RNA-based Spatial Endometrial Cancer Transcriptomics ReSPECT Project

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What is Endometrial Cancer (EC)?

EC Basics

- Nearly 66k women in the US diagnosed with EC in 2022
- 12,500 women will die from EC in the same year
  Nearly 20 percent of women diagnosed with EC do not survive.
- Treatable *if caught early* (Stage 1)
- EC incident rate expected double by 2030 due to
  - High rates of obesity
  - Delayed pregnancy

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What's the EC problem?

The overall survival is 80 percent - Why do we care about EC?

- Higher occurance/lower survival for women of color
- Vague biological/immune requrements to be qualified for immune targeted treatments
- Invasive biopsies make early detection challenging and less accessible

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How can we address EC challenges?

- Spatially Explore Localized Immune Activity Near Carcinoma
  - Within Tumor
  - Within Stroma (forming connective tissue within tumor)
  - Adjecent to tumor region
  - Healthy endometrial tissue
- Create Robust Immune Profile for Treatment Determination

How do we spatially detect immune cells?

In Situ RNA Imaging

- 1) Design 100 different immune transcript probes
- 2) Pretreat Tissue Sample to expose RNA
- 3) Incubate tissue with target immune transcripts (*targets will ligate to RNA*)
- 4) Enzyme amplification of ligated targets (*increases physical size of target*)
- 5) Incubate with fluorescent probes (*binding to enlarges RNA targets*)
- 6) Image using fluorescent microscopy

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Key Immune Transcripts

Transcripts are respresentative of proteins about to be created by a particular cell. These transcripts are used to identify specific immune cells as well as immune system chemical signalling.

Key Transcripts in Endometrial Carcinoma with "Hot" Immune Prescence			
Transcript	Protein Type	Specific Function	Role
CD8B	T-cell Surface Glycoprotein	Activates CD4+ CTLs	Immune
CX3CR1	Immature WBCs Chemokine Receptor	Recruits NK cells through inflammation	Immune Chemot
TGFB1	Growth Factor	Promotes Th17 & Tregs cells	Immune Normal
CD69	T cell, B cell, NK cell Post-activation Antigen	Promotes lymphocyte proliferation	Immune

Example Images

The ReSPECT Project is ongoing. Below are examples of how collected spatial transcriptomic information can be used.