Organoids: How they are used today, and how they might be used tomorrow

Presentation By: Sarah Lundy

Today's Goals…

Acquire

- Acquire a basic knowledge of organoids

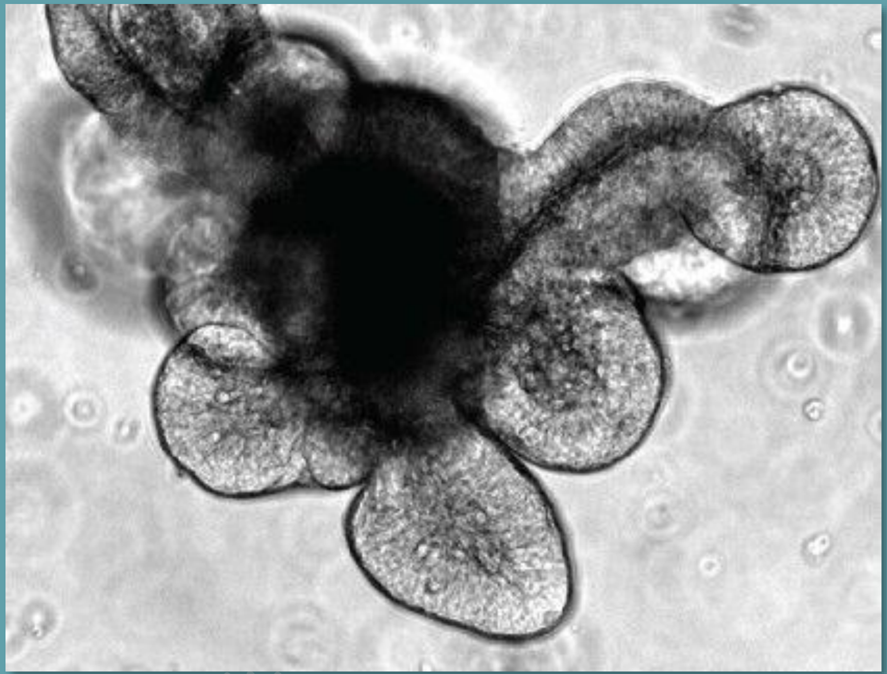
Understand

- Understand ways organoids are currently used

Visualize

- Visualize the future of organoids

What is an Organoid?

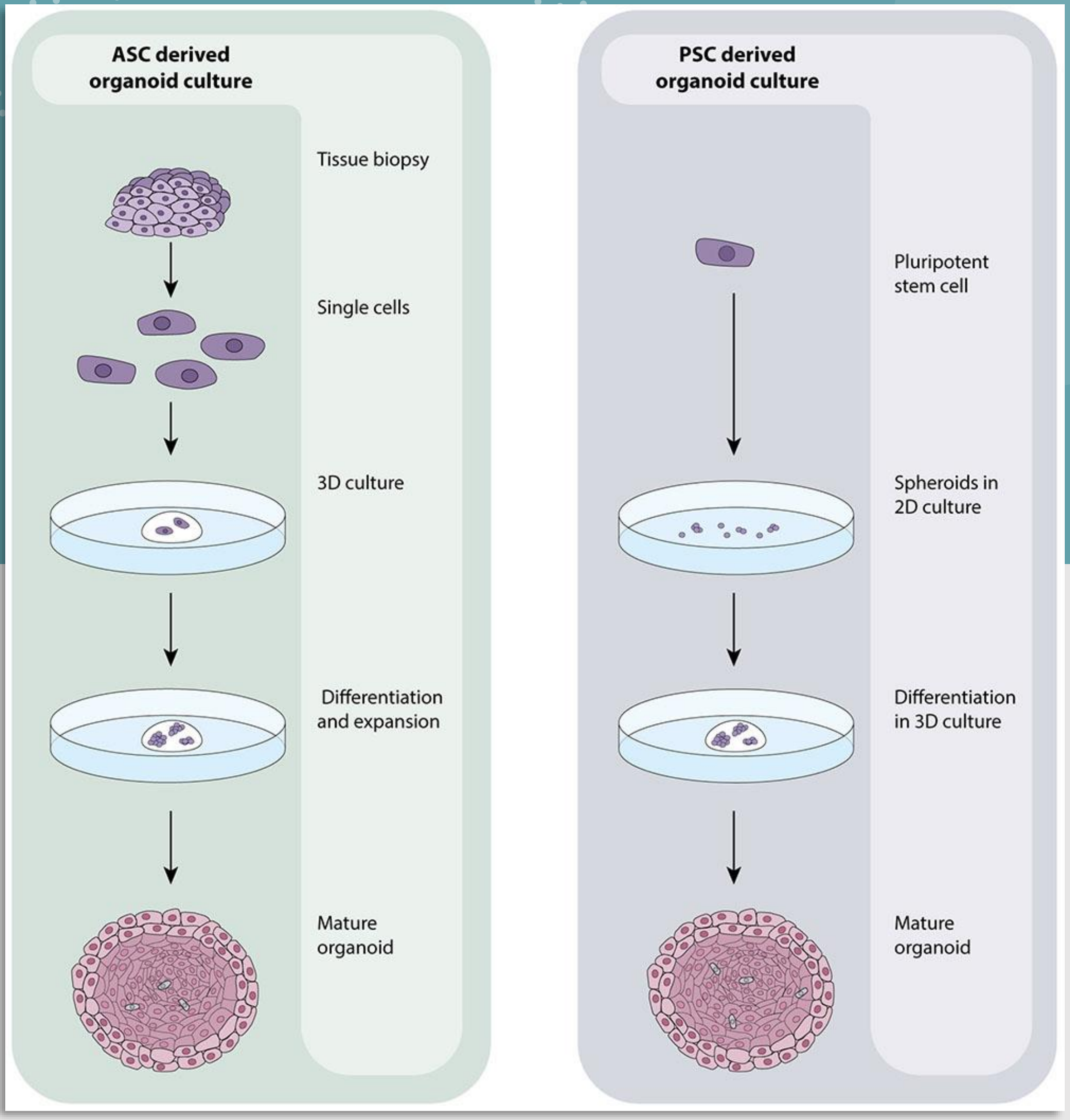


(Conder, 2015)

- 3D stem cell-derived tissue structure, grown *in vitro*
- Models a specific tissue type or organ
- Used in studying diseases and treatments

Organoids can be “grown” from 2 types of stem cells

- <u>Pluripotent stem cell-derived organoids</u>
  - Resemble embryonic tissue development
- <u>Adult stem cell-derived organoids</u>
  - Growth patterns resemble tissue repair mechanisms
- Organoids can also grow from *cancerous cells*



(Lakobachvili & Peters, 2017)

Organoids have a broad range of uses

- The applications for organoids continues to grow

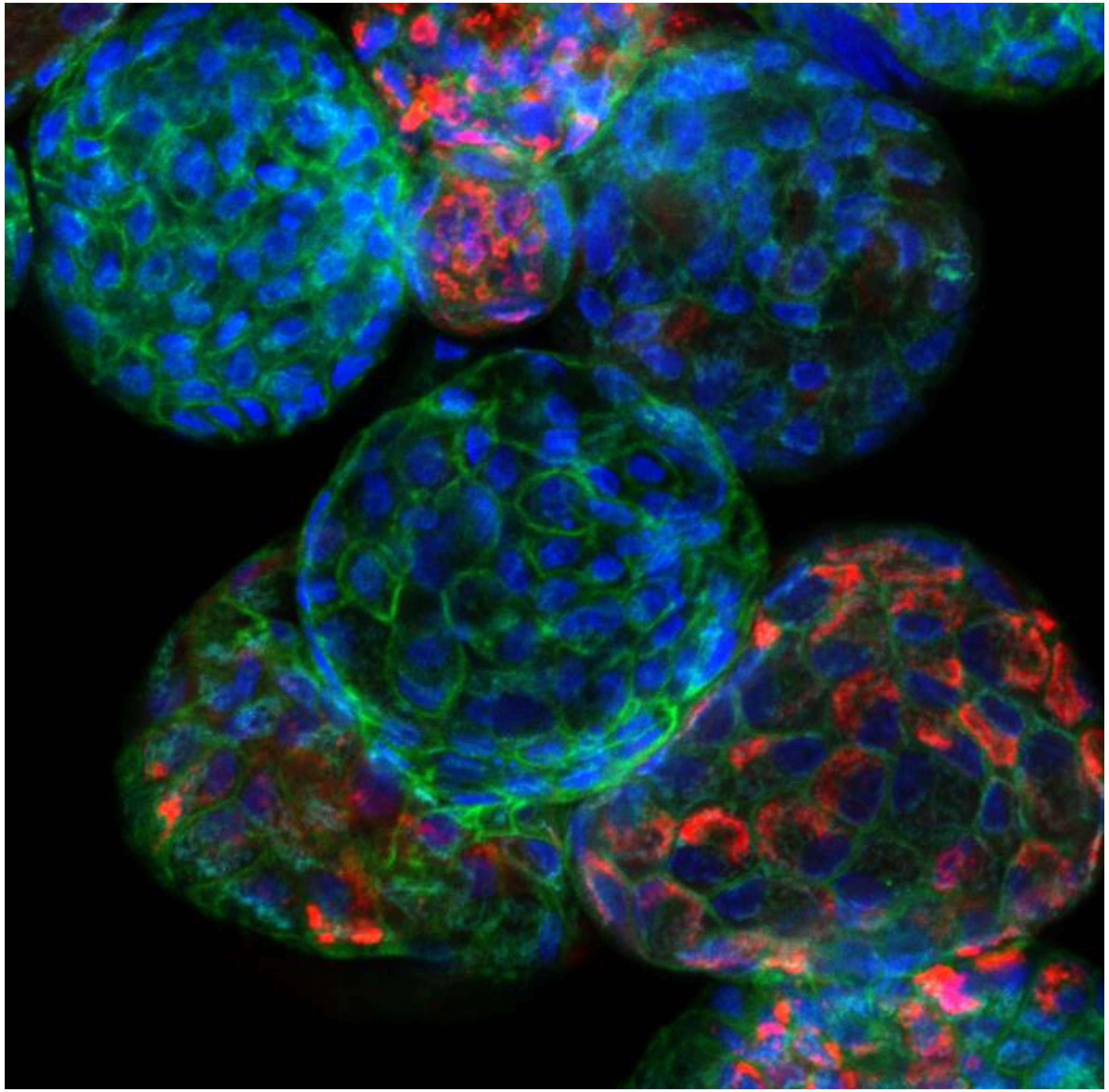
- <u>Some of the most prominent uses include:</u>
  - Developing personalized cancer treatment
  - Modeling Liver Disease
  - Transplantation of liver organoids
  - Evaluating Covid-19's effects on different tissues

Personalized Cancer Treatment

- Cancer cells can be used to form a patient-derived organoid (PDO)
    - Some PDOs mimic the tumor from which they came from
- Various treatments can be tested on the PDO and the most effective one(s) can be determined
- Saves the patient time, money, and discomfort

- Wensink et al. (2021)

Liver Disease Modeling



(Nosengo, 2020)

Liver Disease Modeling

- Organoid was made using a co-culture of…
  - hepatic endodermal cells
  - human mesenchymal stem cells
  - human umbilical vein endothelial cells
- Cells organize into “liver buds” and the organoid develops primitive vasculature
- Organoid can be used to study *disease progression* and *treatment options*
- Cell genetics can be evaluated, and mutations can be identified

- Nuciforo & Heim (2021)

Transplantation of Liver Organoids

- **Liver bud organoids were transplanted to mouse mesentery**
  - The organoid metabolized drugs and secreted albumin into the blood
  - Organoid improved outcome for mouse liver disease model
    - Nuciforo & Heim (2021)

- **Organoids grown from cholangiocytes were implanted into a deceased human liver**
  - The liver and organoid were maintained for over 100 hours
  - Organoid was functional, and could repair bile duct to an extent
    - Sampaziotis et al. (2021)

Evaluating Covid-19s Entry Method Into Respiratory Cells

- Airway and alveolar organoids proved important in determining the entry mechanism of Covid-19 into respiratory tissues

    - Vero cell entry occurs via cathepsin-mediated entry/endocytosis
    - Respiratory organoid cell entry occurs via serine protease-mediated entry

- This highlights the importance of using the appropriate cell types for research

- van der Vaart et al. (2021)

Evaluating Covid-19s Effect On Other Tissues

- Many types of organoids have been used in studying Covid-19
    - *Brain organoids* help evaluate neurological effects
    - *Gastrointestinal organoids* help to study GI response to Covid-19
- Organoids have also been used to study treatment and vaccine options

(Kim et al., 2022)

Challenges with Organoids

- Most organoids do not develop vasculature, so growth is limited
- Growing organoids is a highly sensitive process and can be easily altered
    - This leads to inconsistent development of organoids
- Reducing the variability of organoids will take years of trial and error

Solutions

Blood vessel formation may require co-culturing with proper cell types

Humans will have to adapt to the sensitivity of organoids

Defining culture requirements for growing various organoids would help reduce variability

Future directions

- Continue and enhance use in personalized cancer treatment
- Working to define the needs of different types of organoids
- Develop methods so the organoids better physically resemble the organ
- Growth of organ parts to replace faulty anatomy

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