Project Objective: Identify the hallmarks of the tumor microenvironment

Motivating Factors:

1. We have characterized the "hallmarks of cancer." but no such high-level map exists for the tumor microenvironment
2. There exist 3 primary models for the study of cancer:
   (a) Cell culture
   (b) Lab animal
   (c) Human (clinical)

   Yet, none of these models is adequate for the study of the tumor microenvironment (i.e., cancer's functional interactome). Namely,

   (a) Cell cultures compress a tumor into a 2D environment and fail to replicate the full microenvironment with which the tumor interacts
   (b) Animal models may lack fidelity with respect to human cancers and findings may be difficult to translate into clinical applications
   (c) Human models are limited to clinical trials and lack the flexibility found in cell and animal models.
3. A high-fidelity *ex vivo* model with tightly-controlled microenvironmental parameters that mimic the human tumor environment is needed to fill this gap
   (a) 3D organ scaffolds may offer a solution to this
   (b) Such a solution must be:
      i. Easy to produce in batch;
      ii. Functional replicates of human systems; and
      iii. Tightly controlled with respect to the microenvironment
   (c) I.e., any solution must have all the benefits of a human model without the drawbacks of committing a felony in your research

Anticipated Challenges:

1. What can be grown? Are we restricted to tissue types? To hollow organs? What are the technological challenges of allowing for growth of multiple tissue types/organs?
2. How do we achieve functional maturity of the organs once grown?
3. What types of cancer is this model suited to study? How does this relate back to the types of organs and tissues that we are able to grow?
4. How detailed can we reasonably make our models without replicating every organ system in the entire body? Where do we draw the line between the model lacking fidelity and being over-engineered?
5. How can any findings be validated and then translated into new therapeutics?
6. Will any new therapies actually be worth this initial investment in the technology?

Research Timeline:
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