Organoid Cultures for the Study of Cancer in Bloom Syndrome

Stronger Together

Bloom Syndrome Association Conference 2022

Rosemont IL

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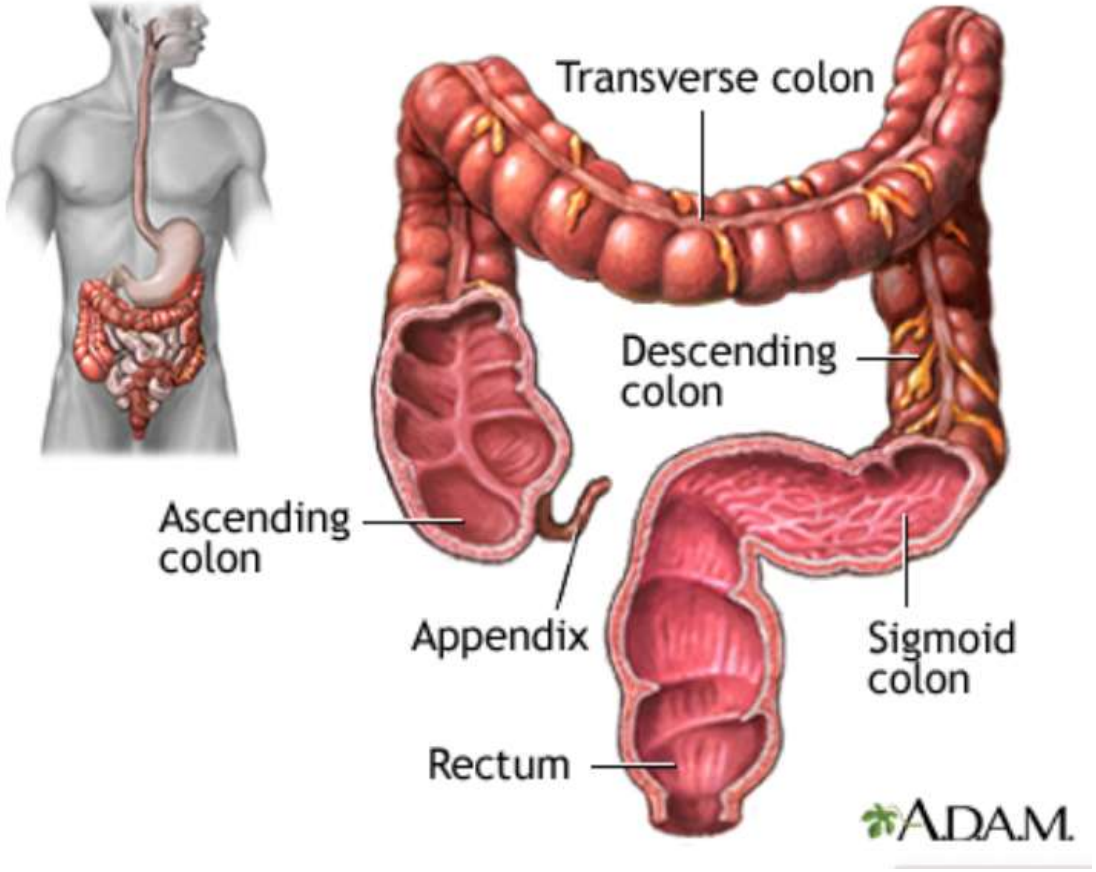
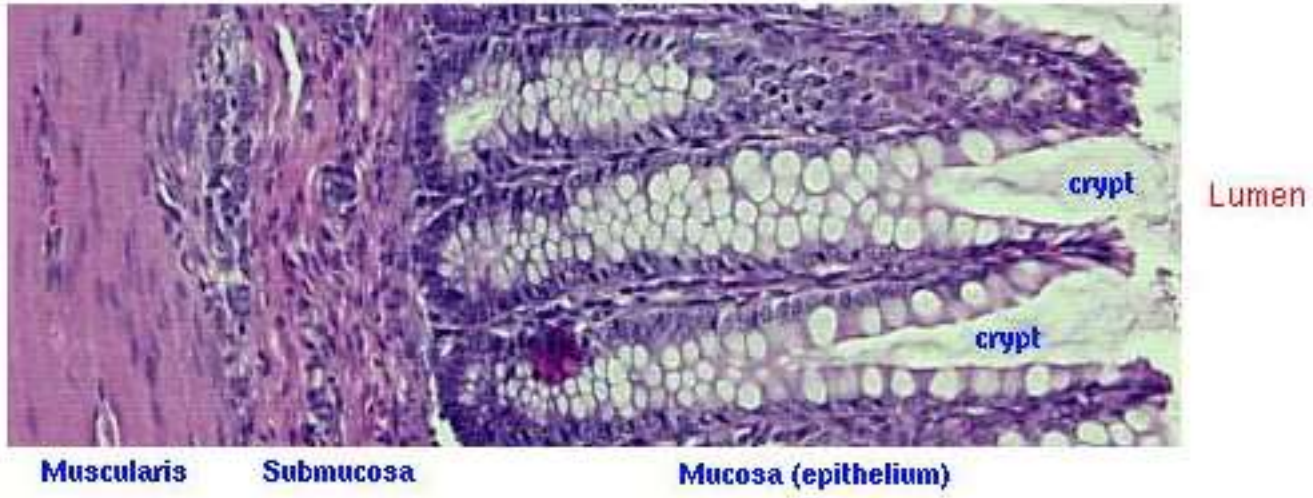
RECQ meeting
Chicago -- 2008

We need to know a lot more about cancer cell biology in Bloom syndrome

- What we are lacking:
  - Gap in knowledge about the specific mechanisms and disease-causing lesions that drive cancer in Bloom syndrome
  - What transcriptional pathways are impacted in cancer development and how are the transcription factor networks deranged and re-arranged?
  - Lack of knowledge about how Bloom cancer cells behave in response to specific genetic and therapeutic challenges – what are their vulnerabilities?
- What we need:
  - Direct analysis of resected tumors
  - Cancer cell lines from Bloom cancers – MODELS MODELS MODELS!!!
  - Preserve tissues for later study in anticipation of new technological developments

Tissues are organized by cell type and functional morphology
Large intestine (example)





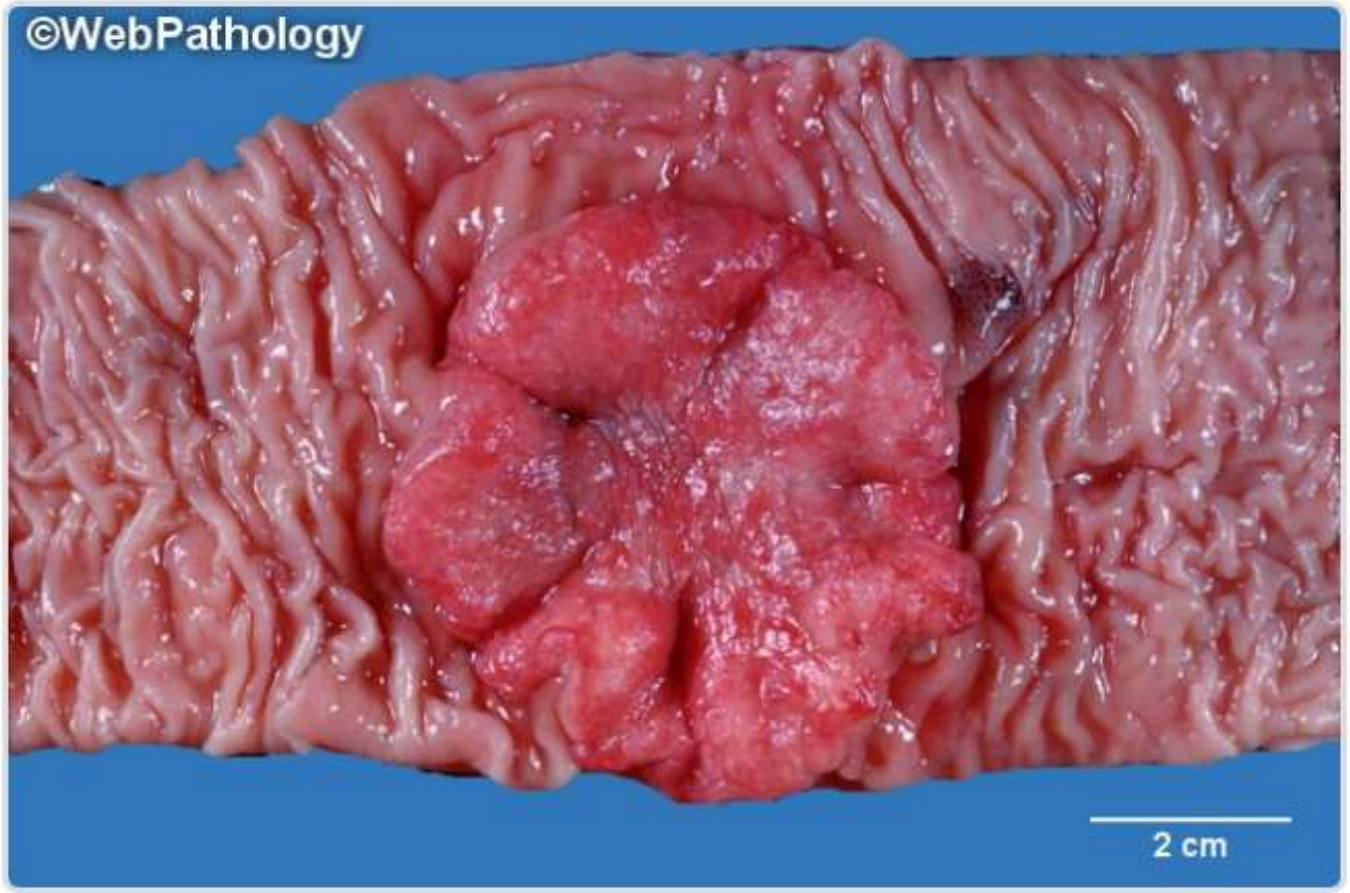
Stem cells

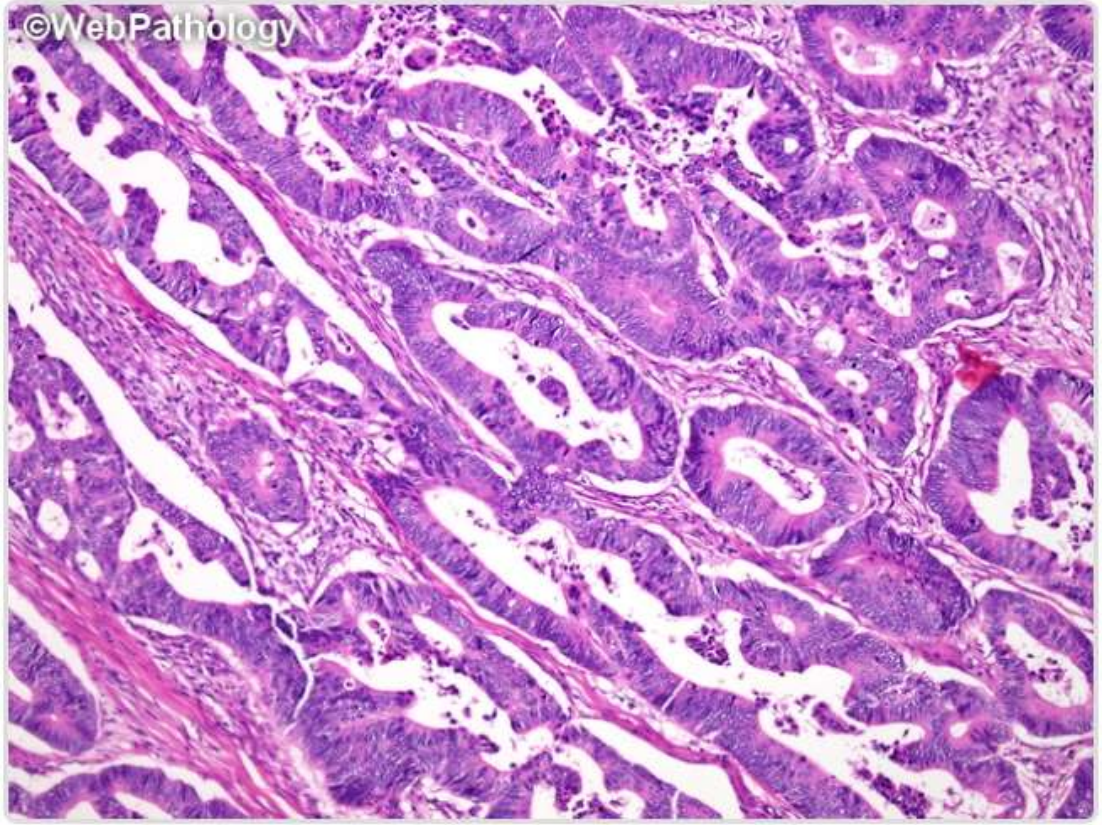
Differentiated cells

Mesenchymal layer; fibroblasts, smooth muscle, lymphocytes

Epithelial cell layer; Absorbtive, goblet, neuroendocrine etc.

Adenocarcinoma of the colon retains features of original tissue but are disorganized, proliferative, hyperplastic





Carcinogenesis is Multistep – The Vogelgram

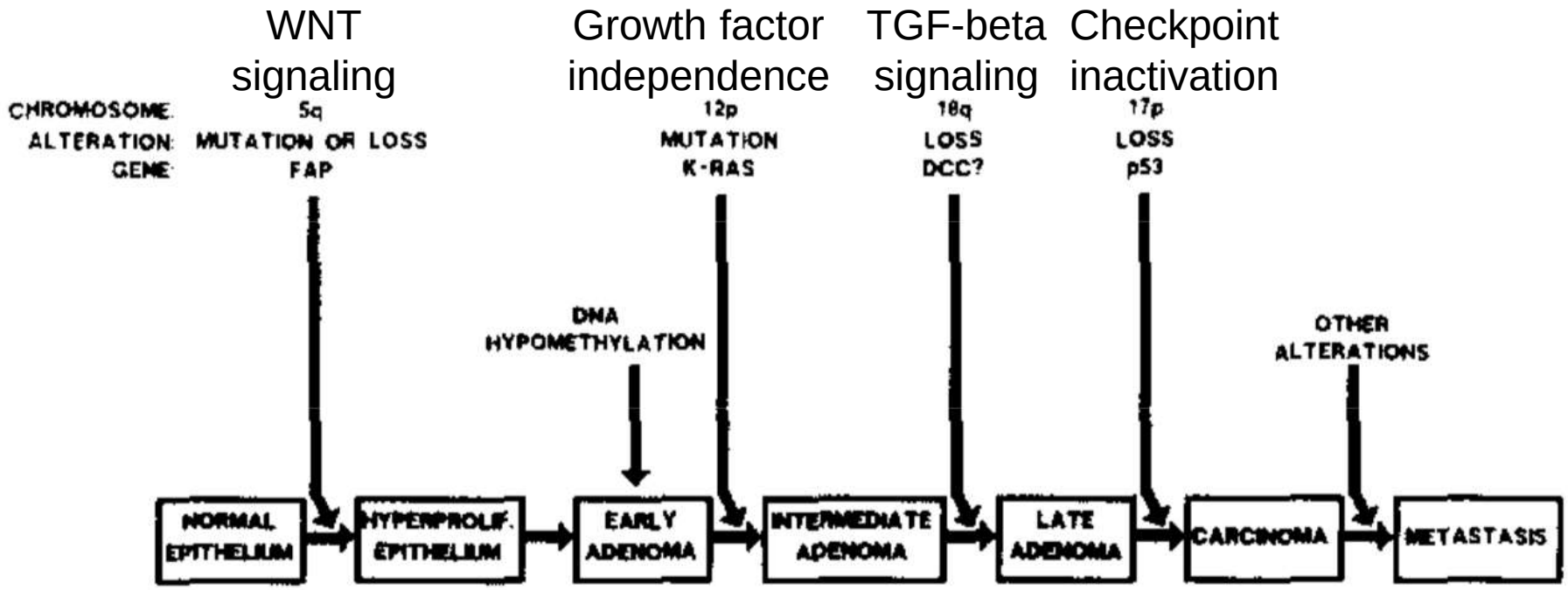
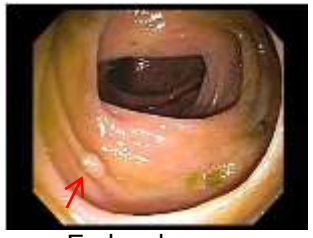


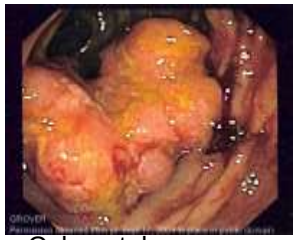
Figure 3. A Genetic Model for Colorectal Tumorigenesis


"clean colon"


Aberrant crypt focus

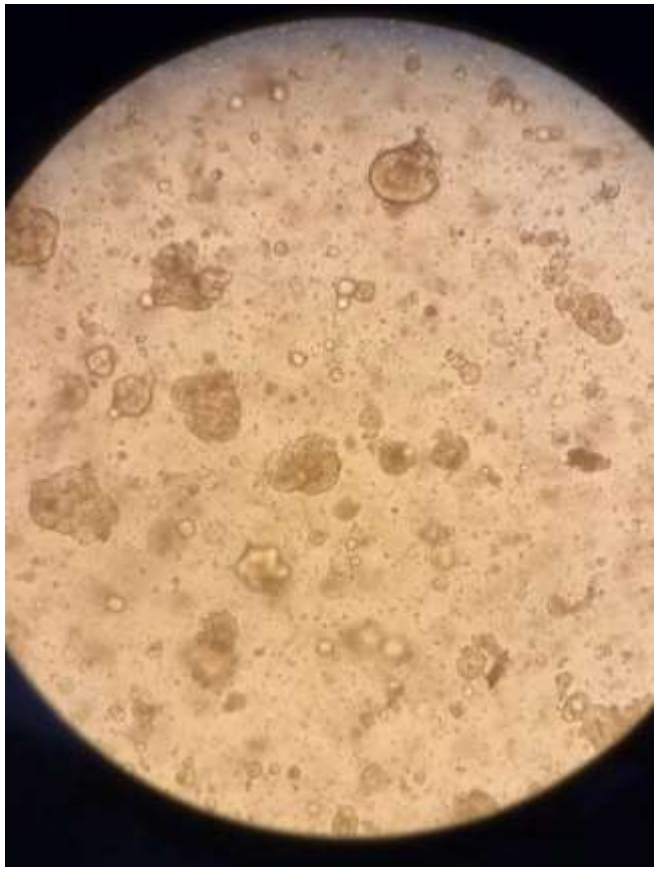

Early adenoma


Advanced adenoma

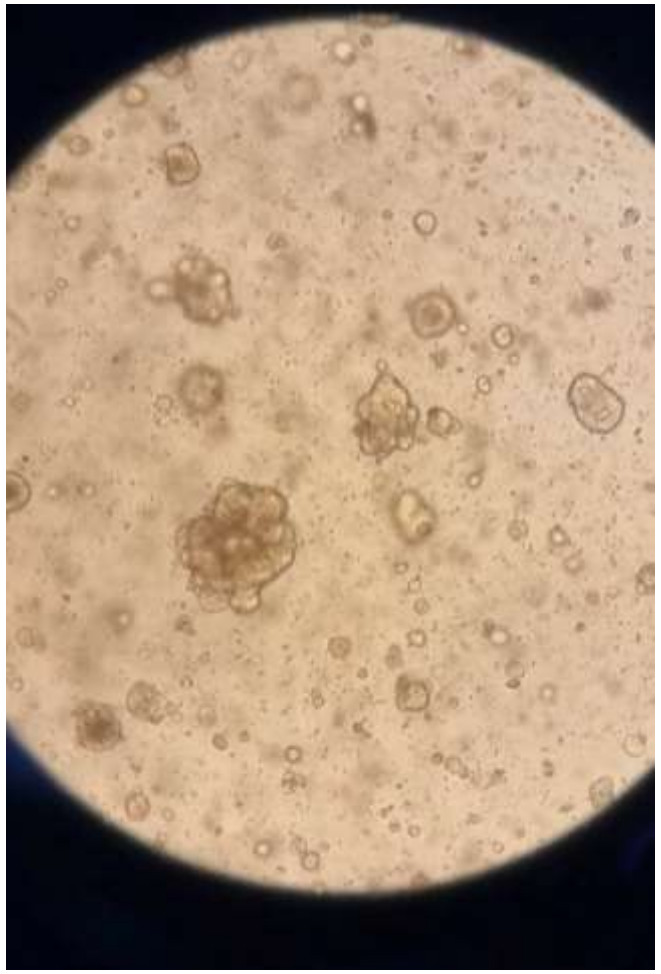

Colorectal cancer

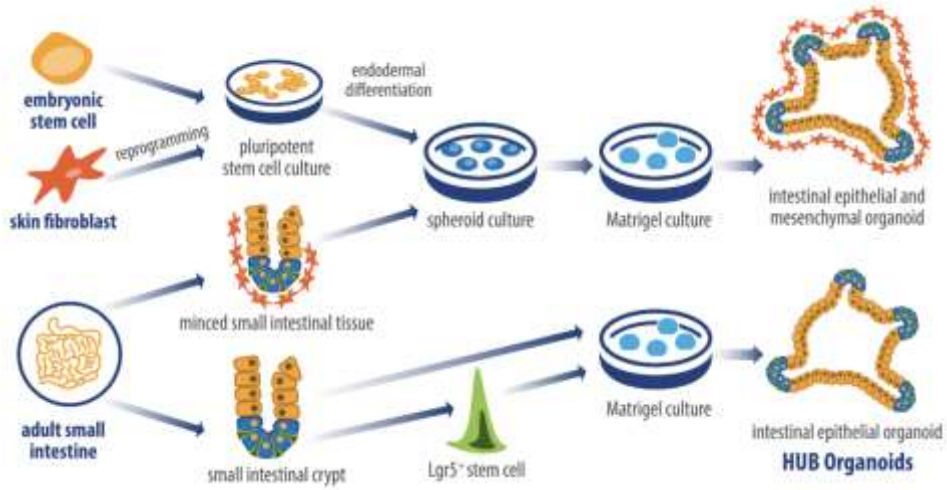
Vogelstein and Fearon, 1990

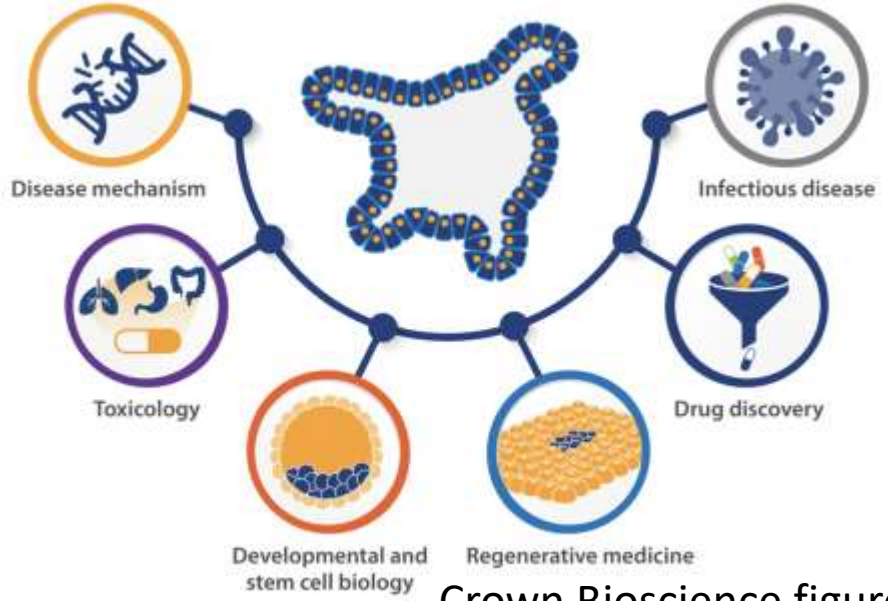
Cancer Organoid Models are the current best method to study human cancer



Human colorectal cancer organoids







Crown Bioscience figures

What can you do to help?

- To make cancer organoid models, WE NEED
  - FRESH CANCER TISSUE FROM THE OPERATING ROOM AS SOON AS IT CAN BE OBTAINED FROM THE SURGEONS AND PATHOLOGISTS – we need to get the tissue in Arizona within 24 hours of surgery
- We have IRB APPROVAL to do this through the BLOOM SYNDROME REGISTRY
- If you have Blooms or you are a parent of a minor with Blooms, and the person with Blooms is diagnosed with a cancer: ALERT YOUR SURGEON you want FRESH TUMOR TISSUE preserved in transport media to be couriered to NATHAN ELLIS and CALL THE REGISTRY to arrange for the tissue transfer (material transfer agreement).
- With your help, we will makes these organoid cultures. We will make them generally available for study and we have lots of plans ourselves on how to study them. THIS COULD BE TRANSFORMATIVE FOR TREATING BLOOM CANCERS!
- We are supported by you, the Association, the Registry, and the Upenn Orphan Disease Center. Their pilot funds will lead to large federal grants.