

Studying Stomach Cancer in the Lab

StoCAN Webinar

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From Bench to Bedside

Scientific
Discoveries

- basic science research
- animal models



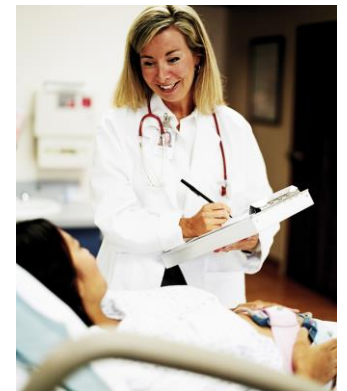
Clinical Trials

- 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



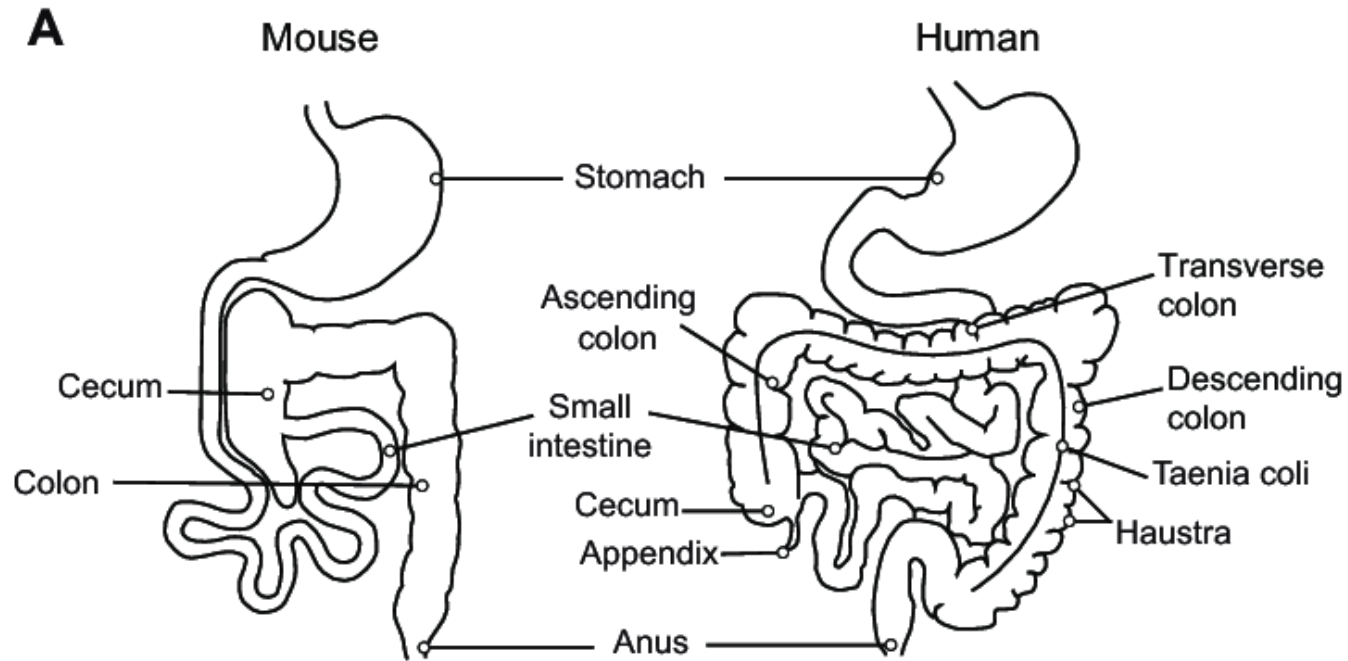
80% genetic similarity

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



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

Healthy Mouse Stomach



Gastric Cancer Mouse Stomach



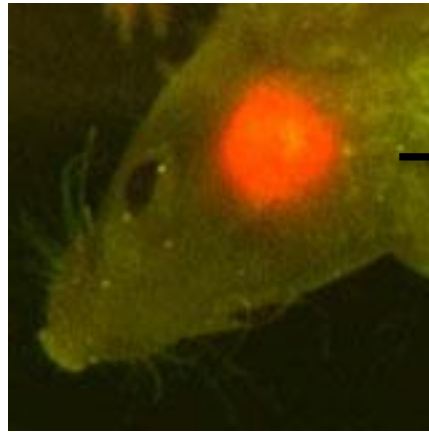
What are we studying in our Gastric Cancer mouse models?

- Biomarkers for early detection and recurrence
- New treatments to slow/prevent metastases or spread of disease
- Biological pathways that drive gastric cancer

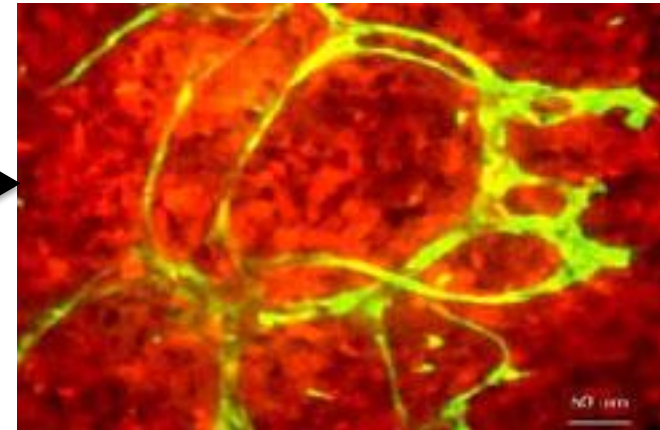
Mice Can be Engineered with Molecular Markers to Follow Cancer Progression



GFP mouse



Brain
tumor



RED = tumor cells
GREEN = blood vessels
from mice

We Can Monitor Gastric Cancer Progression in our Mice

Yellow Protein labeled Gastric Cancer Mice

Healthy Mouse

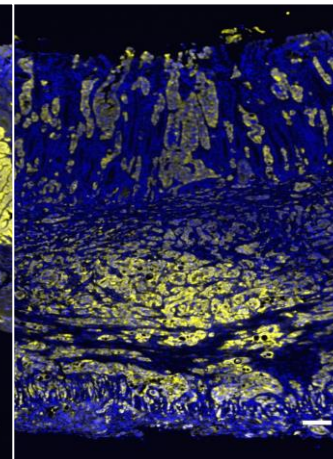
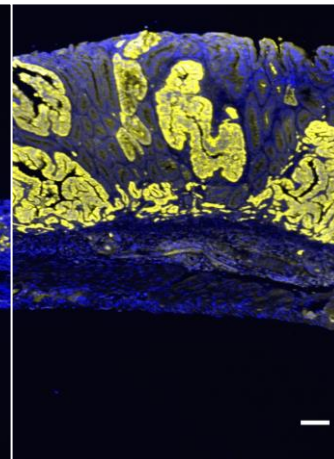
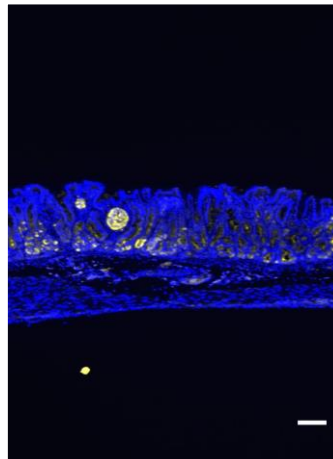
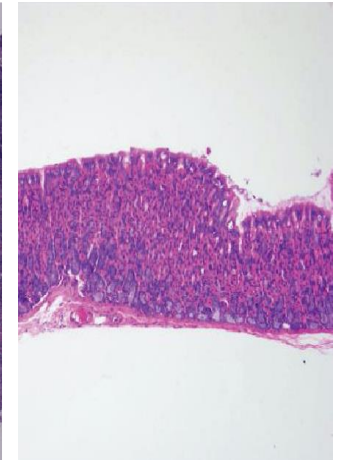
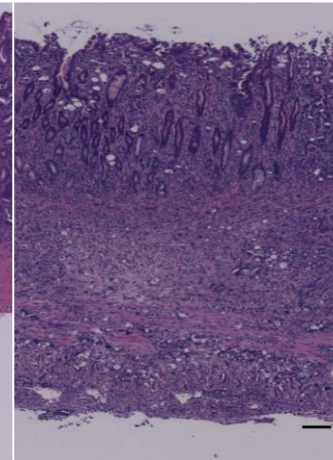
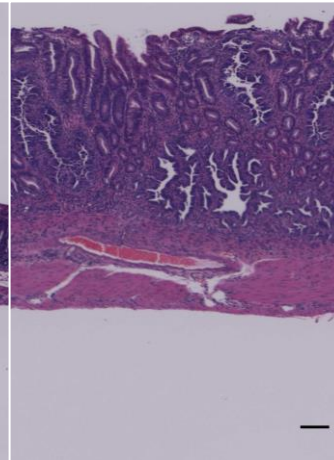
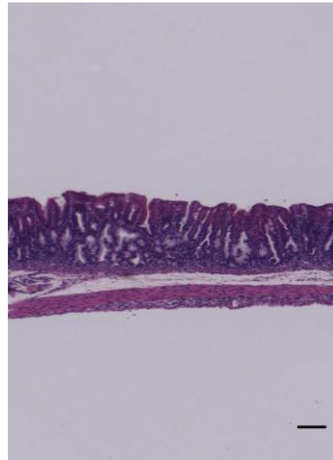
3 weeks old

6 weeks old

9 weeks old

9 weeks old

Stomach



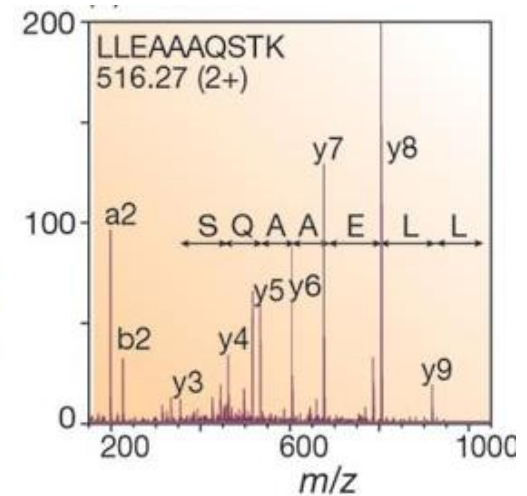
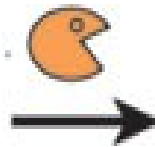
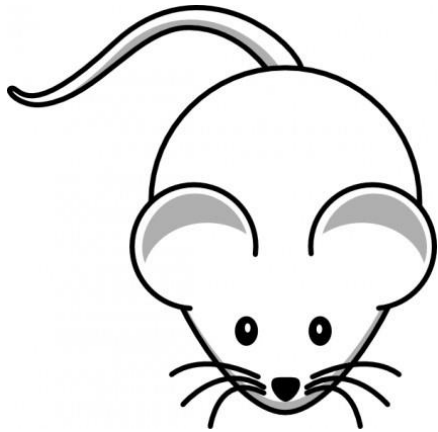
Yellow = Cancer cells
Blue = All cells

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

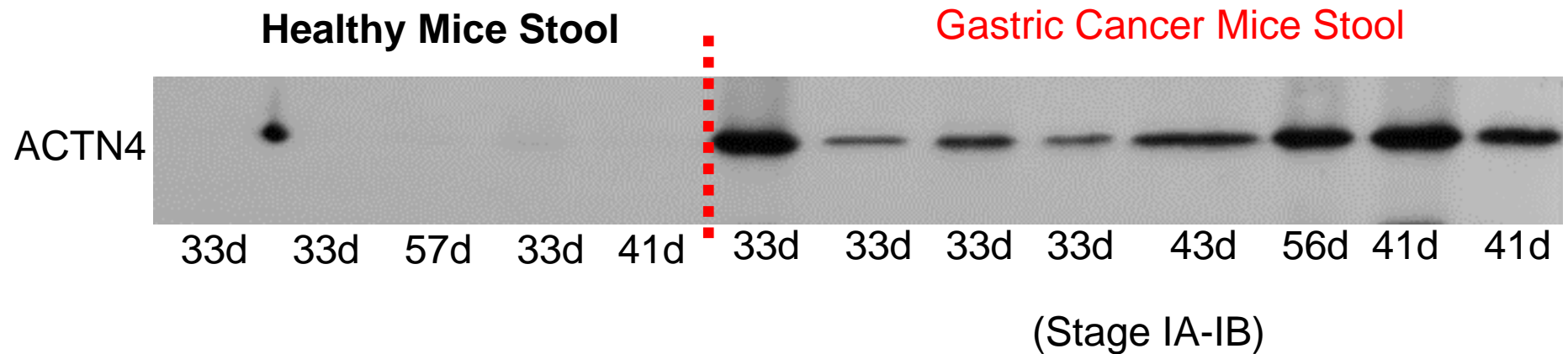
- 4 weeks (early)
- 12 weeks (late)

Prep Samples

- Digest
- Label (barcode)

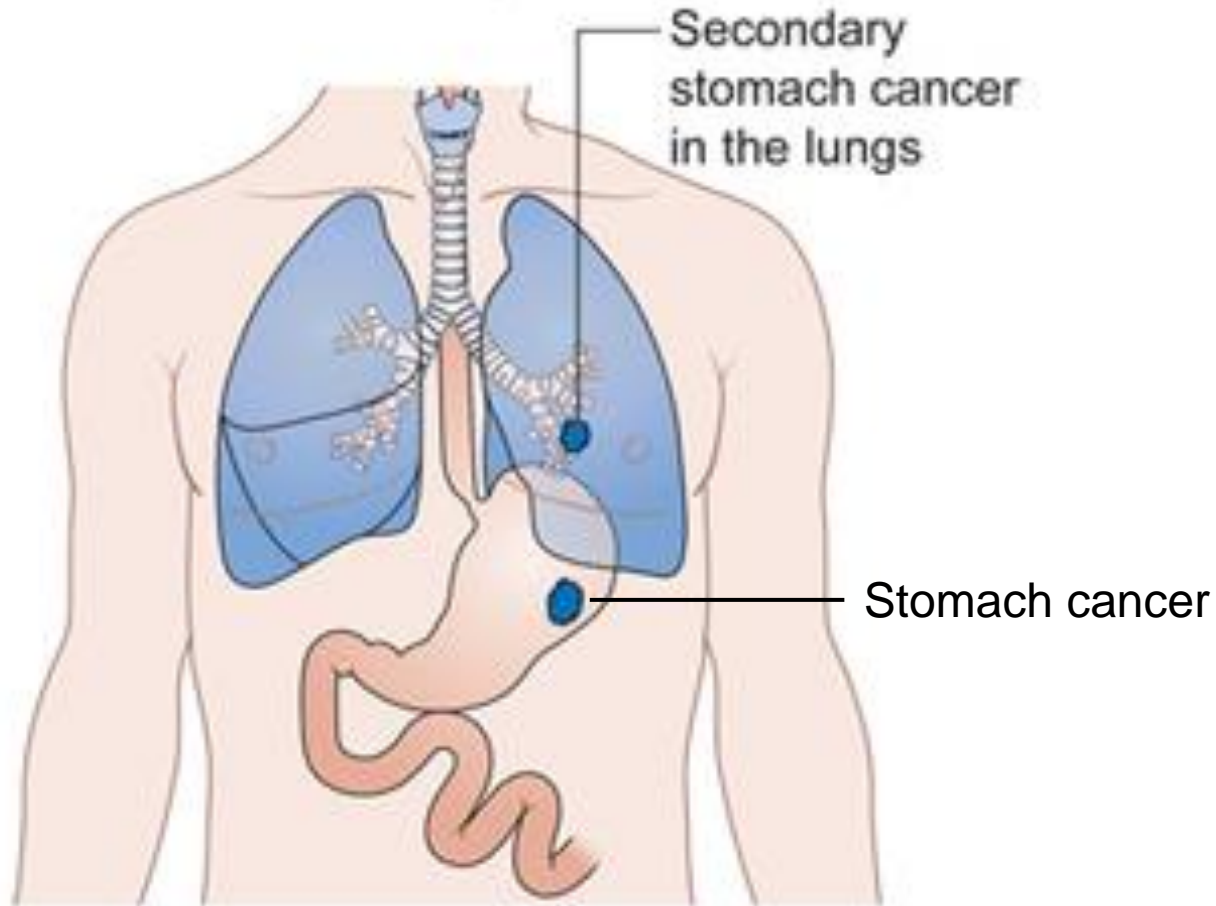
Mass
Spec
Analysis

Possible Biomarkers of Early-Stage Gastric Cancer



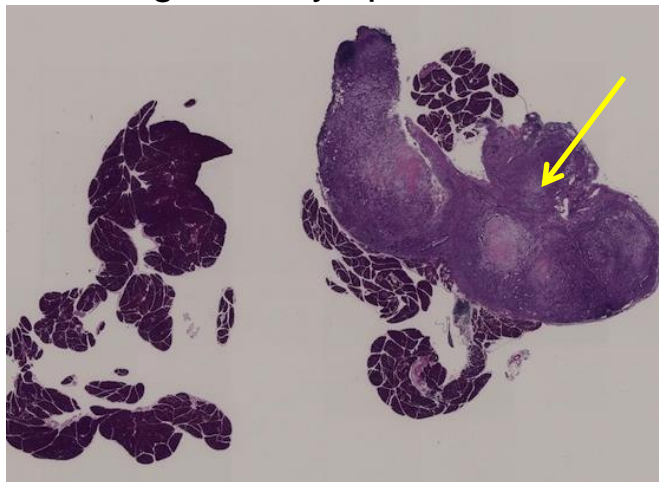
- Can we screen the stool of everyone with risk factors for GC?
- Can we use these biomarkers to detect GC recurrence?

Advanced Gastric Cancer: Metastatic Progression

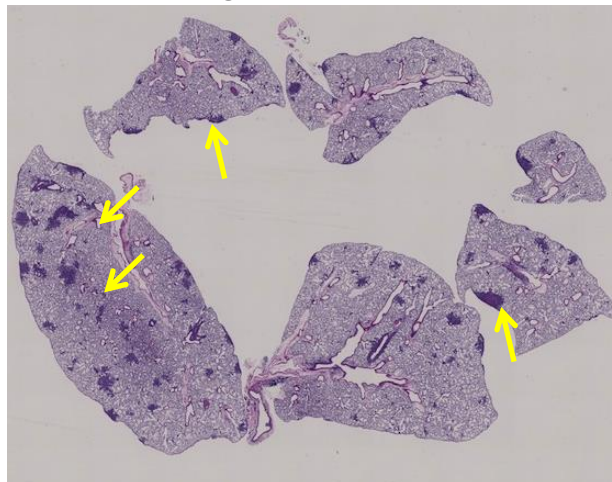


Gastric Cancer Mice Metastasize to Lymph Nodes, Lung and Liver

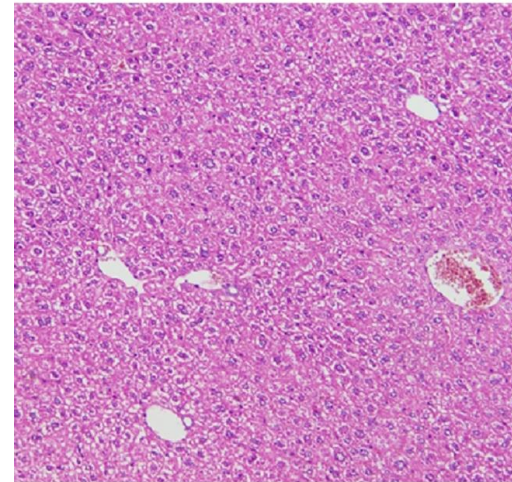
Perigastric Lymph Node Mets



Lungs Metastases



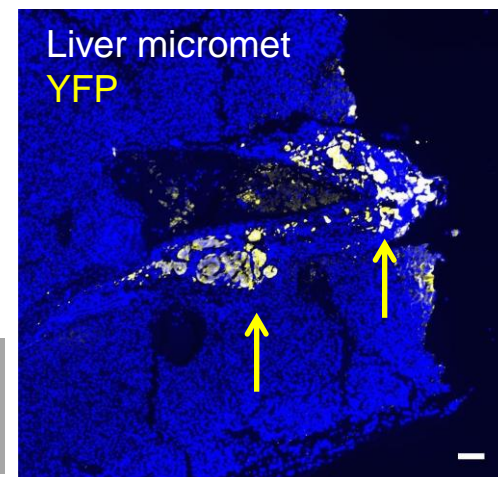
Liver Micrometastases



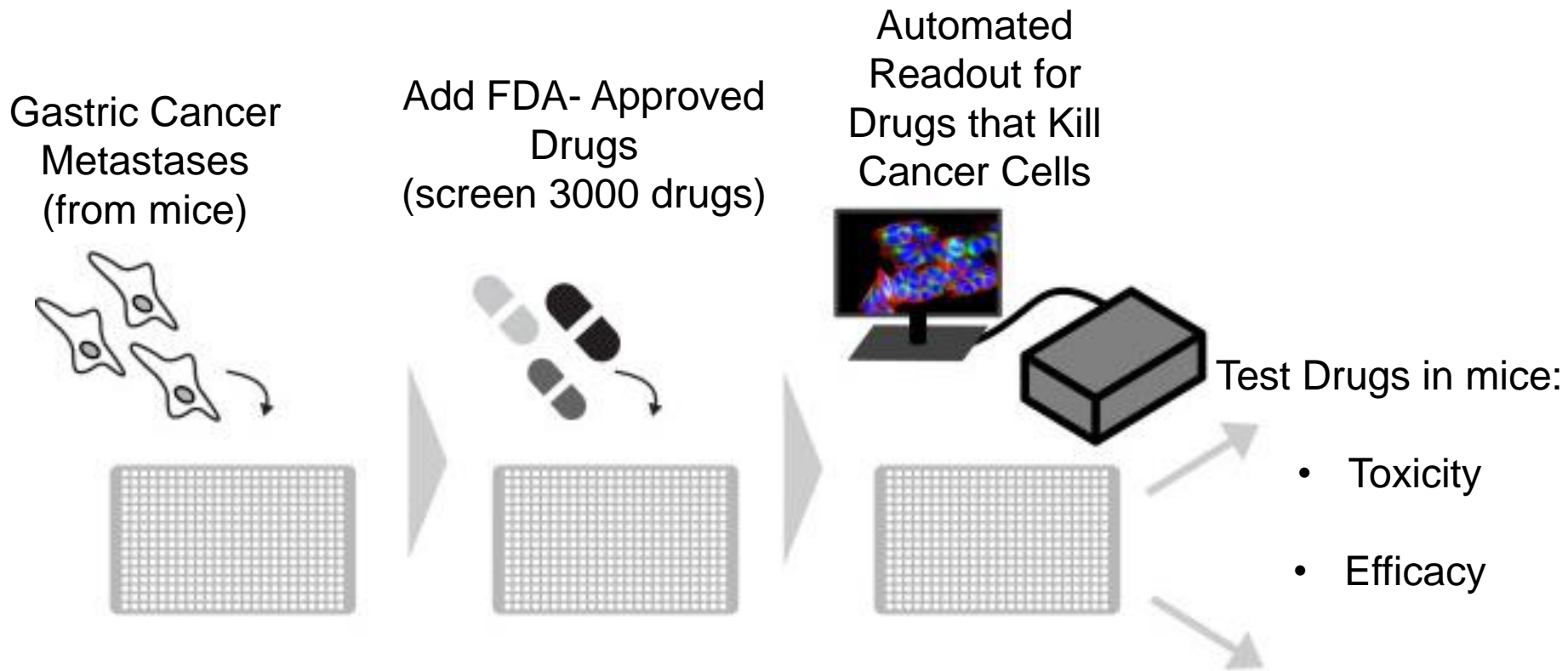
Liver mets
not detected
by imaging



Yellow = Cancer cells
Blue = All cells



Drug Discovery for Metastatic Gastric Cancer

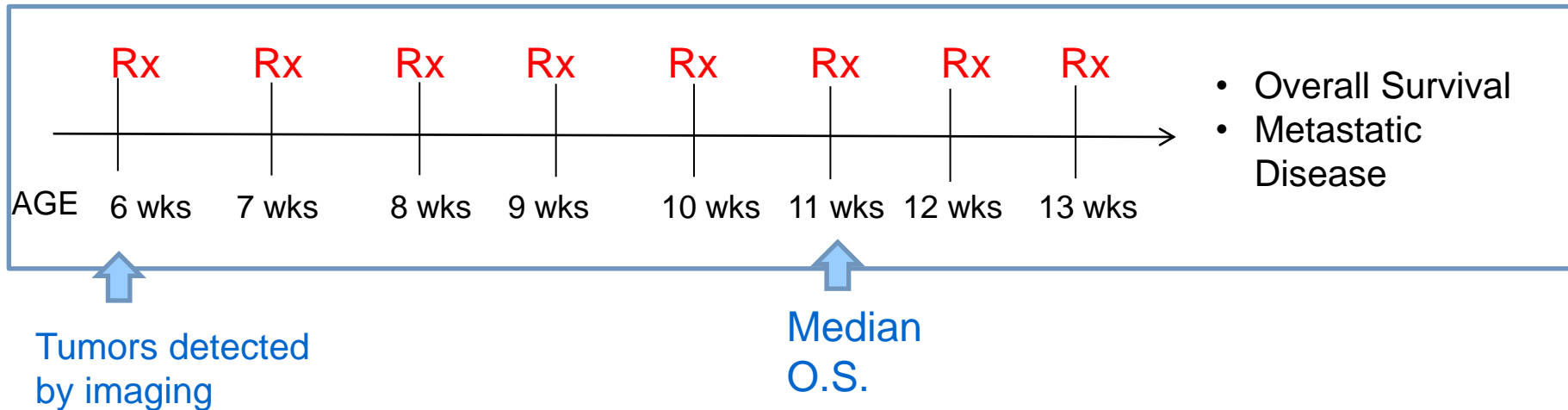


Clinical Trials in Gastric Cancer Mice

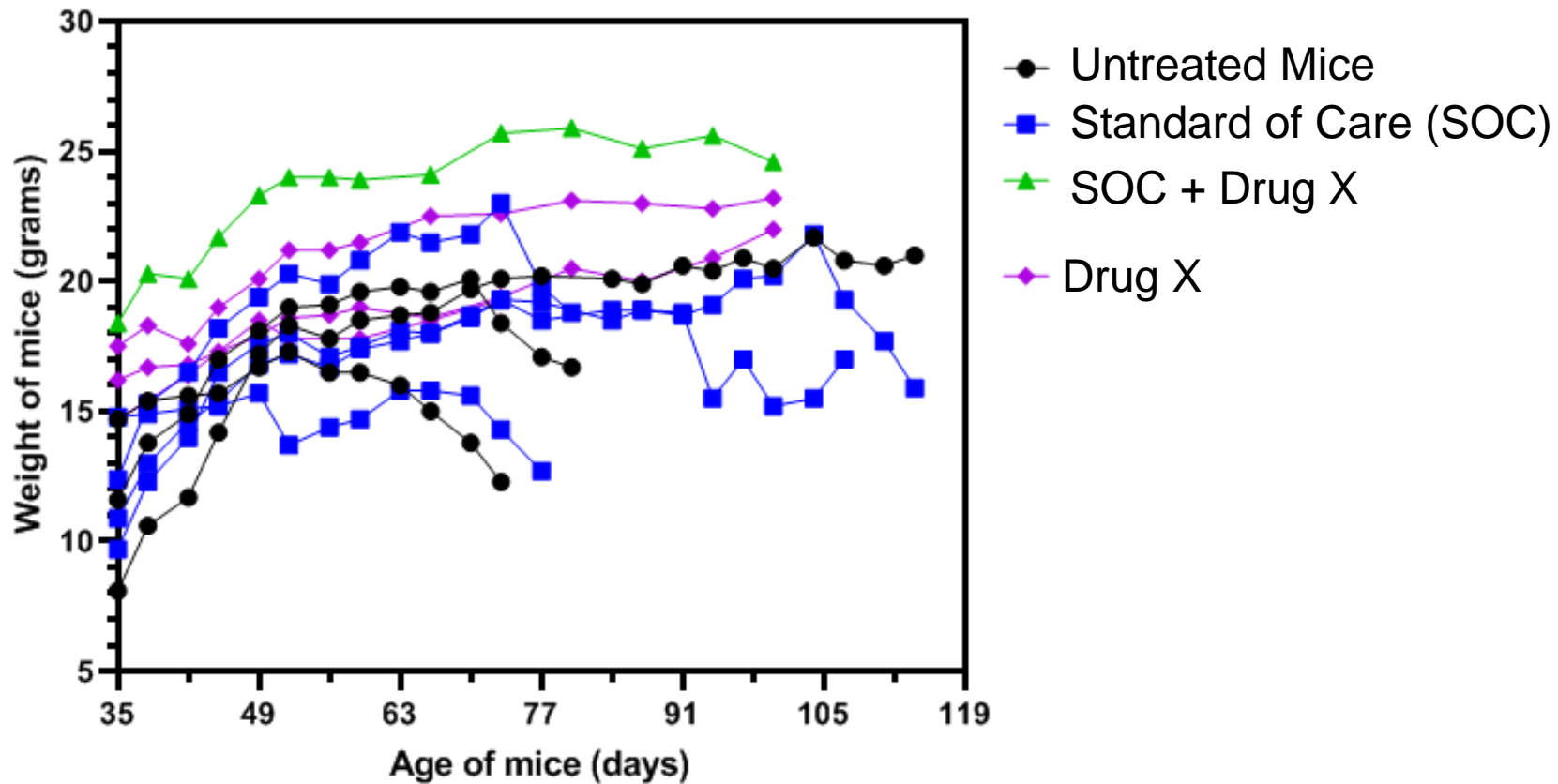
ARM I: 5FU + Oxaliplatin
Standard of Care

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

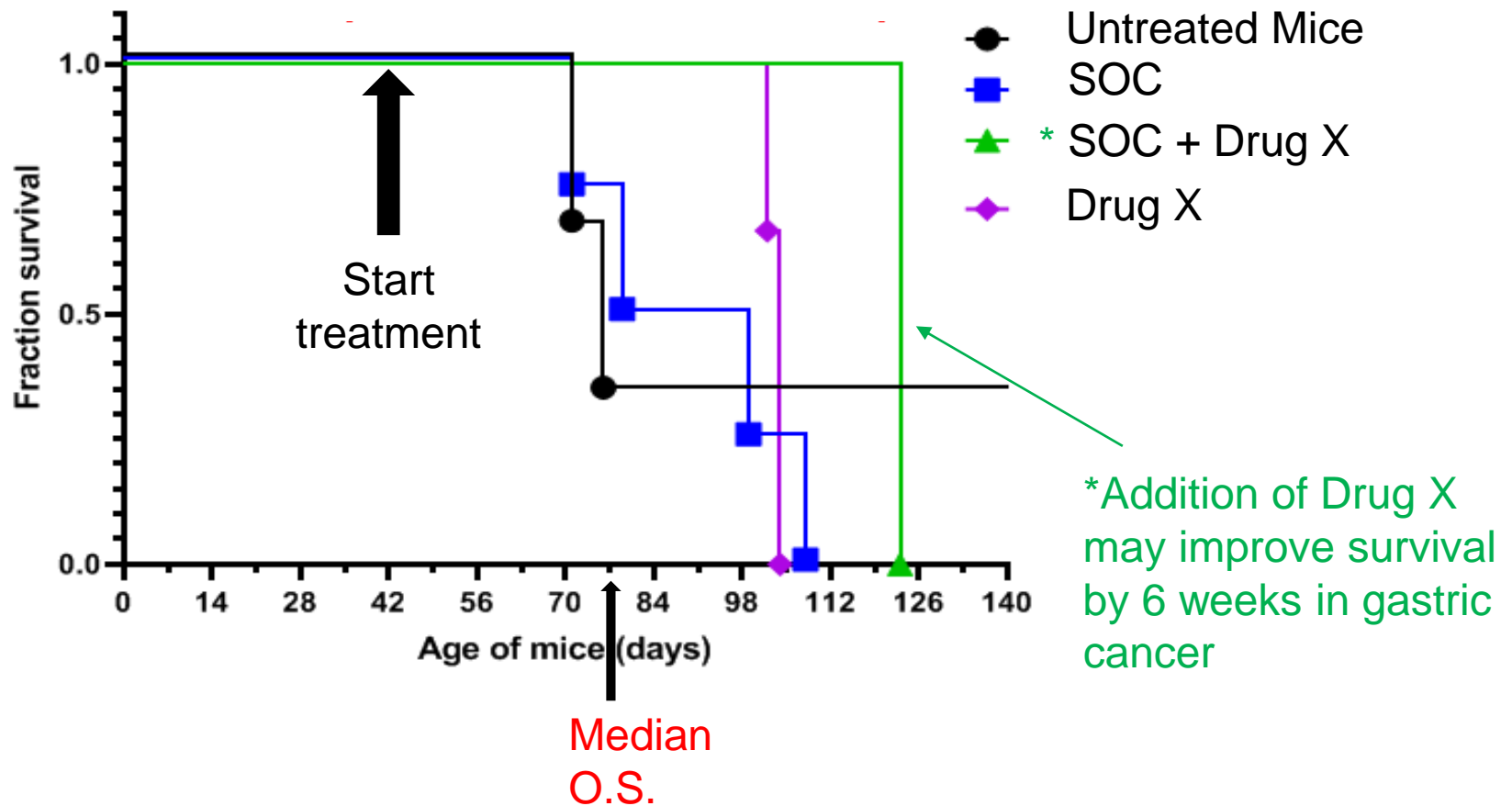
Experimental Schema



New Treatment Regimen is not Toxic to Mice



Can New Drugs Extend Survival for our Gastric Cancer mice with Advanced Disease?



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