# The Differentiation of Stem Cells into Specialized Kidney Cells with Organ-Chip Tech

Zeke, Jonathan, Yui, Rahul, Shilp, Melissa

# The Need for Organs

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1475508/ - this is a sim study

https://atlasofscience.org/building-an-artificial-kidney-from-human-stem-cells/ - actual article
Uh someone read and summarize lol

Background -zeke

Article - rahul

Similar studies? - jon

impact / application - yui

Cited Article summary -shilp

Kahoot questions - melissa

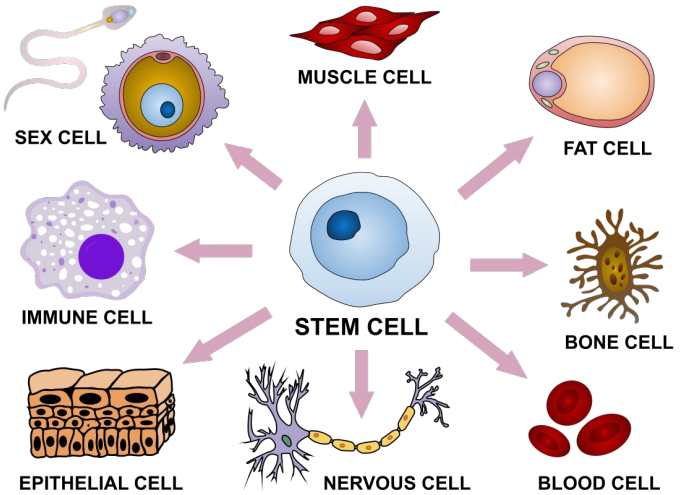
# Background: Stem Cells

Differentiation

- Totipotent: can differentiate into all cell types
- Pluripotent: can differentiate into almost all cell types
- Multipotent: can differentiate into a related family of cell types
- Oligopotent: can differentiate into a few different cells
- Unipotent: can produce one cell type only

Signaling and Growth Factors

- Cytokines
  - Renewal vs. differentiation
- Environment
  - Neighboring cells
  - Physical factors



# Background: Making Stem Cells

Embryonic Stem Cell (ESC)

- Timeline
  - Mouse (1981)
  - Human (1998)
- Harvested from ~5 days after fertilization
- Autoimmune disorders and mismatch rejection
  - Ongoing research to reduce risk
- Controversial
  - Less likely to be favored for large scale production

Induced Pluripotent Stem Cell (IPSC)

- First Developed by Shinya Yamanaka's team  in 2016 (relatively new!)
  - Won the Nobel Prize
- Transform adult (somatic) cells into PSC
  - Demonstrated skin -> eye cells
- Takes longer (3-4 weeks for human)
  - Expensive
- Decreased Risk of Rejection

# Background: From Stem Cells to Organs

We turned our stem cells into organs! Now how can we test these organs out?

Unfortunately, organs are complex systems

- Physiological
- Mechanical

We don't can't do this in a petri dish!

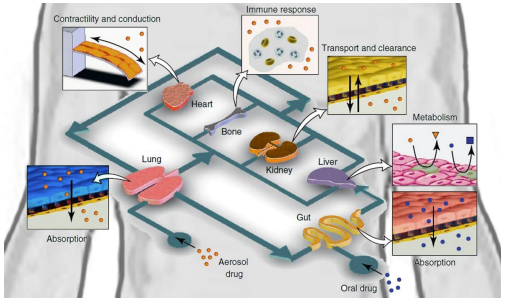
Animal testing is inefficient, expensive, and FDA regulated. It's also very inconvenient to do an organ transplant for every case study.

The new way to do it is: Organs on a Chip!

# Background: Organs on a Chip

A “Chip” contains:

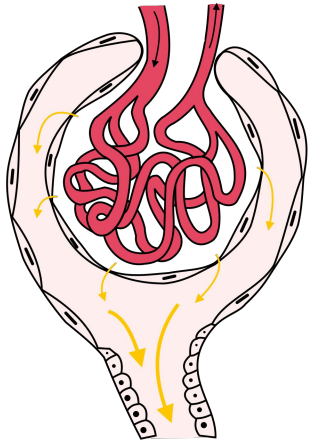
- Microfluidic Channels w endothelial tissue lining
  - Incorporates fluid flow
    - Pressure gradients
    - Dynamic influx/output
  - We can inject hormones and signaling factors reminiscent of in vitro cases
- Controlled via computational systems and automated homeostasis
  - Simulations overnight
  - Minimize human error



# Article Summary

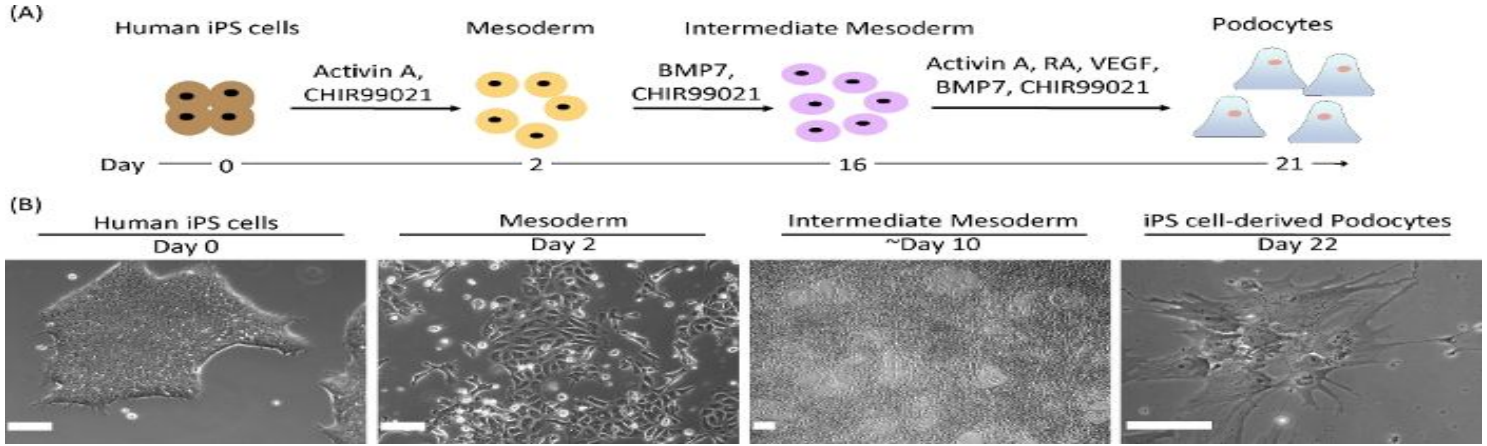
# The Problem

- Diseases and drugs effect on the glomerulus
- No good  In Vitro models of the glomerulus
  - Lack of functional podocytes



# Solution

- Human induced pluripotent stem (hiPS) cell-derived podocytes



# What Next?

- hiPS cell-derived podocytes and organs-on-chip technology
- Major improvement

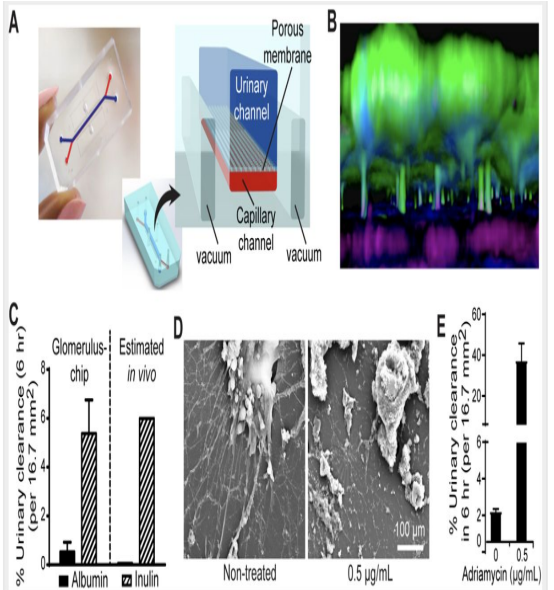



Fig. 2. Establishment of a functional human kidney glomerulus-on-a-chip. (A) Microfluidic organ-on-a-chip device showing dedicated compartments to mimic the vasculature (capillary channel) and podocyte layer (urinary channel). (B) 3D reconstruction of the human kidney's blood filtration barrier modeled using iPS cell-derived podocytes (green) and primary glomerular endothelium (magenta). (C) Selective filtration of molecules in the engineered glomerulus-on-a-chip compared to an estimated in vivo values. (D) Modeling podocyte injury induced by the chemotherapy drug Adriamycin. Scanning electron micrographs showing damage to podocytes exposed to clinically relevant concentration of the drug. (E) Glomerulus-on-a-chip models adriamycin-induced albuminuria. Bar graphs represent the concentration of albumin in the urinary compartment or loss of albumin protein into urine, a hallmark of kidney disease.

# Importance

- Kidney Disease
- Drugs
- Kidney Development
- Lower Cost
- Regenerative Medicine

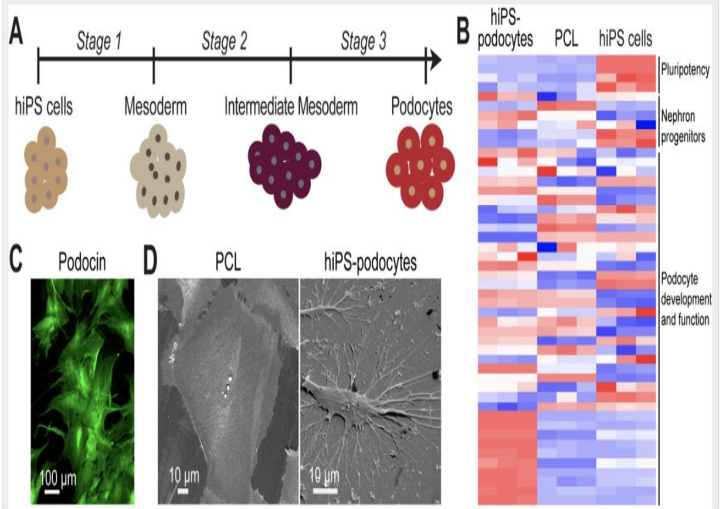
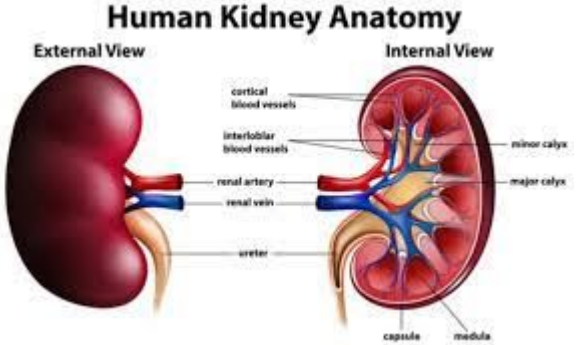


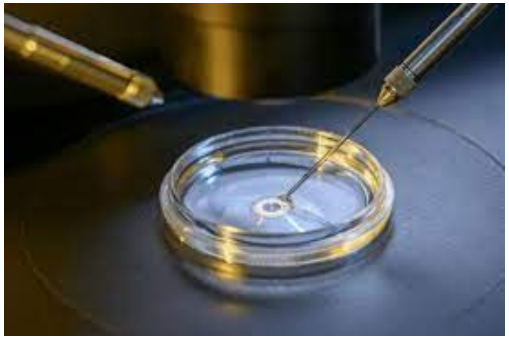

Fig. 1. Directed differentiation of human iPS cells into mature kidney cells. (A) Schematic illustration of the method for human iPS cell differentiation into kidney glomerular podocytes. (B) Transcriptome analysis of genes involved in different stages of kidney development. Red, up-regulated; Blue, down-regulated. (C) Immunofluorescence staining showing the expression of podocin (green), a podocyte lineage identification marker, in the human iPS cell-derived kidney cells. (D) Scanning electron micrographs of human iPS cell-derived kidney podocytes compared to an established human podocyte cell line (PCL) which lacks morphological features necessary for kidney function.

# Application

# Applications of Modeling Kidney Function

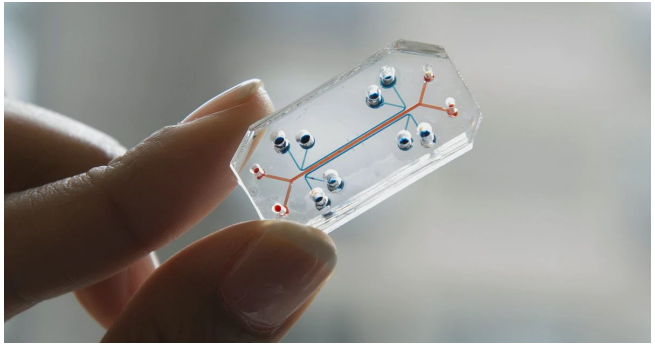
- Modeling kidney development and function
- In vitro system of drug screening and delivery
- Ability to study early and late onset of disease
- More ethical alternative to animal studies
- Possible to use the human iPS cell-derived podocytes as an injectable form of cell therapy

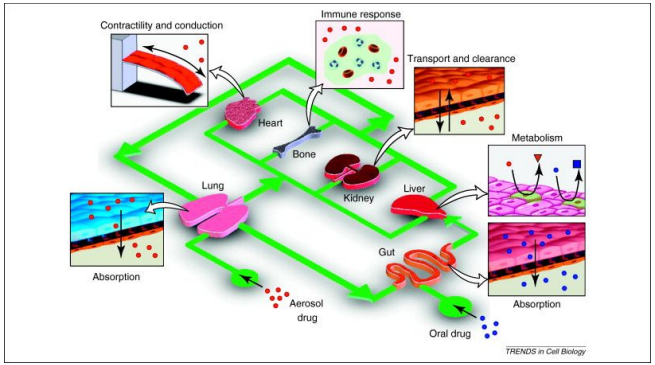


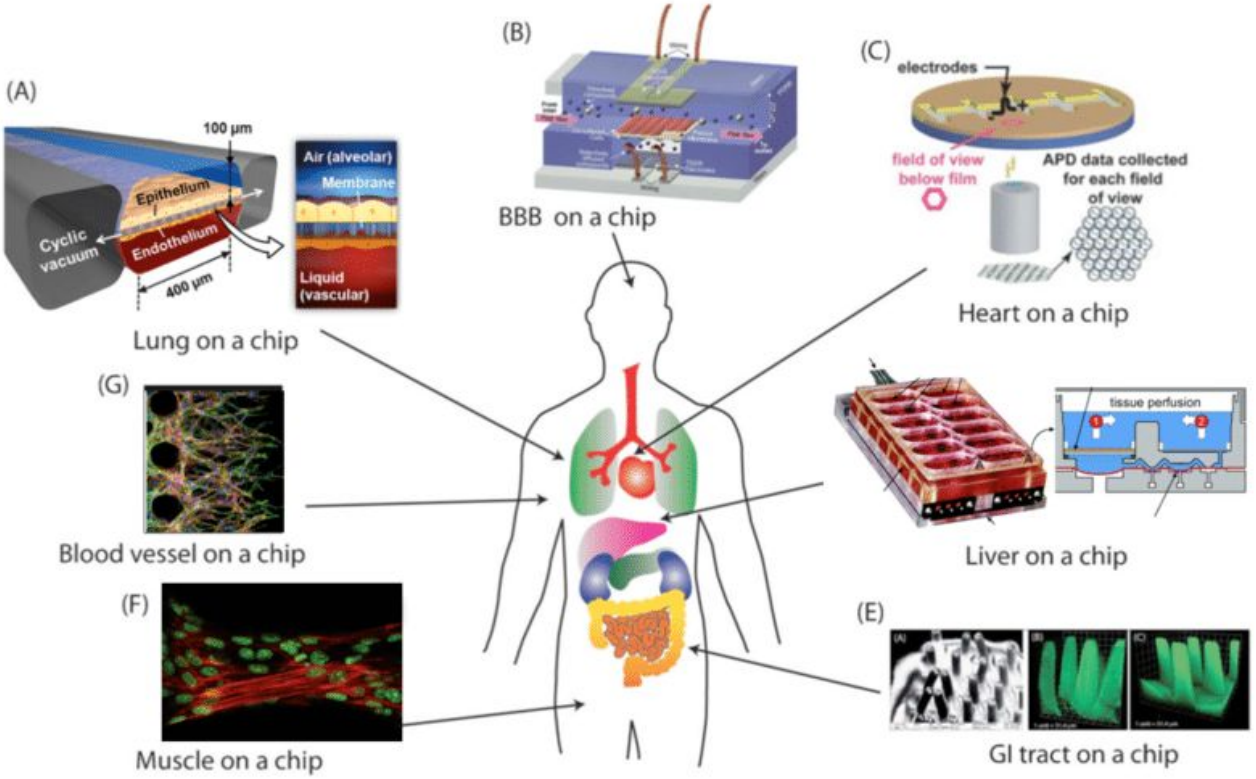
# Applications of organ-on-a-chip technology

- Alternative animal model for low-cost drug screening
- Mimics the function of human organs or tissues
- Can incorporate physical, biological, and chemical aspects of disease
- Can be coupled to other microscale liquid technologies ex:microbots





# What Has Been Modeled?



# Similar Studies

*"The Future of Organ Replacement: Needs, Potential Applications, and Obstacles"*
- Cascalho, Platt 2006

# Conditions for the Future of Organ Replacement

1. The need » particularly how the number of organs to be replaced will change over time
2. Set of applications and new technologies that will be available to replace those organs
3. Set of obstacles (biological, and societal) possibly hindering the replace of organ function

# How has the need for organ replacement has changed over the years?

- Contrary to popular belief within the discussion of transplantations, prevalence of organ failure will continue to increase, and so is the demand for transplantation
- Preemptive transplantations could expand this demand drastically
- Factors increasing demand include increased longevity in the population, more nuanced solutions to organ failure, and more personalized & long-term treatment

# Current Organ Replacement Technologies & Pitfalls, and Possible Solution

- Xenotransplantation » requires severe immunosuppression and is more or less a temporary solution
- Fully Implantable Devices » last resort, limited to cardiac replacement, and engenders additional risks like infection
- Stem Cells » limited to fetal microenvironments, and may require immunosuppression if stem cells do not originate from patient
- Solution could be with mixing multiple technologies

# Significance to the Kidney Study & other organ regeneration studies

- In spite of these limitations and pitfalls, scientists are optimistic about using stem cells due to high versatility and efficiency
- Research done by Musah's research group can be used in relatively most regenerative medicine / therapy research on other organs
- Set's a basis for regenerative biomedical therapeutics and opens up new doors for future organ replacement / regeneration research

# Future goals in Organ Regeneration Research

- Major vascularization in engineered tissues
- Replication of most organ functions
- Organ regeneration in vivo is still very far in the future
  - Current goals in the field:
    - Regenerate damaged portions of certain organs through tissue engineering
    - Ensuring that stem cells can differentiate into specific sub-lineages
    - Maximizing efficiency and effectiveness of stem cell differentiation