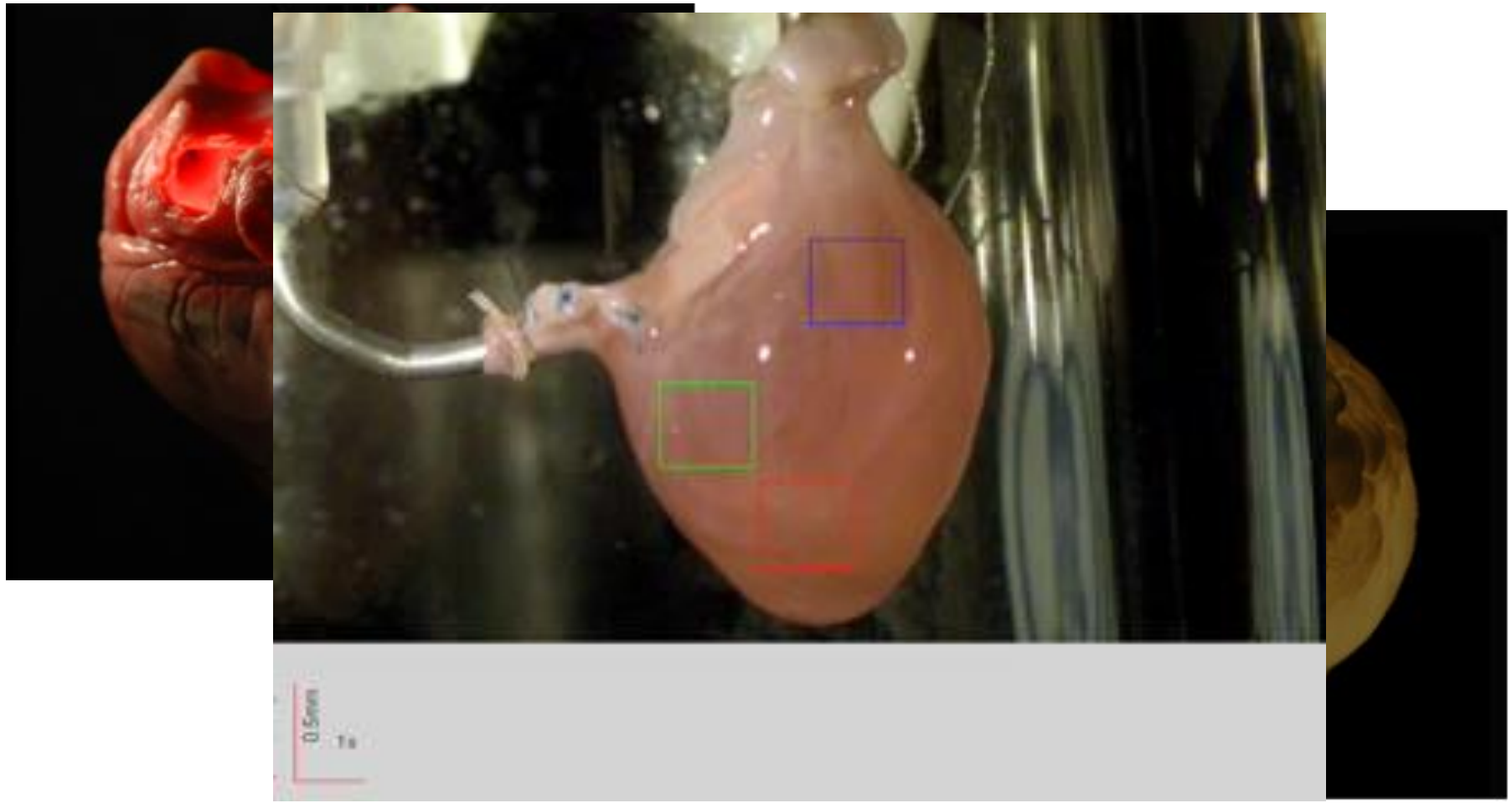
BIOENGINEERING ORGANS AND TISSUES

3D PRINTING





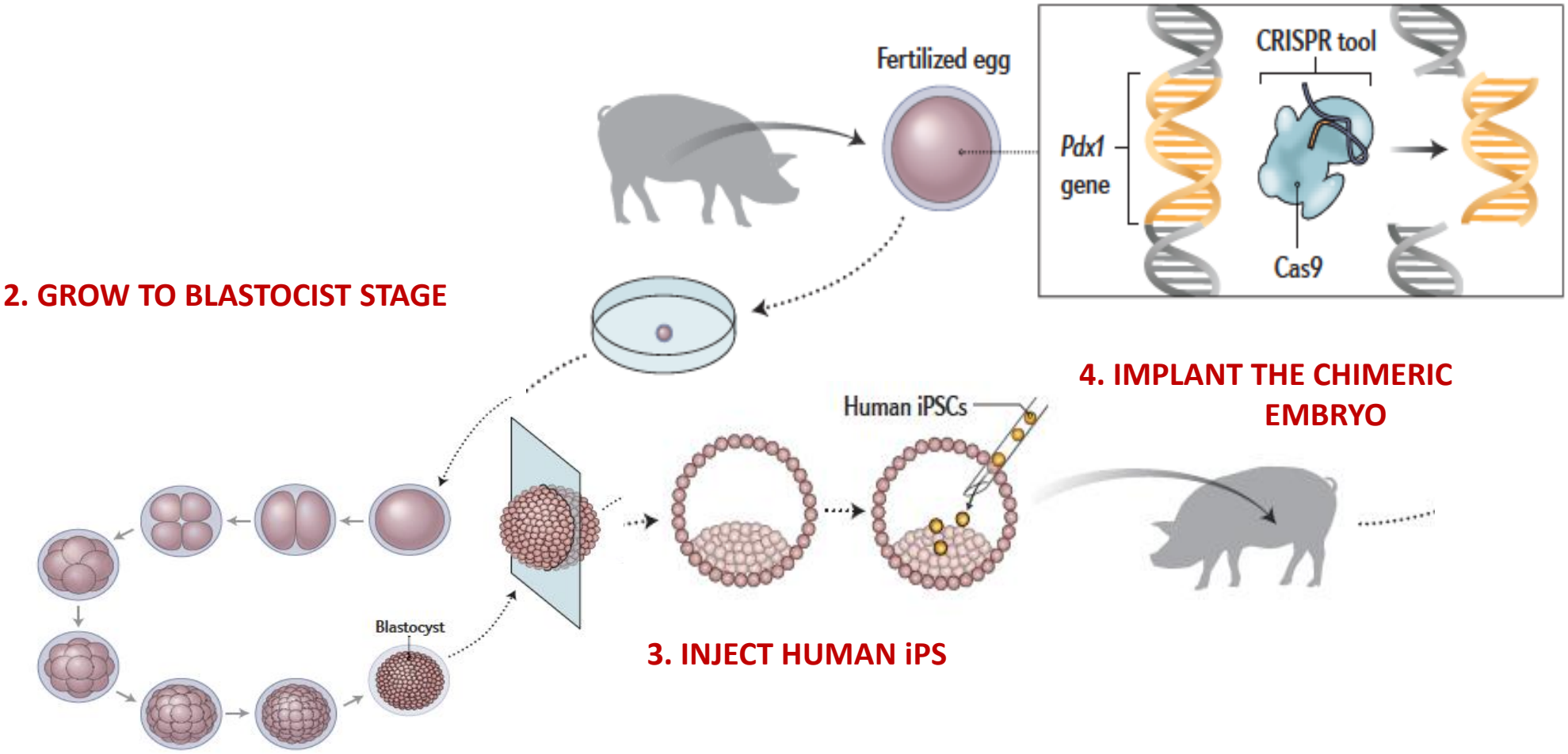
BIOENGINEERING ORGANS AND TISSUES



USING BIOREACTOR-ANIMALS AS A SOURCE

1. GENE EDIT THE EMBRYO

Delete Pdx1

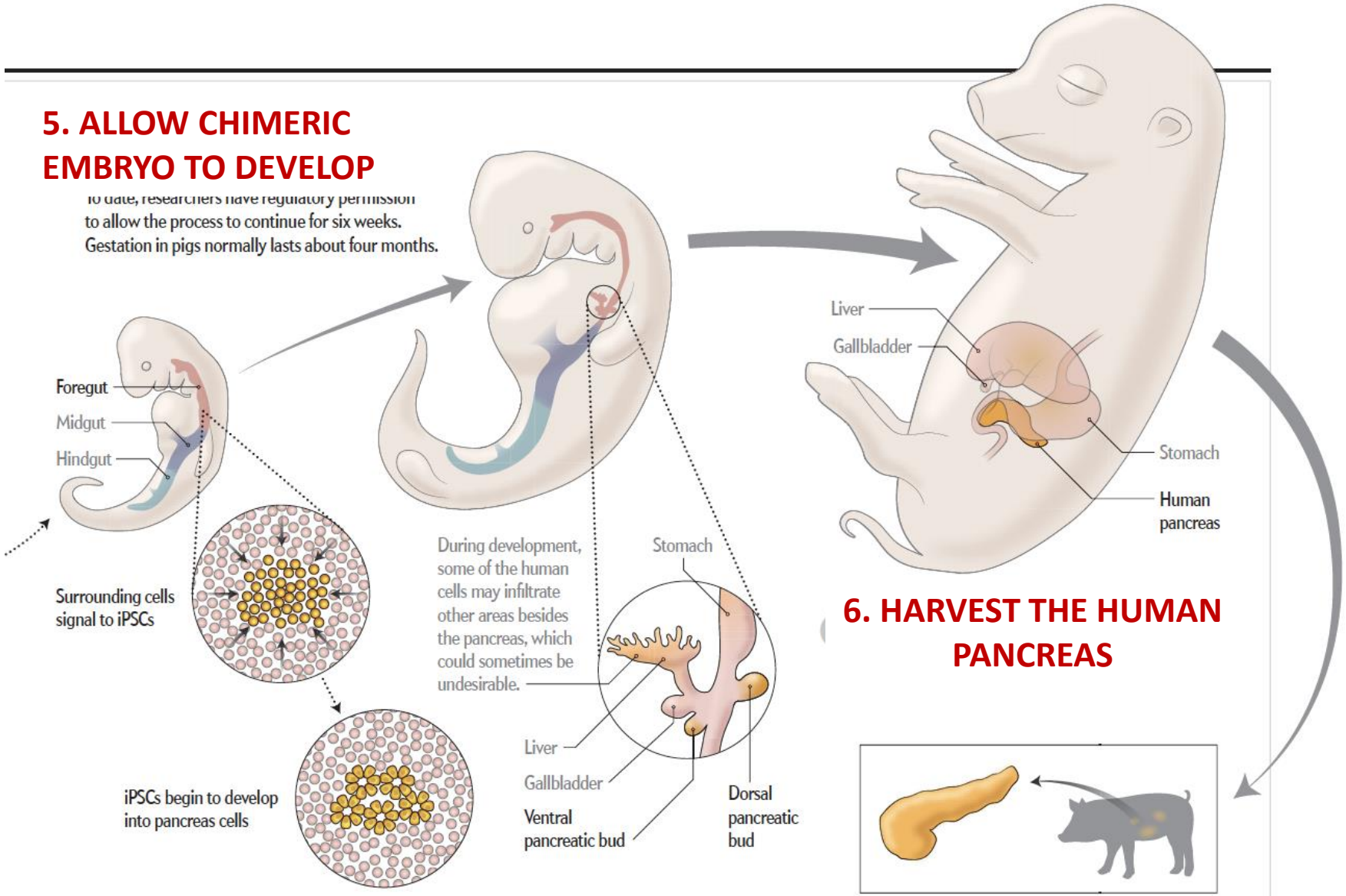


2. GROW TO BLASTOCIST STAGE

3. INJECT HUMAN iPS

4. IMPLANT THE CHIMERIC EMBRYO

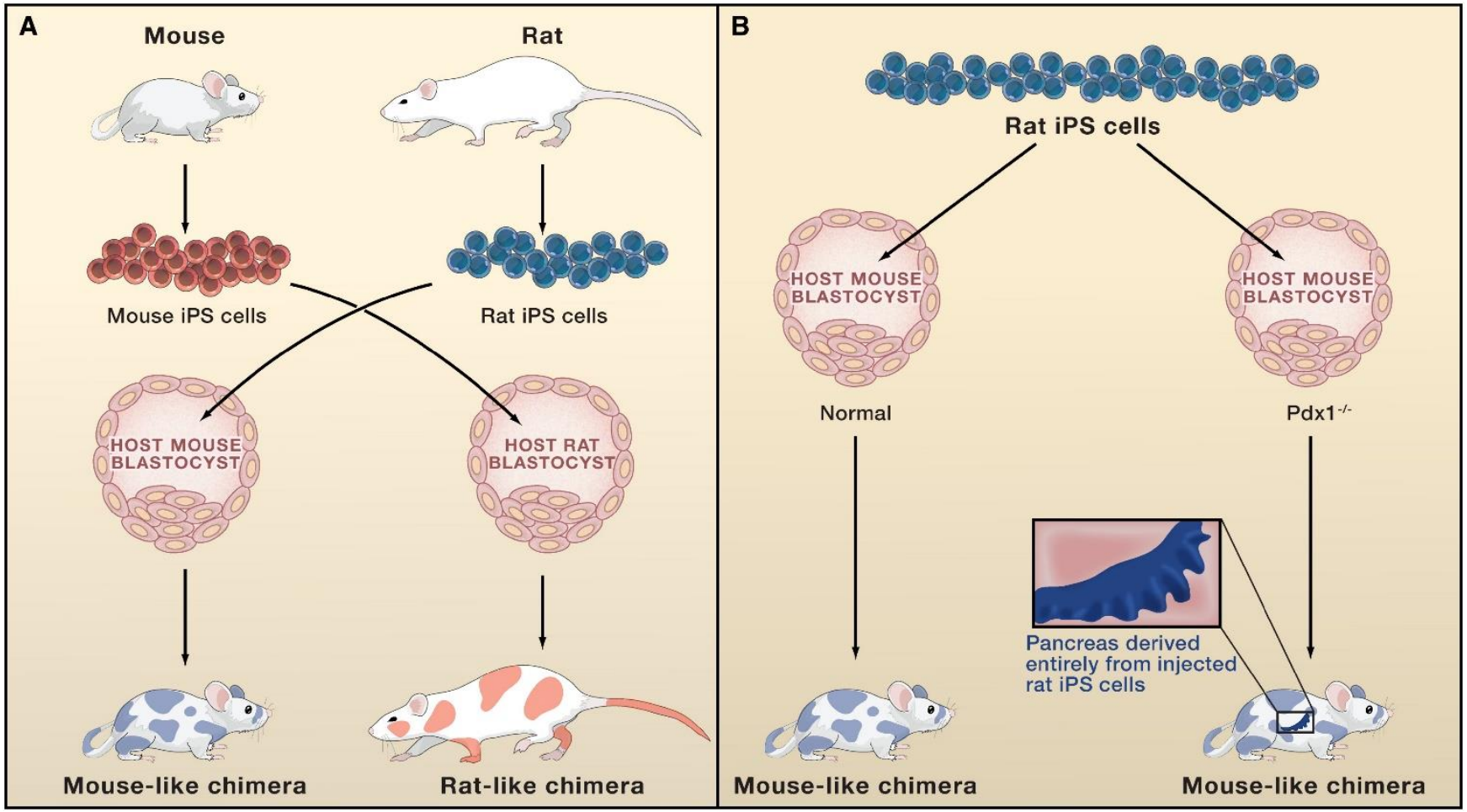
5. ALLOW CHIMERIC EMBRYO TO DEVELOP



6. HARVEST THE HUMAN PANCREAS

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

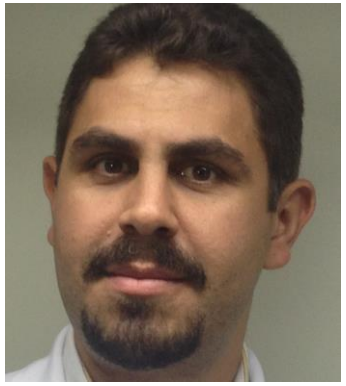
Gustavo

Adriana

Emiliano

Regina

Fernando



Glauber

Jorge

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