Synthetic Biology:

A Perspective On Its Potential In Regenerative Medicine

Kevin Munnelly, President and CEO, Gen9
Stem Cells & Regenerative Medicine Congress
September 15, 2014

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Shameless Self Promotion

20+ years in pharmaceuticals, life science tools and molecular diagnostics

Applied Biosystems

life technologies™

MILLENNIUM®

BioTrove

Board Member

OH_2 Laboratories
A Factory for Drug Discovery

Providing functional water soluble variants of any GPCR or membrane protein

EVE BIOMEDICAL

Fast, accurate, inexpensive gene sequencing using molecular motion

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Gen9 – *Synthesizing the Future*

Founders

Fabrication

Joe Jacobson
MIT

Genetics

George Church
Harvard

Bio-engineering

Drew Endy
Stanford

Investors

Agilent Technologies

THE KRAFT GROUP

DRAPER FISHER JURVETSON

Founded 2009
35 Employees
Located in Cambridge, MA, USA

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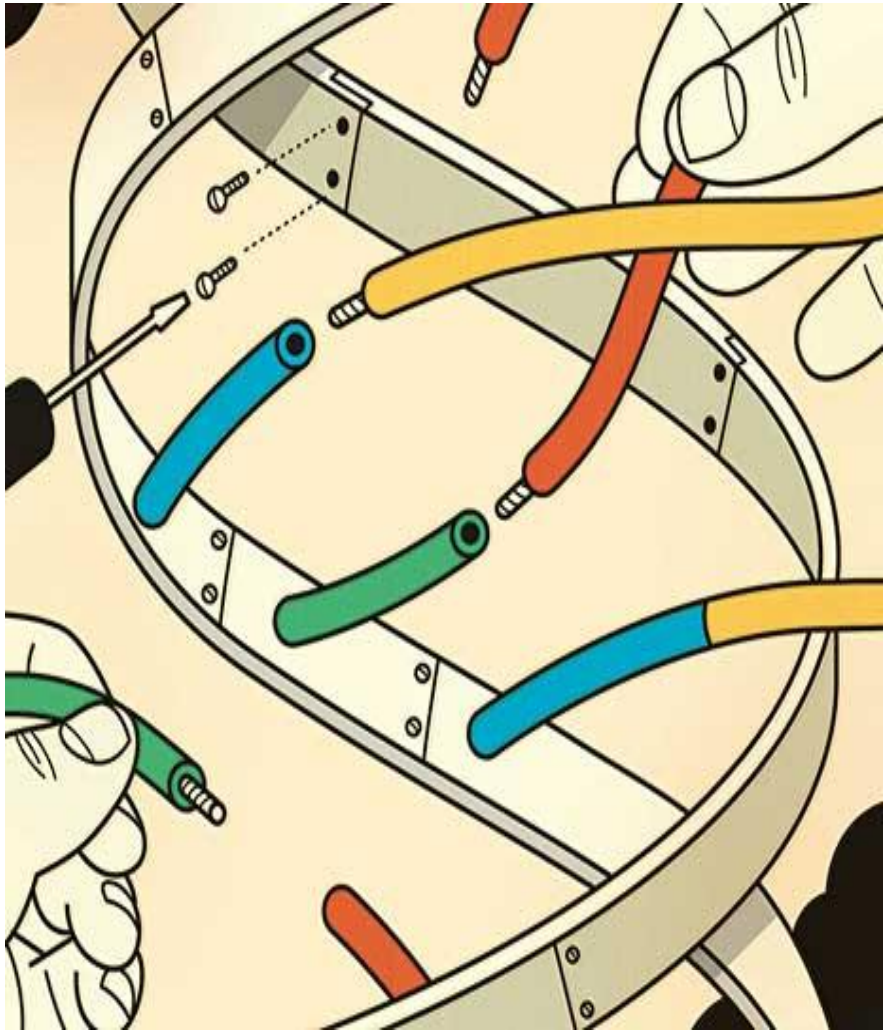
What is Synthetic Biology?



"Synthetic biology is:
a) the design and construction of new biological parts, devices and systems and;
b) the re-design of existing natural biological systems for useful purposes."

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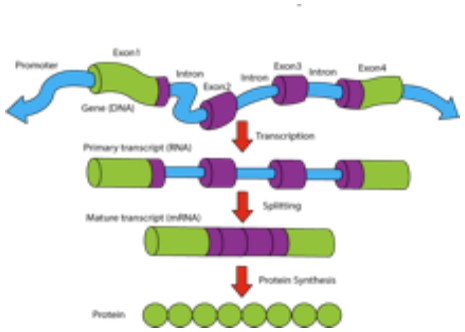
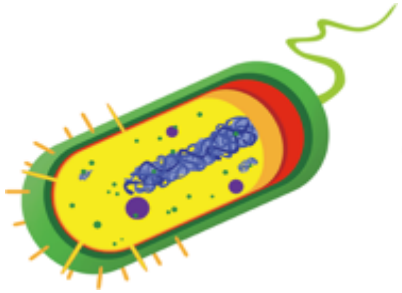
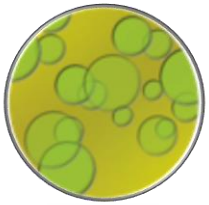
Synthetic Biology is Creating Future Factories…

…for the Production of Pharmaceuticals, Biofuels and Chemicals





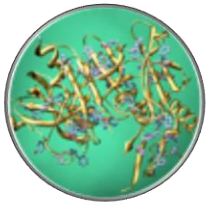
Using Synthetic Genes… **to Create Cellular Factories …** **to Make High Value Products**



Bio-Fuels

Chemicals

Pharmaceuticals



Enzymes

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Products of Synthetic Biology

Synthetic Biology in Medicine

Systems Biology
- Construction and analysis of synthetic regulatory networks
- Sophisticated Perturbations

Bimolecular synthesis and fabrication
- Optimized drug synthesis
- Molecular-scale device fabrication

Biomedical
- Artificial immune systems
- Cancer and other disease therapies
- Tissue generation and regulation
- Biosensing
- Diagnostics

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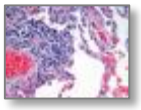
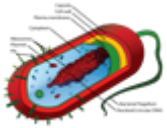
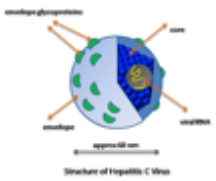
The Progress of Synthetic Biology







2020

Metazoan

Tissue/Organ

2015

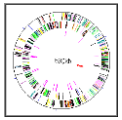
Eukaryote

S. cerevisiae Chromosome synthesized

Prokaryote

2010

De novo Mycoplasma Genome synthesized



Designed Proteins

2005

Parts Libraries

BioBricks repository established

Synthetic Circuits

Bi-stable Switch in E. coli

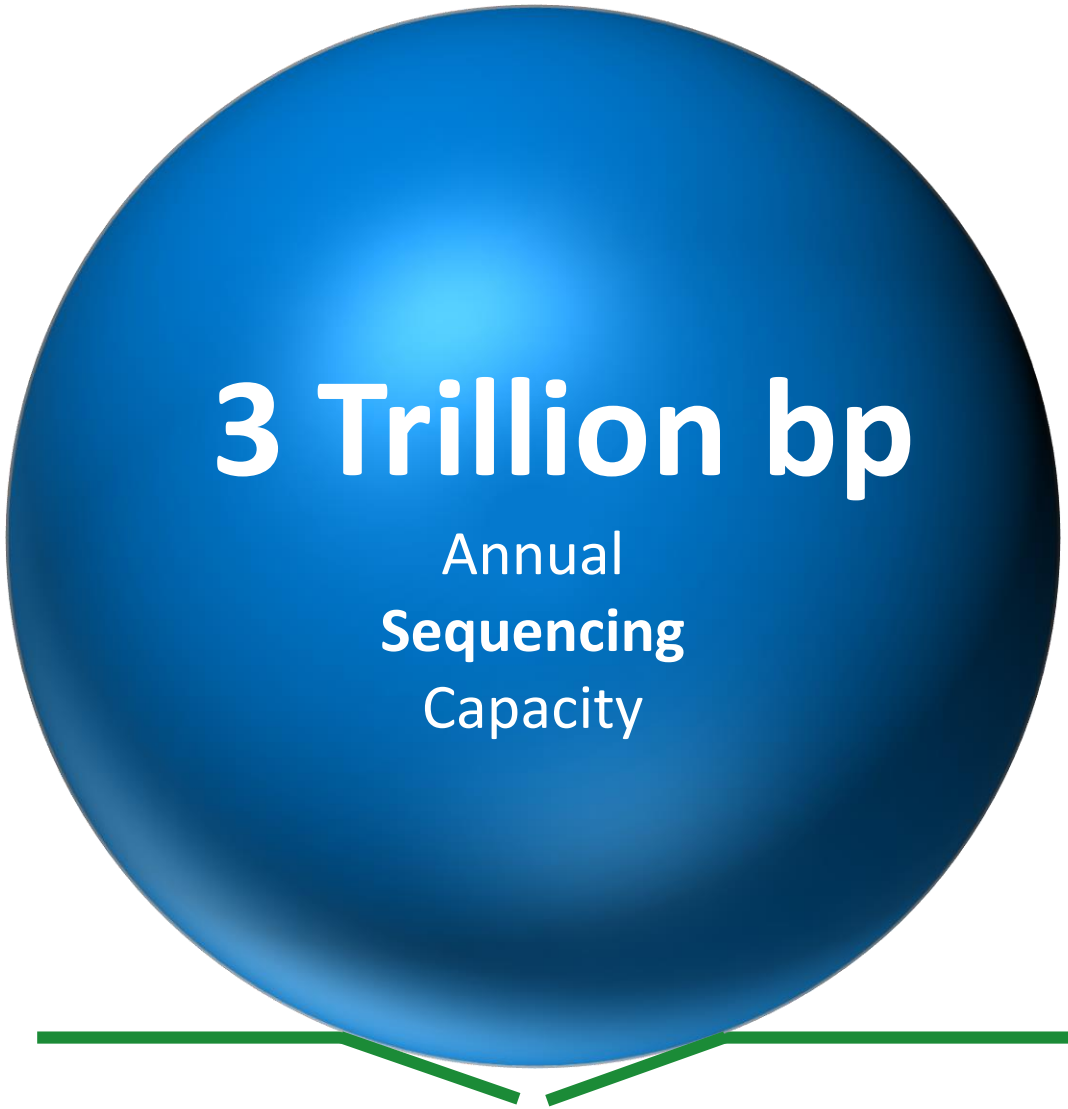
2000

DNA

1995

What is Holding Us Back?

The Opportunity: Reading vs. Writing DNA



10,000X
Discrepancy

300 Million bp
Annual
Synthesis
Capacity

Capacity in Base Pairs Per Year

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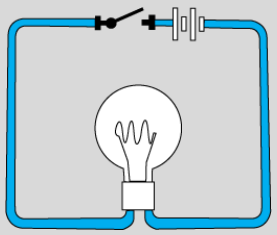
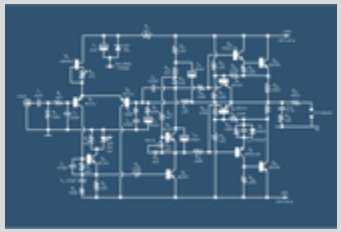
Gene Synthesis: A new Demonstration of Moore's Law

Disruptive Technologies



Simple Circuit



Complex Circuit

Integrated Circuit

Oligo Synthesis

Gene Synthesis

Gen9 BioFab®

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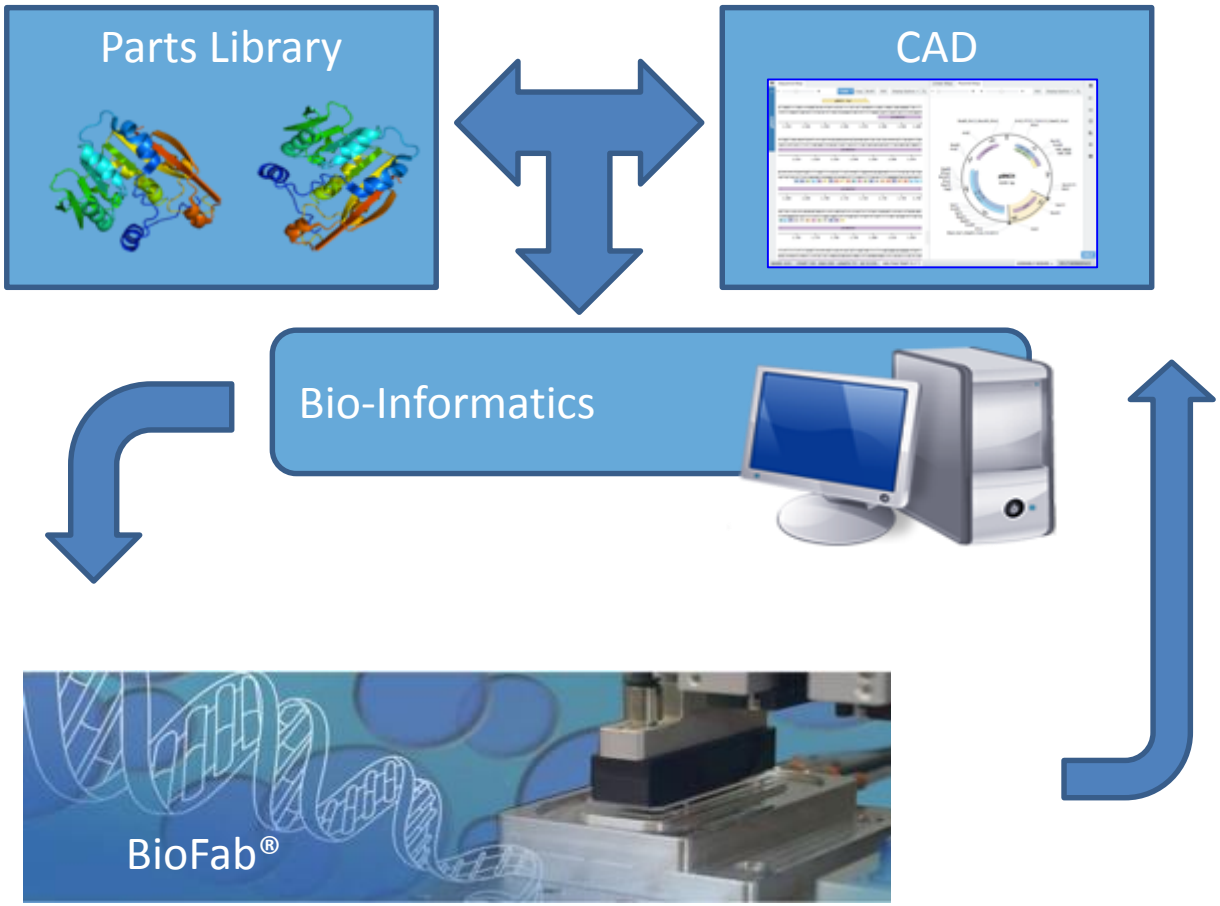
Gene Synthesis Ecosystem



On-Demand DNA Applications

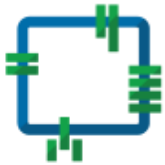
single genes*

minimal life

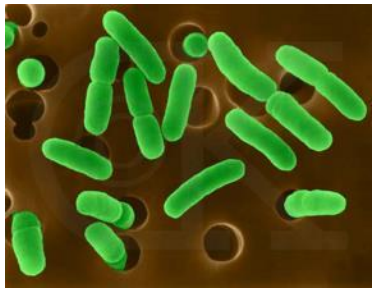
base pairs

10^2 10^3 10^4 10^5 10^6 10^7

genetic circuits
Pathways



genome rewrite



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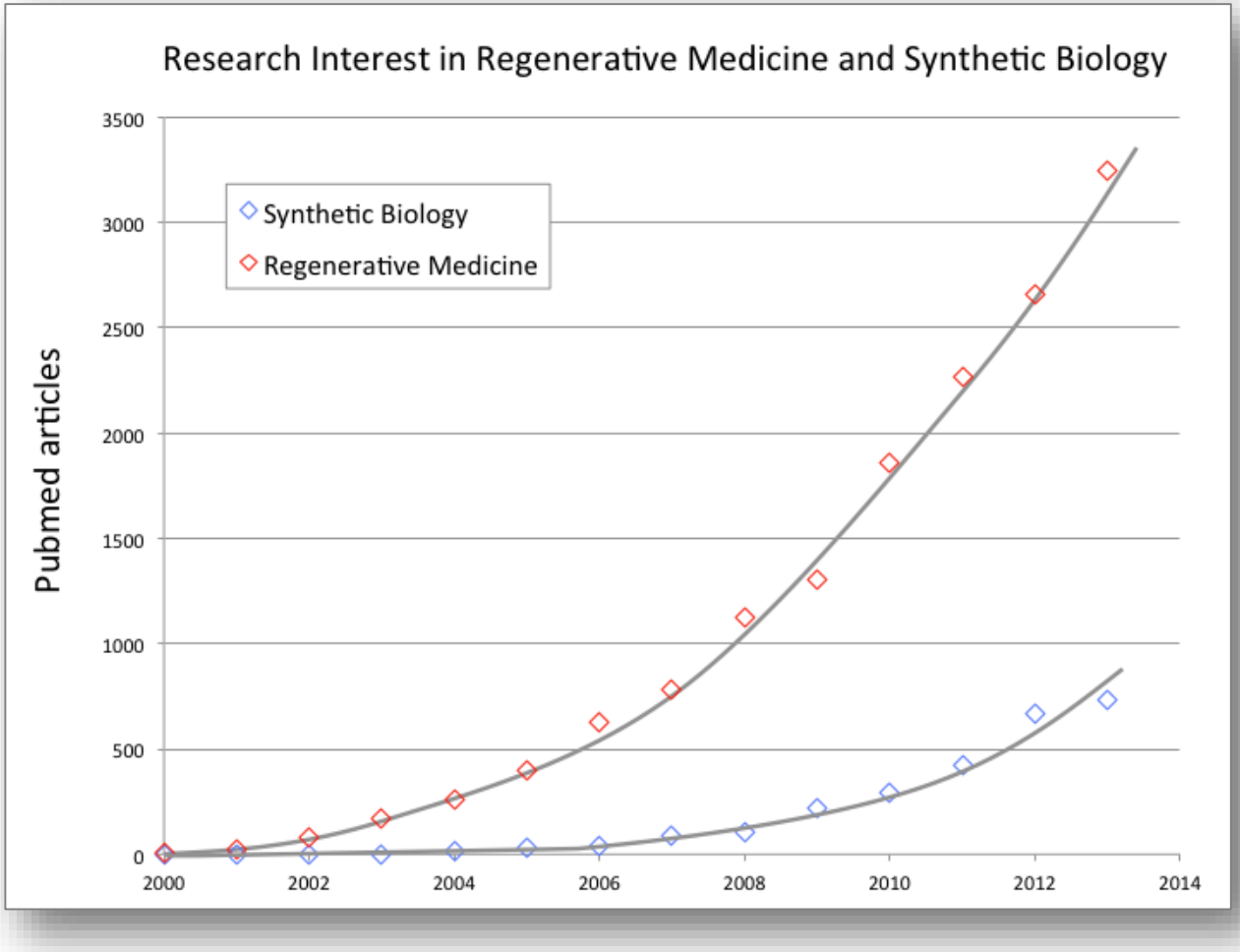
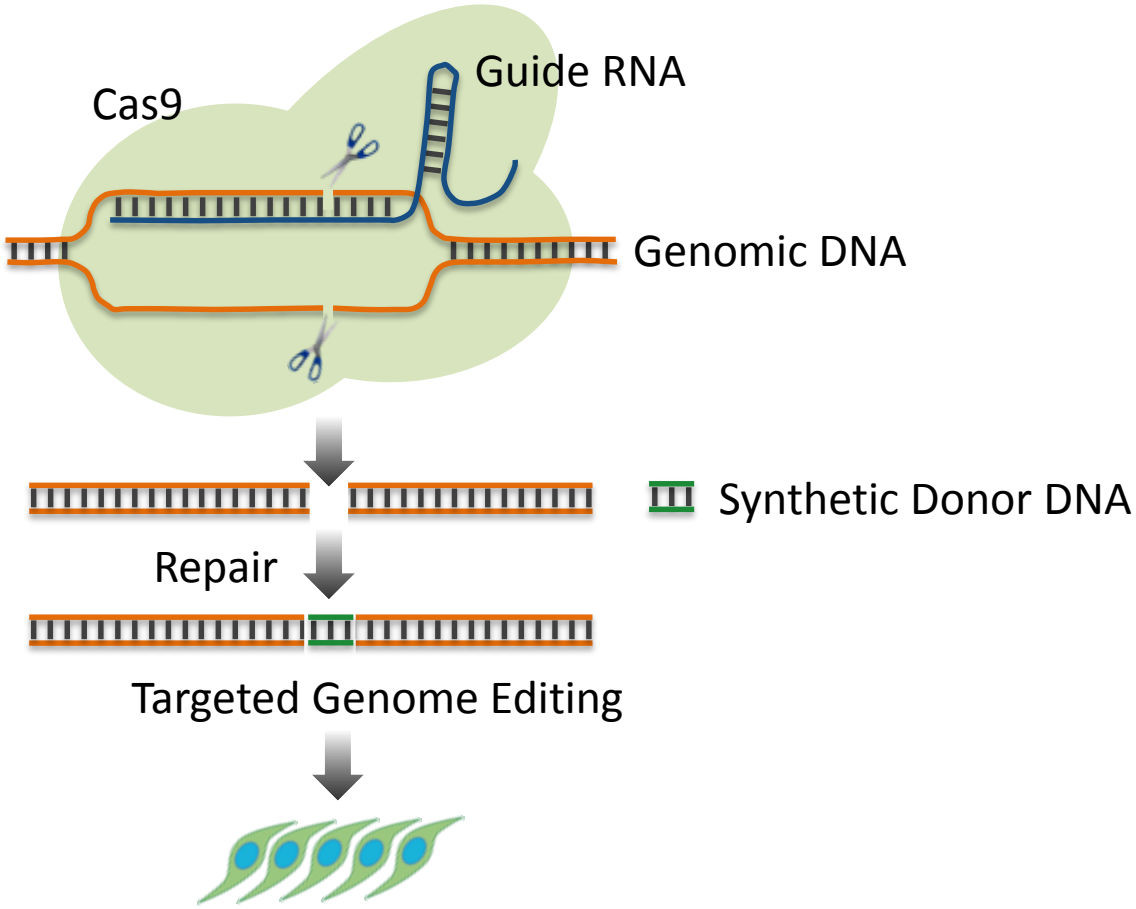
The Promise of Synthetic Biology

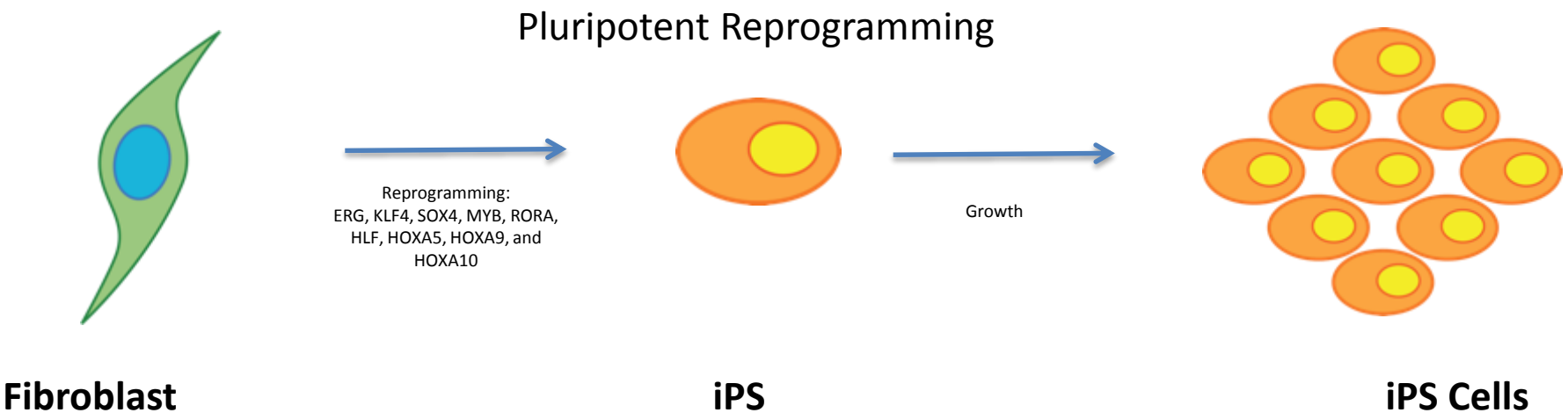


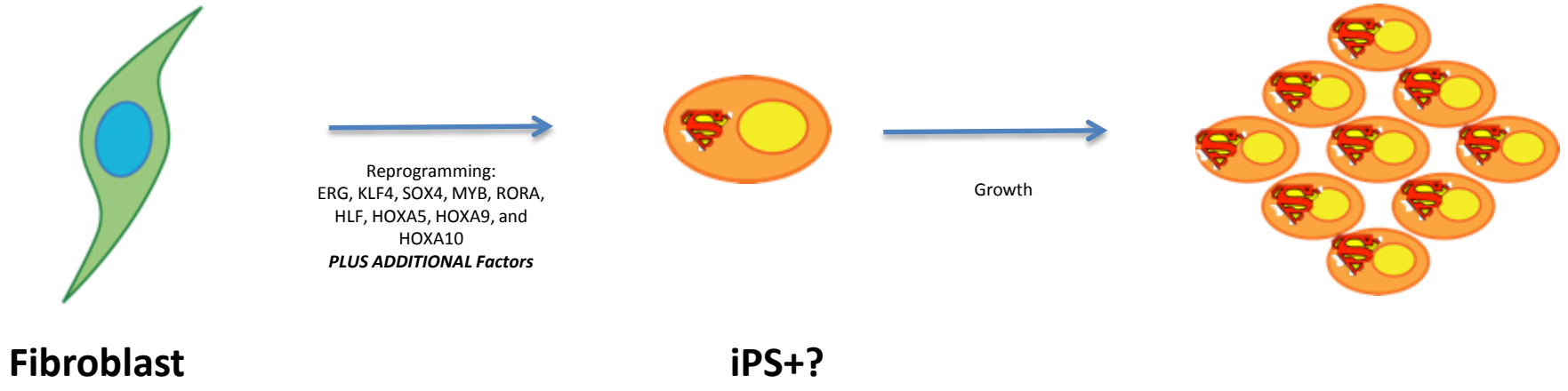
Editing Genomes

Advancements in technologies for precision editing



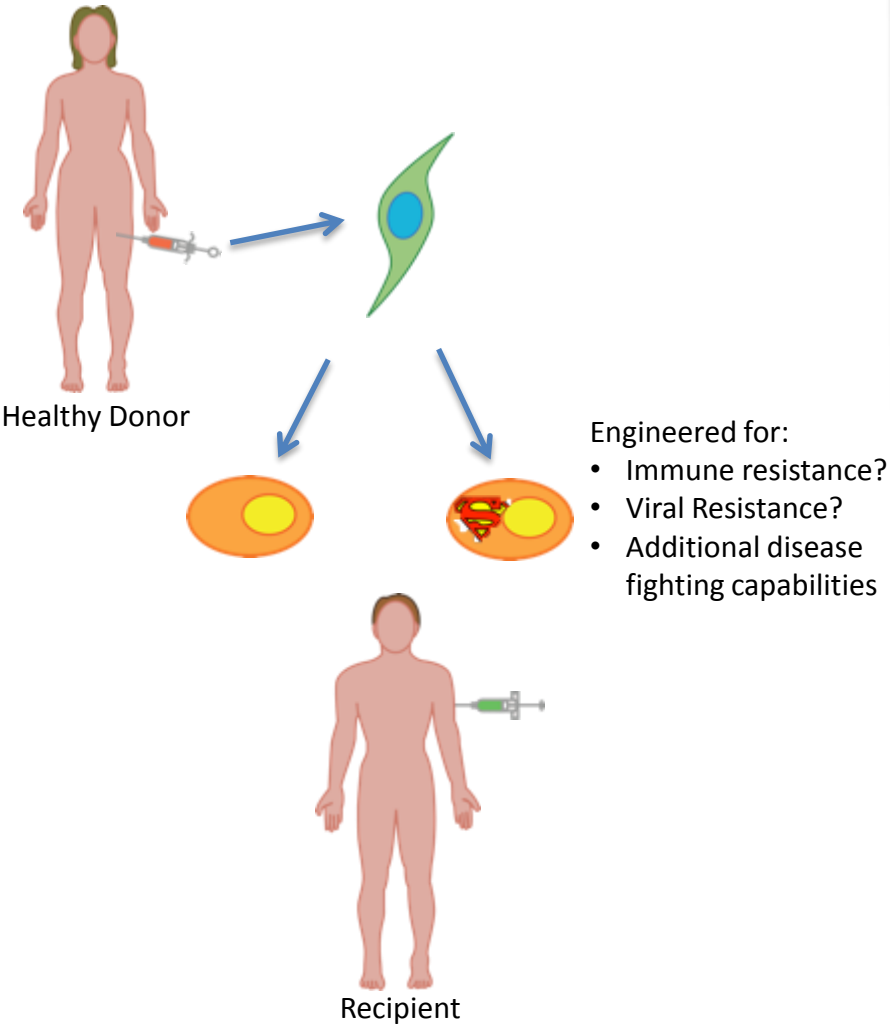
Creation of Pluripotent Cells



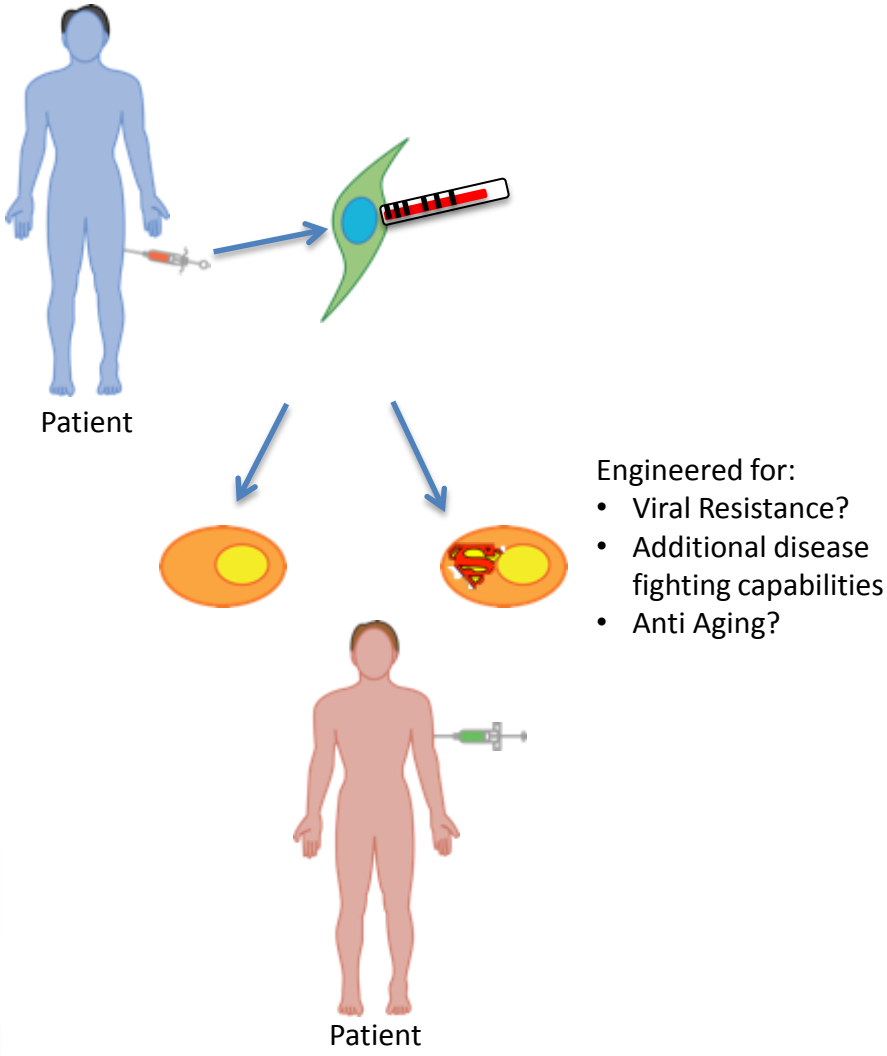


Better Options for Therapy

And Disease Treatment



Engineered for:
- Immune resistance?
- Viral Resistance?
- Additional disease fighting capabilities



Engineered for:
- Viral Resistance?
- Additional disease fighting capabilities
- Anti Aging?

New Therapeutic Companies in Editing Space

CRISPR THERAPEUTICS

CRISPR THERAPEUTICS RAISES $25 MILLION IN SERIES A FINANCING AND ANNOUNCES FOUNDING TEAM OF WORLD-RENOWNED ACADEMICS AND CLINICIANS

Basel, Switzerland – 24 April 2014

CRISPR Therapeutics, a biopharmaceutical company focusi raised $25 million in a series A investment from Versant Ve comprising high-profile experts in diverse fields of science i drug delivery technologies, RNA interference and gene silei

The funding and the team's collective expertise will allow C gene medicines that have the potential to cure serious gen

Cas9 is an enzyme that can be easily programmed with RN deletion, insertion or correction of target genes with surgic interest and to correct specific target genes, to tackle both editing offers significant advantages over traditional gene tl correcting some recessive genetic disorders.

editas MEDICINE

FOR IMMEDIATE RELEASE

Editas Medicine Created to Discover and Develop Novel Class of Genome Editing Therapeutics

Company Founded by Five World Leaders in Genome Editing; Secures $43 Million Series A Financing Led by Flagship Ventures, Polaris Partners and Third Rock Ventures

Cambridge, Mass., November 25, 2013 -- Editas Medicine, a transformative genome editing company, today announced it has secured a $43 million Series A financing led by Flagship Ventures, Polaris Partners and Third Rock Ventures with participation from Partners Innovation Fund. Following an explosion of high profile publications on CRISPR/Cas9 and TALENs, genome editing has emerged as one of the most exciting new areas of scientific research. These recent advances have made it possible to modify, in a targeted way, almost any gene in the human body with the ability to directly turn on, turn off or edit disease-causing genes. Editas' mission is to translate its genome editing technology into a novel class of human therapeutics that enable precise and corrective molecular modification to treat the underlying cause of a broad range of diseases at the genetic level.

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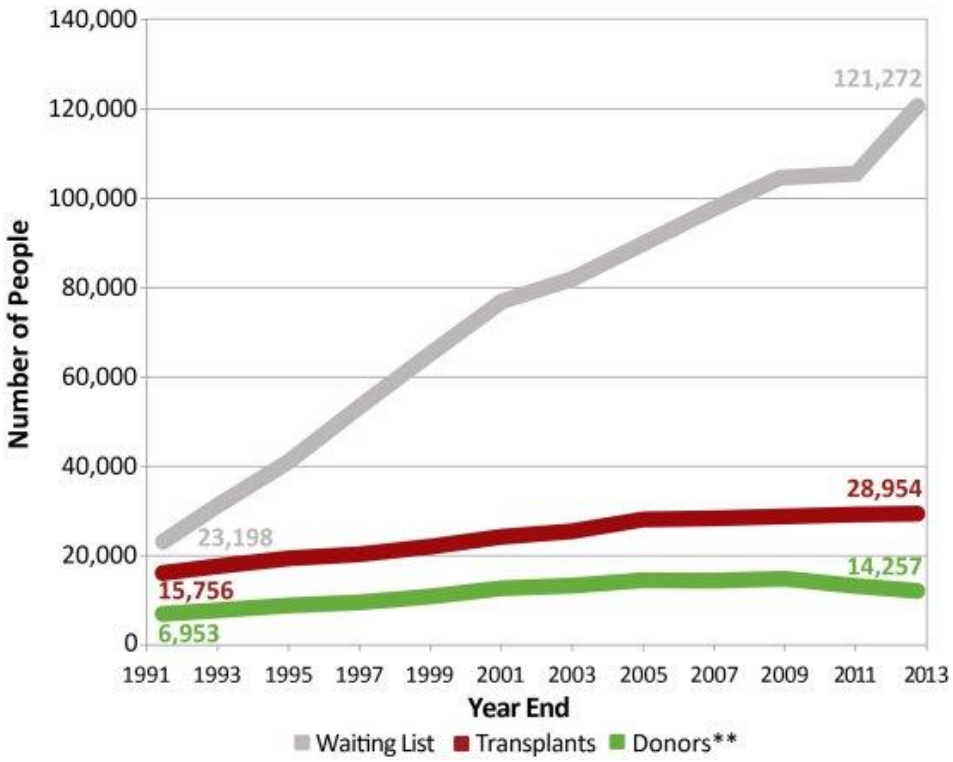
Need for Organs



Each day, an average of 18 people die waiting for transplants due to organ shortage (>6500 year)

Data from optn.transplant.hrsa.gov and OPTN/SRTR Annual Report.
** Data include deceased and living donors

Humanized Pigs?

Immune Resistant Model Organisms

Humanized pig organs to revolutionize transplantation

Initial focus: the almost 400,000 people who die from lung disease, including cancer, each year

May 7, 2014

Genome pioneer J. Craig Venter's Synthetic Genomics Inc. (SGI) is teaming up with United Therapeutics Corporation subsidiary Lung Biotechnology Inc. to use synthetic genomic advances to develop humanized pig lungs.

The collaboration will focus on creating organs that are safe and effective for use in human patients in need of transplantation, with an initial focus on lung diseases — addressing specifically the urgent need for transplant organs for people with end-stage lung disease.

SGI plans to use its unique DNA design, DNA synthesis, genome editing, and genome-modification tools to develop engineered primary pig cells with modified genomes. This will involve modifying a substantial number of genes at an unprecedented scale and efficiency, the company says.

[+]

(Credit: iStock)

400,000 people die annually from lung disease

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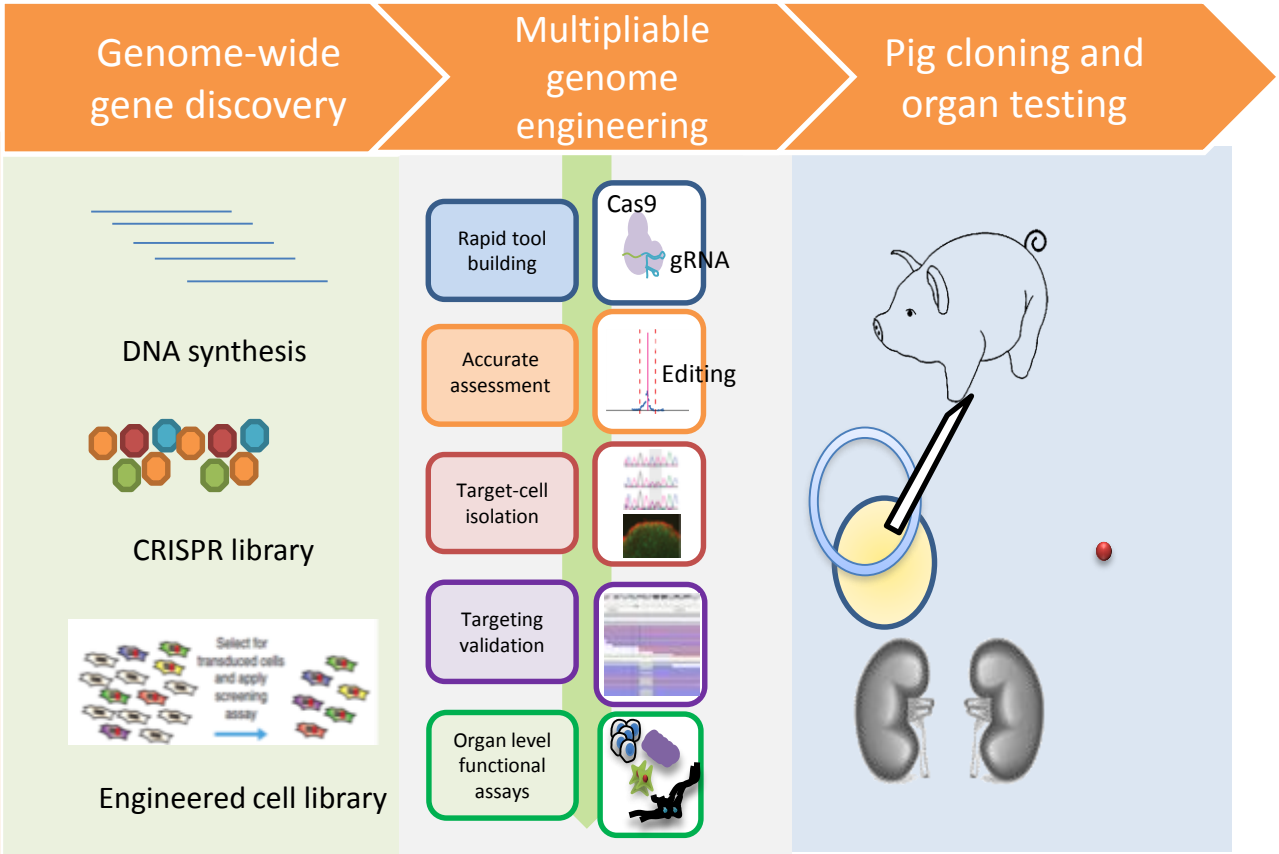
Iterative genome editing approach to synthesize human compatible organs from animals

egenesis
ENGINEERING LIFE

Iterative humanization of pig organs



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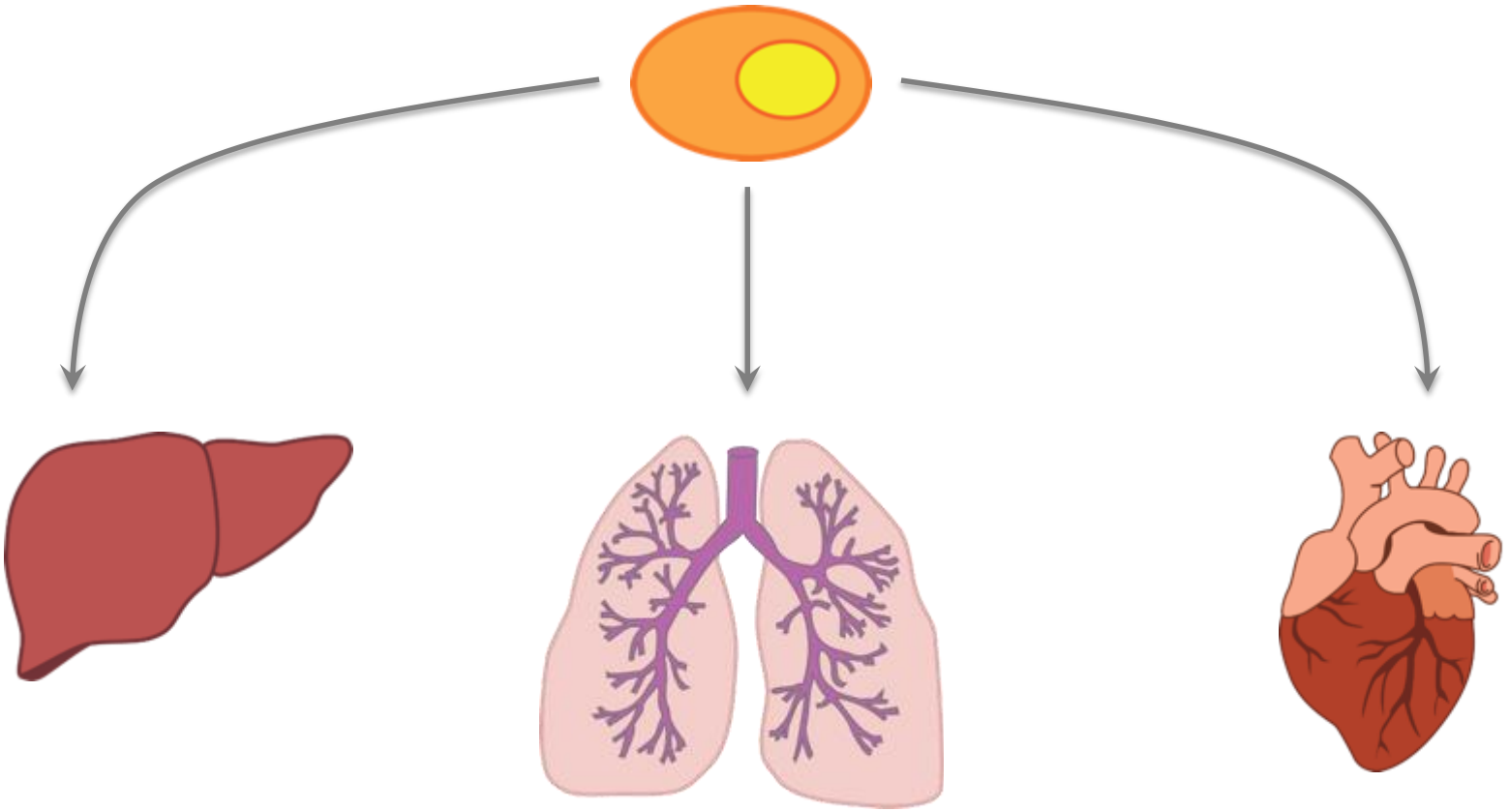
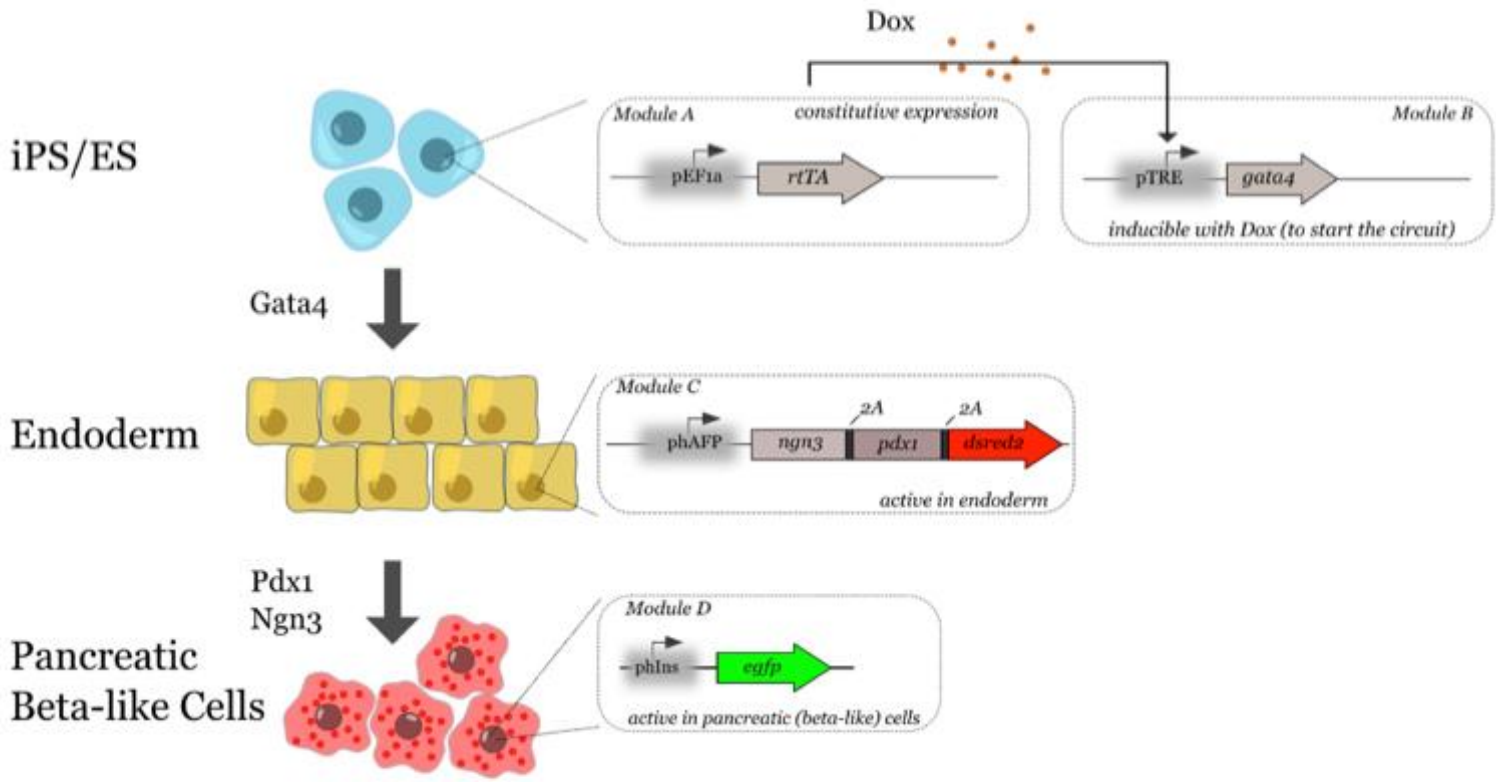
Can We Create Large Scale Functional Tissues?



Defining, Writing and Manipulating Genetic Programs

A Self-Timed Genetic Program for β cell Differentiation



From the Weiss lab (MIT Synthetic Biology Dept)

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A Sampling of Cell Fate Regulators

Targets for Synthetic Biology Reprogramming

Endoderm
- Gata4, Gata6, Sox17

Muscle
- MyoD

Trophectoderm
- Cdx2

Pancreas
- Ngn3, Pax4, Nkx2.2, Pdx1

Adipocytes
- Pparγ

Neuronal
- Nkx2.2, Nkx6.1, Pax6, Ngn1

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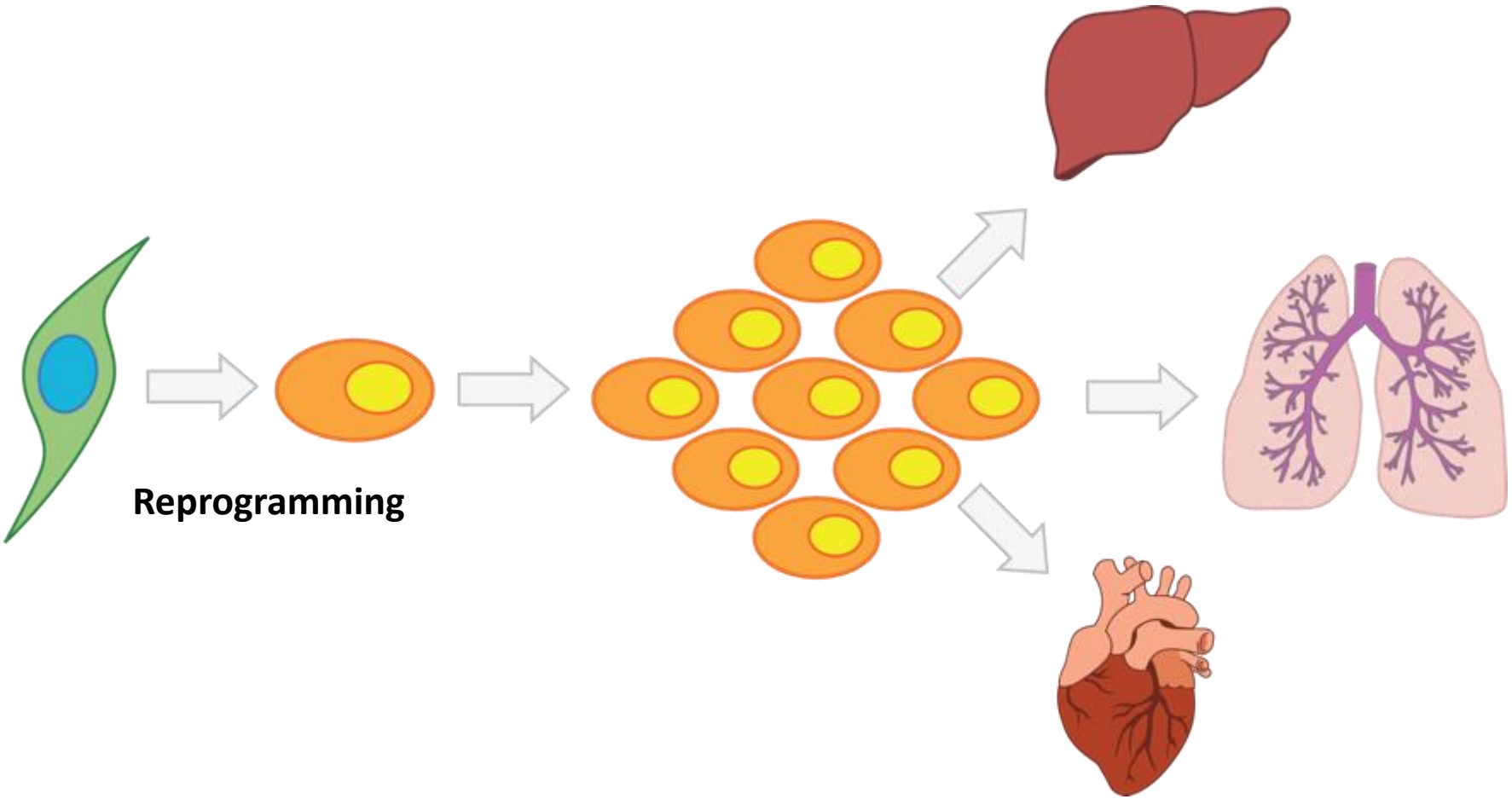
Path to Organ (re)Generation



Printed Organs

Organovo and Johnson & Johnson Team to Evaluate 3D Bio-printed Tissue Use

BY BRITTNEY SEVENSON - JULY 24, 2014

Like 76 Tweet 127 8+1 59 Share 48 56 2 points

It's only a matter of time before 3D bio-printing really takes off. One of the leaders in the space is Organovo, a company who has already been able to 3D print living liver tissue, and has an ultimate goal of 3D printing a functioning liv

organovo™

Before we get th applications to 3 used today. One such application is that of drug discovery testin performing clinical trials on potential new drugs for the market. oftentimes being put at some risk. Liver toxicity testing, in partic samples from cadavers, meaning it's not all that easy to obtain s researchers to do, is create live human tissue, which can then be reactions a particular drug may have on that tissue. Once scaled much tissue as is needed for research, as well as tissue of extre

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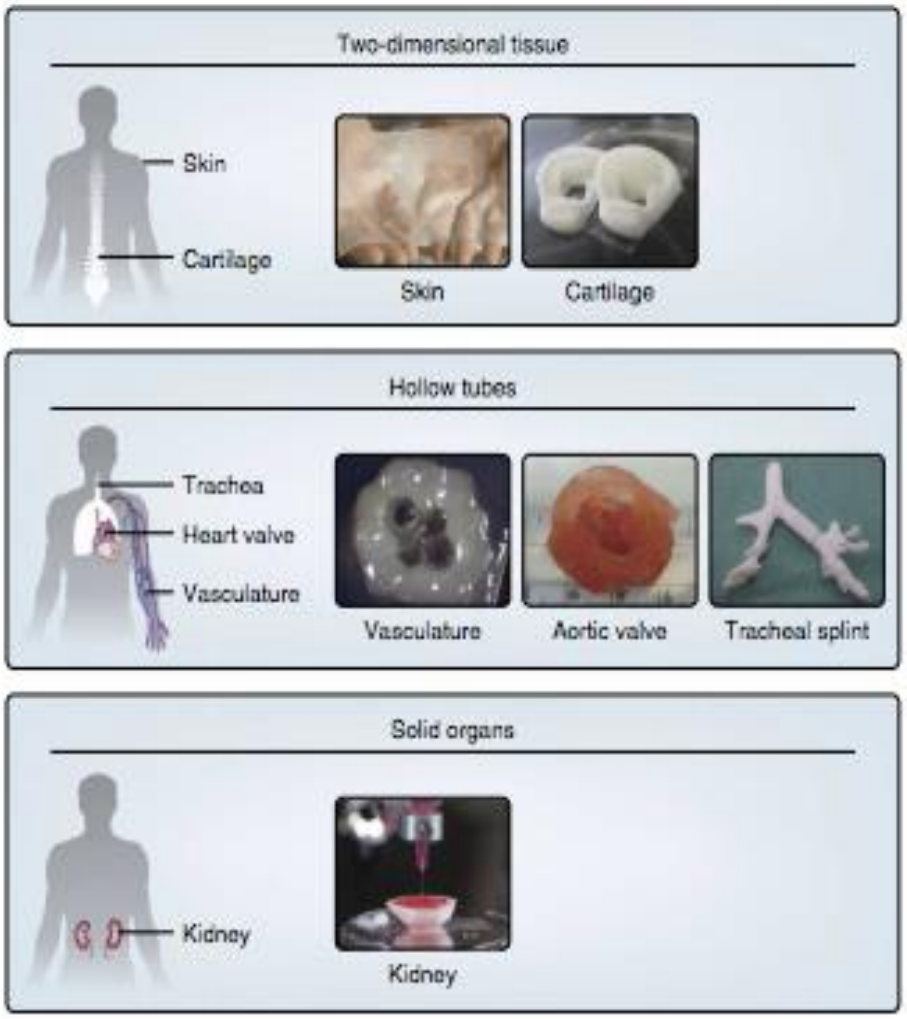
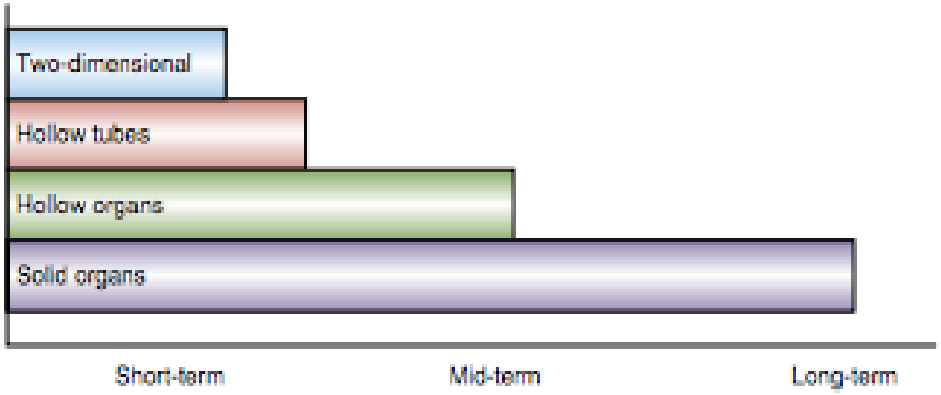
Development Timeline for 3D Tissues/Organs





Murphy and Atala. Nature Biotechnology Vol 32, No. 8 (2014)

Looking Ahead

- Advancement of developmental biology research
- iPS reprogramming
  - Therapies
  - Tissues
- Applications of amphibian based genetics?
- Generic and personalized model organisms
- SynBio + 3D printing
- Nuclei editing in Brain and neurons
- Anti Aging?

Potential to unlock many of life's mysteries!


Gen9
GeneBit
perfect
Gene
vector
clonal
plus
Variant
service
GeneByte
synthesized
sequence
products
dsDNA
BioFab
base pairs
Collaboration
Innovation
USA
Sequence-perfect
DNA
design
process
Next-generation
constructs
genes
libraries
Custom
order
Integrity
synthesis
Dedication