Studying Stomach Cancer in the Lab

StoCAN Webinar

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From Bench to Bedside

Scientific Discoveries

- basic science research
- animal models

Clinical Trials

- Phase I, II, III trials to test new therapies for patients

Treating patients

- New drugs
Why mice?

99.5% genetic similarity

96-99% genetic similarity

90% genetic similarity

80% genetic similarity
Mouse Models to Study Cancer

- Mice have 75% genetic similarity to humans but 99% of mouse genes have human analogs

- Small & easy to breed

- Experiments are completed quickly and better controlled than human studies
Mice and Humans have Similar Anatomy

A

Mouse

Stomach

Cecum

Colon

Human

Transverse colon

Descending colon

Taenia coli

Haustra

Ascending colon

Small intestine

Cecum

Appendix

Anus

B Mouse fore and glandular stomach

C Human glandular stomach

Gastric Cancer in Mice - Linitis Plastica

- Gastric cancer mice with enlarged dysmorphic stomach

- Thick, rigid, and whitened Similar to Linitis Plastica or Leather Bottle stomach seen in patients
What are we studying in our Gastric Cancer mouse models?

• Biomarkers for early detection and recurrence

• New treatments to slow/prevent metastases or spread of disease

• Biological pathways that drive gastric cancer
Mice Can be Engineered with Molecular Markers to Follow Cancer Progression

GFP mouse

Brain tumor

RED = tumor cells
GREEN = blood vessels from mice

Zimmer et al. 2015
We Can Monitor Gastric Cancer Progression in our Mice

Yellow Protein labeled Gastric Cancer Mice

3 weeks old  6 weeks old  9 weeks old

Healthy Mouse

9 weeks old

Stomach

Yellow = Cancer cells
Blue = All cells
Can we detect gastric cancer before we can visualize it?

- Blood
  - Circulating tumor cells, tumor DNA

- Stool and Urine
  - Tumor proteins, tumor DNA

- Gastric Lavage
  - Tumor cells, tumor proteins, tumor DNA
Mass Spectrometry Analysis of Stool from Mice with Early-Stage GC

**GC mice**

Collect stool
- 4 weeks (early)
- 12 weeks (late)

**Prep Samples**
- Digest
- Label (barcode)

**Mass Spec Analysis**
Possible Biomarkers of Early-Stage Gastric Cancer

- Can we screen the stool of everyone with risk factors for GC?
- Can we use these biomarkers to detect GC recurrence?
Advanced Gastric Cancer: Metastatic Progression

Secondary stomach cancer in the lungs

Stomach cancer
Gastric Cancer Mice Metastasize to Lymph Nodes, Lung and Liver

Perigastric Lymph Node Mets
Lungs Metastases
Liver Micrometastases

Liver mets not detected by imaging

Yellow = Cancer cells
Blue = All cells
Drug Discovery for Metastatic Gastric Cancer

- Add FDA-Approved Drugs (screen 3000 drugs)
- Automated Readout for Drugs that Kill Cancer Cells

Test Drugs in mice:
- Toxicity
- Efficacy
Clinical Trials in Gastric Cancer Mice

**ARM I**: 5FU + Oxaliplatin  
*Standard of Care*

**ARM II**: 5FU + Oxaliplatin + **Compound X**  
*Experimental Arm*

**Experimental Schema**

- Overall Survival
- Metastatic Disease

**Rx**

- AGE 6 wks
- 7 wks
- 8 wks
- 9 wks
- 10 wks
- 11 wks
- 12 wks
- 13 wks

Tumors detected by imaging

Median O.S.
New Treatment Regimen is not Toxic to Mice
Can New Drugs Extend Survival for our Gastric Cancer mice with Advanced Disease?

- *Addition of Drug X may improve survival by 6 weeks in gastric cancer*

**Diagram Description:**
- Untreated Mice
- SOC
- SOC + Drug X
- Drug X

**Key Points:**
- Median O.S.
- Start treatment
- Addition of Drug X may improve survival by 6 weeks in gastric cancer
Short-term Goals

• Validate stool biomarkers in patient stool

• Investigate whether stool biomarkers decrease after chemotherapy - can they detect recurrence?

• Test new drug combinations in GC mice