Prevention and Early Detection: New Tools and Research Opportunities

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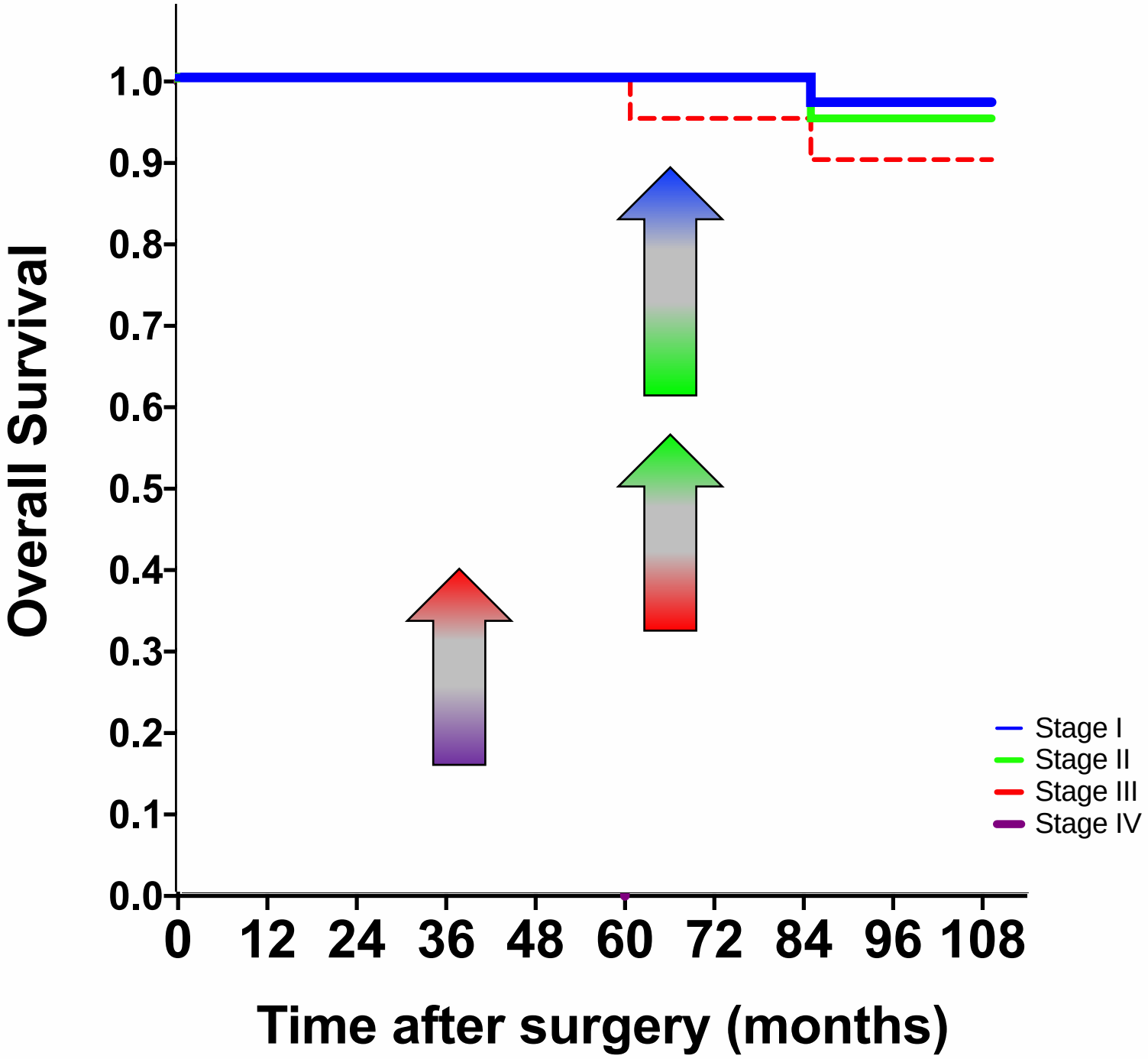
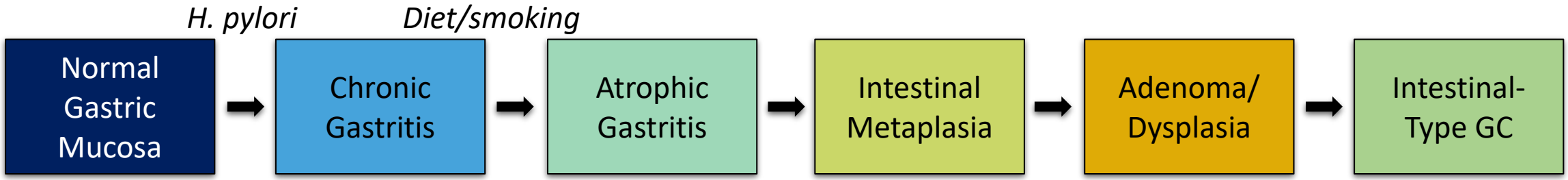
Massachusetts General Hospital

October 15, 2021

Shifting the curve



How can we detect GC early?



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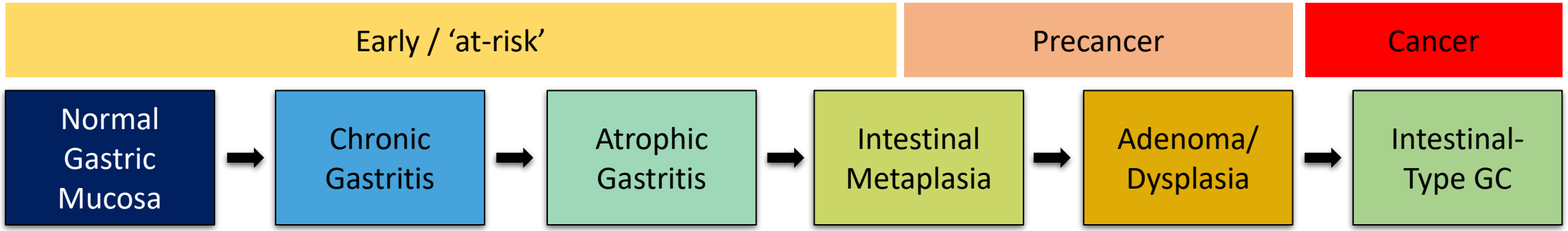

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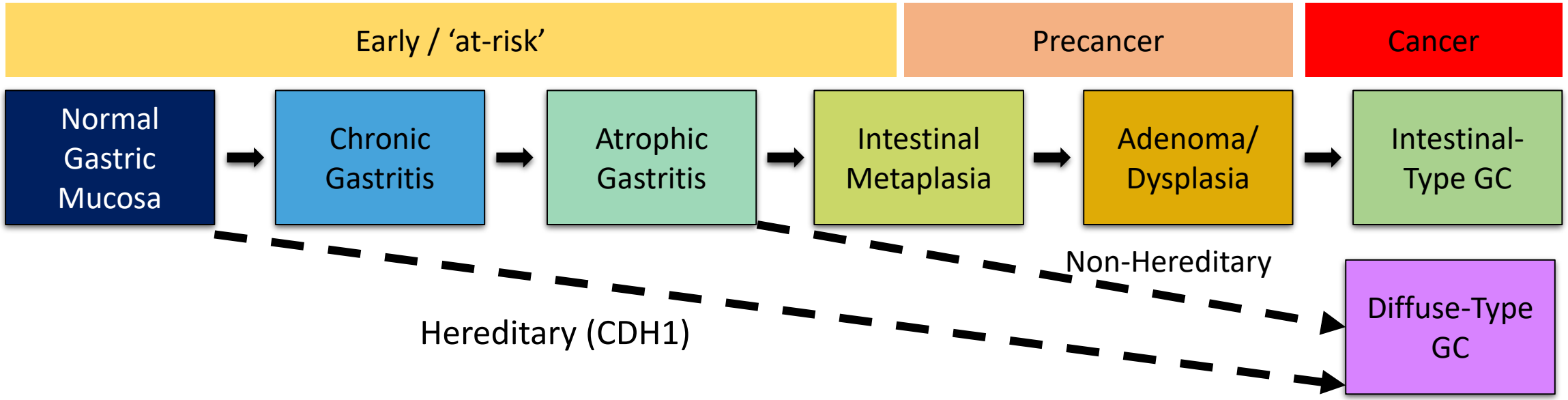
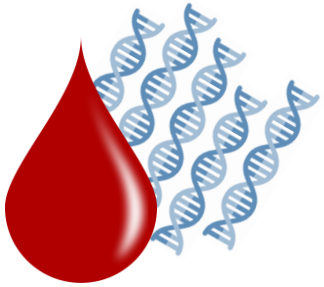


How can we detect GC early?

Early detection and improved interception in clinical practice

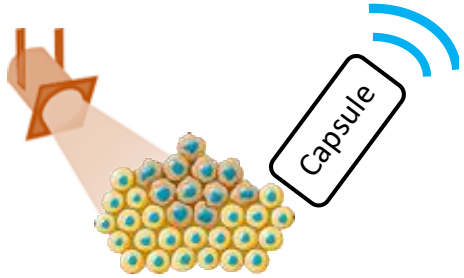


Blood Biomarkers:

Circulating Tumor Cells

Cell-free DNA

Exosomes



Advanced Imaging Approaches:

Near Infrared Molecular Imaging

Minimally-invasive Capsule Imaging

Clinical practice

Early / 'at-risk'

Precancer

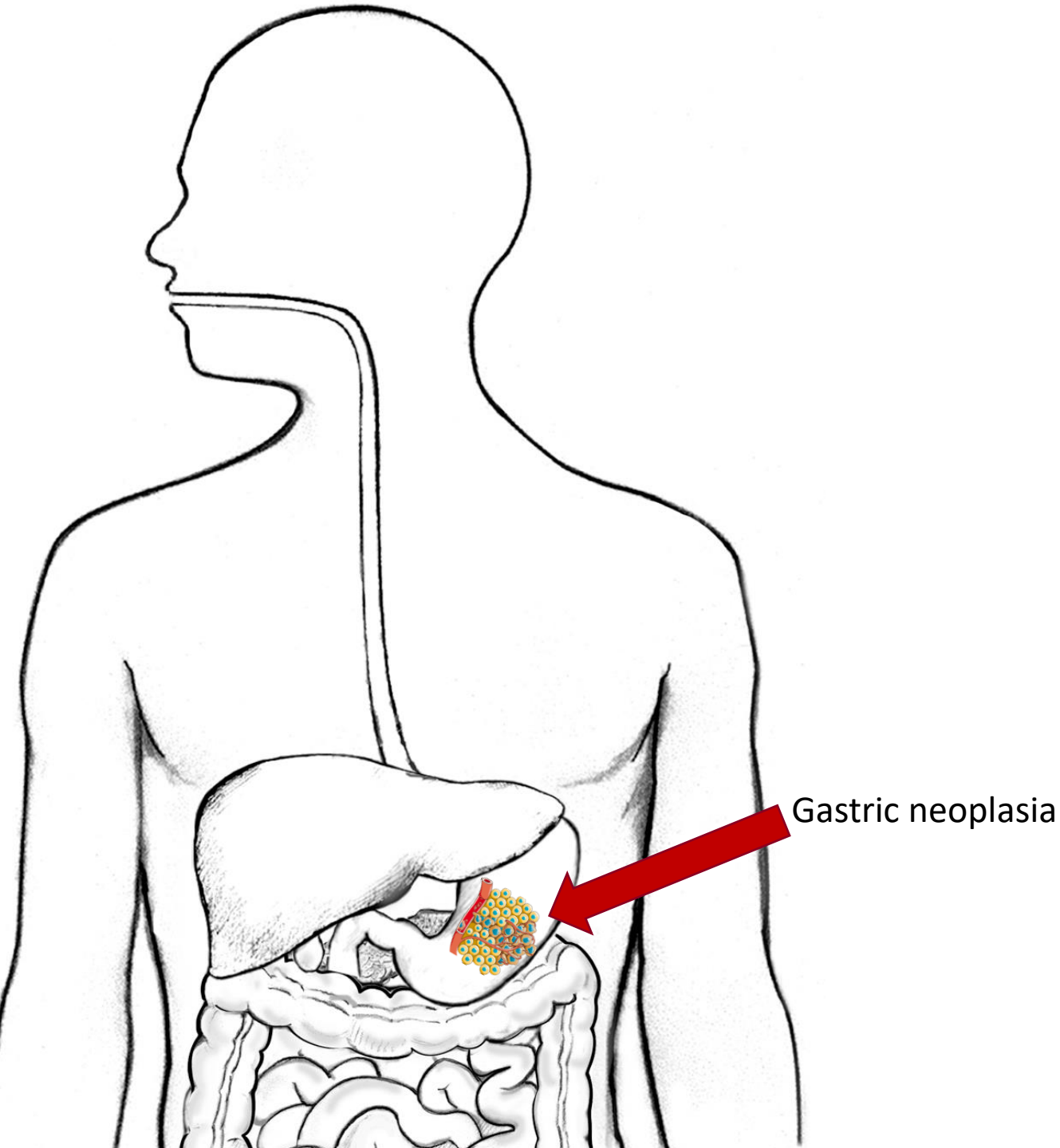
Cancer

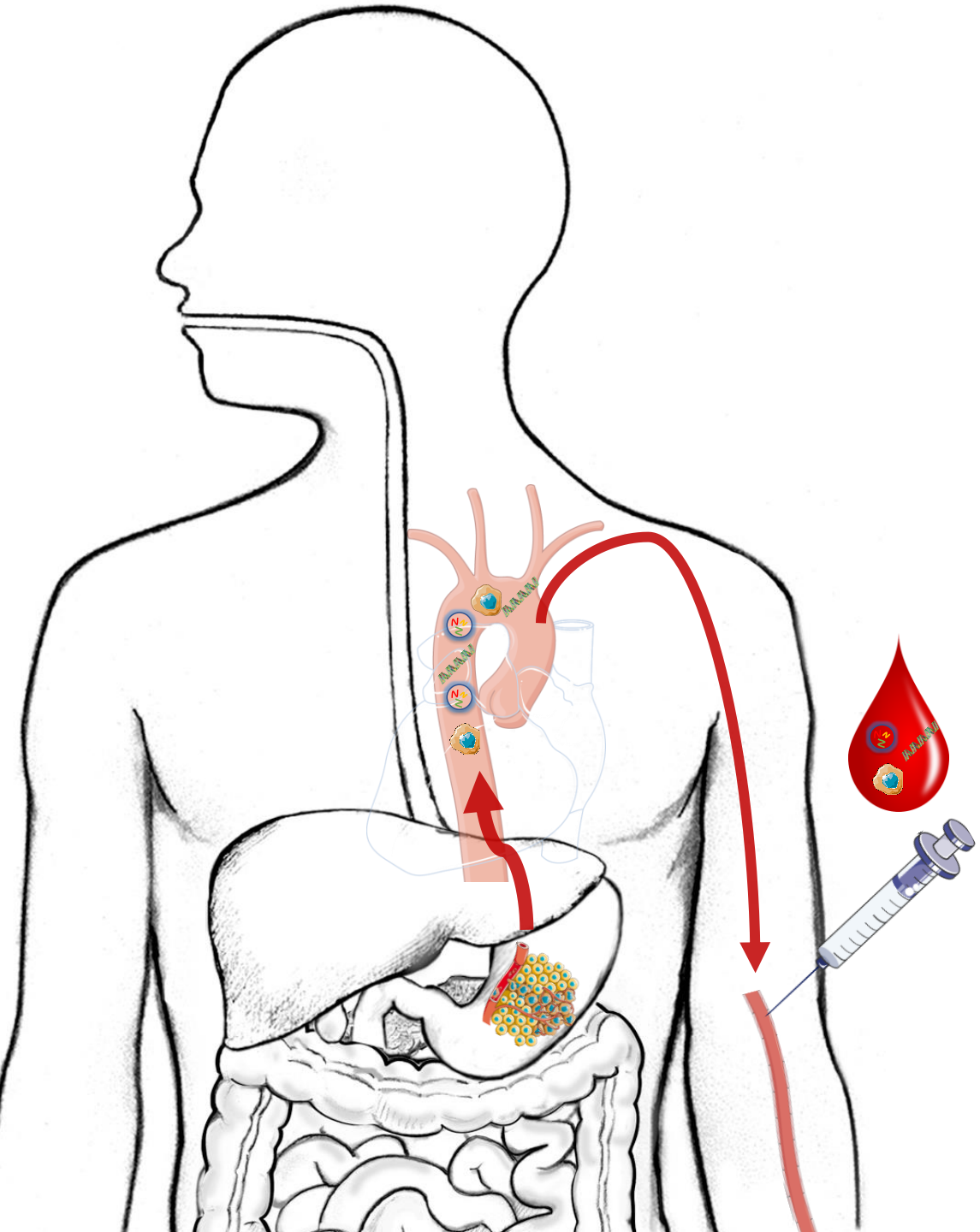
Normal Gastric Mucosa → Chronic Gastritis → Atrophic Gastritis → Intestinal Metaplasia → Adenoma/ Dysplasia → Intestinal-Type GC

Non-Hereditary

Hereditary (CDH1)

Diffuse-Type GC


Gastric neoplasia



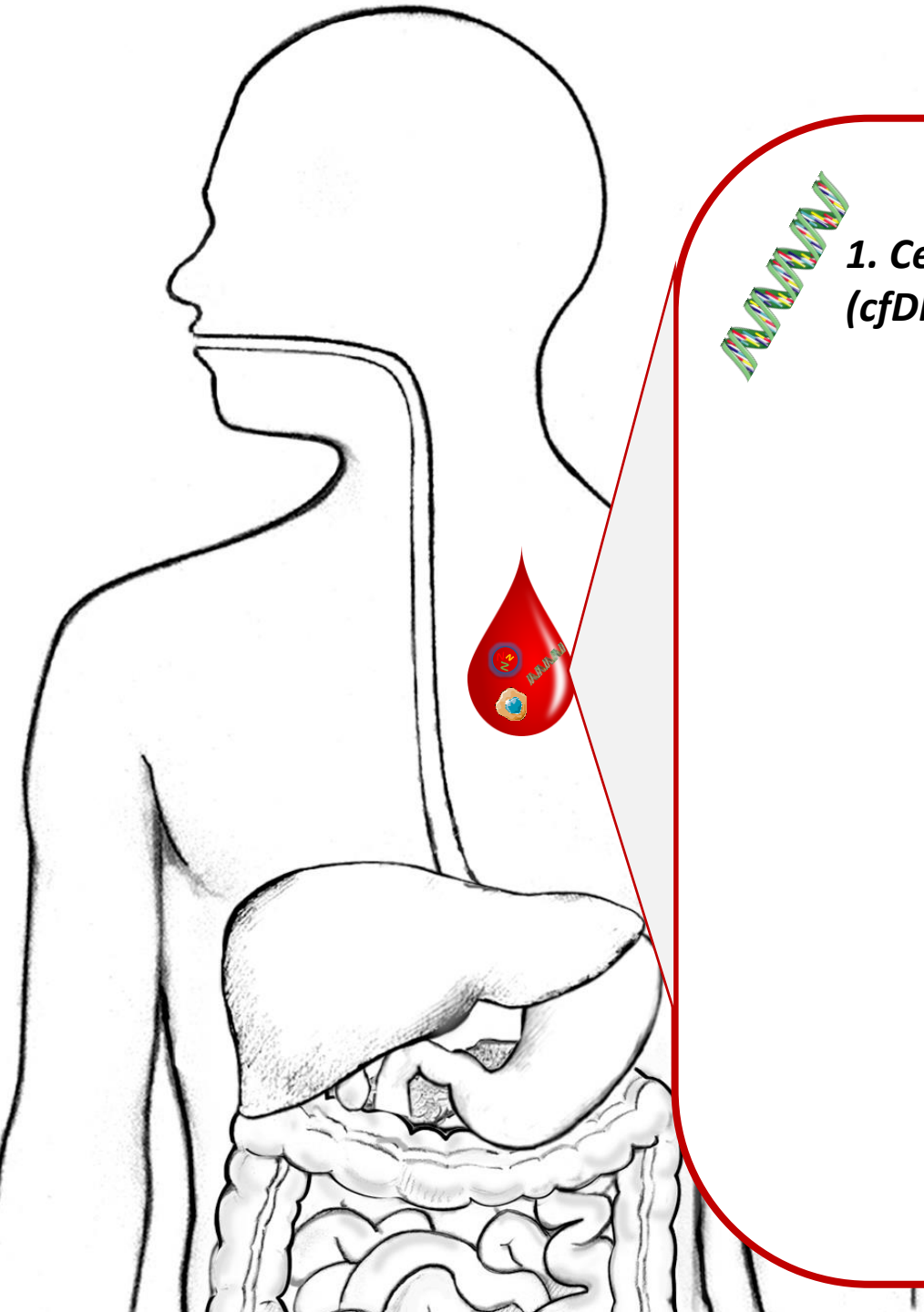
1. *Cell free DNA (cfDNA/ctDNA)*

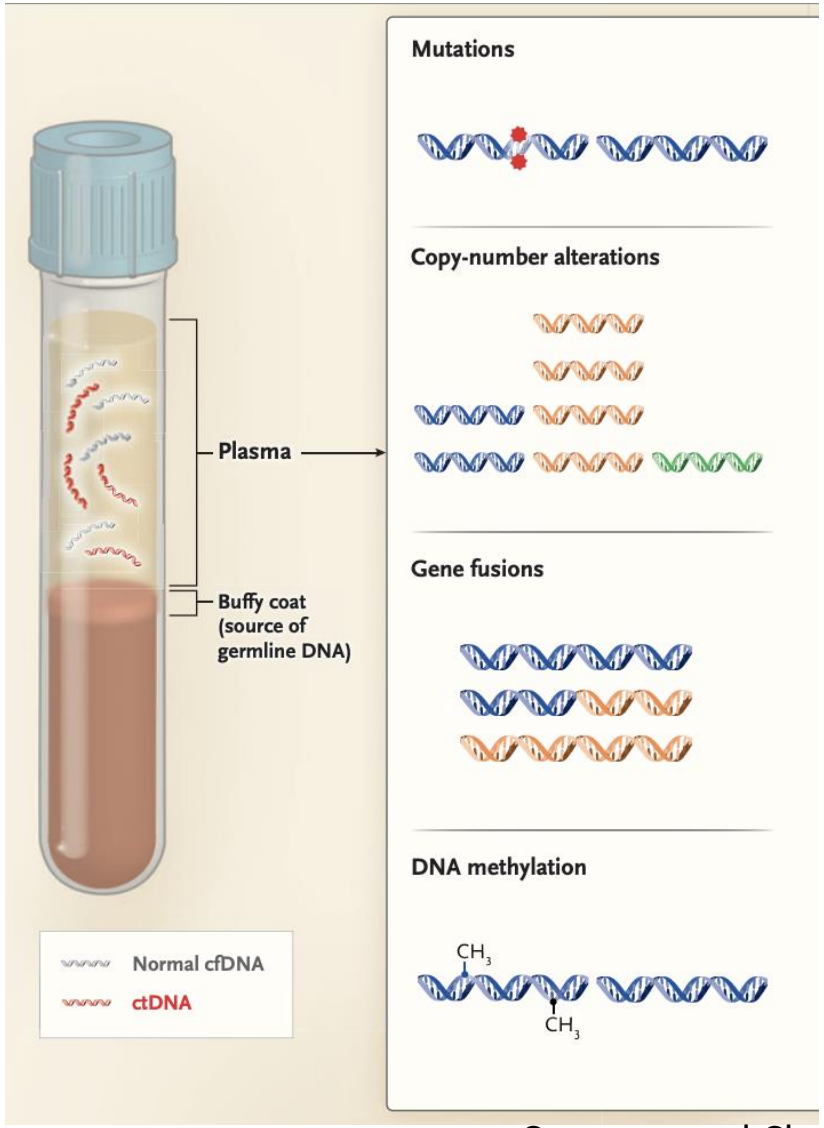
2. *Circulating Tumor/Epithelial Cells (CTC/CEC)*

3. *Exosomes*

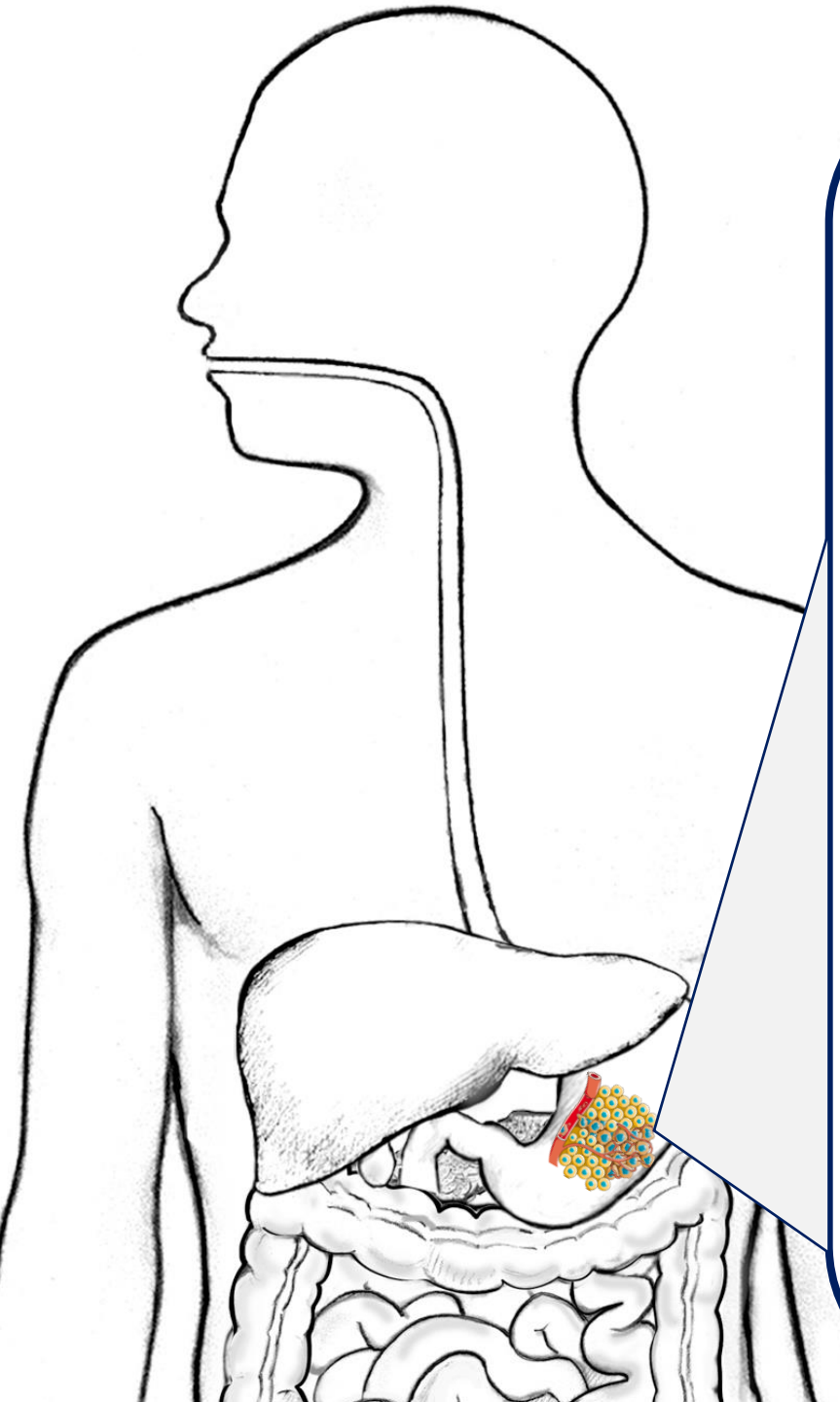
Blood-based biomarkers

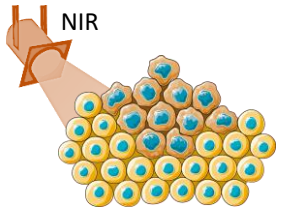
1. Cell free DNA (cfDNA/ctDNA)





Corcoran and Chabner *NEJM* 2018

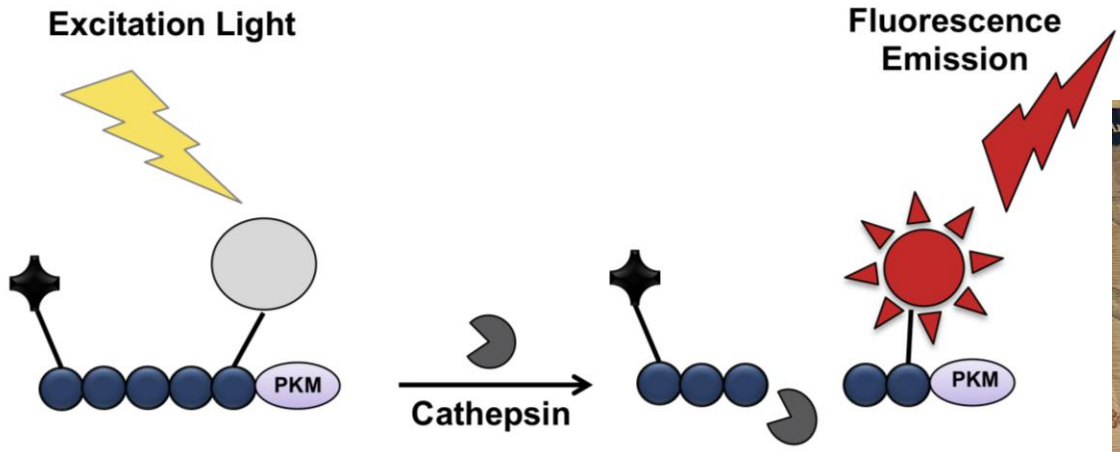


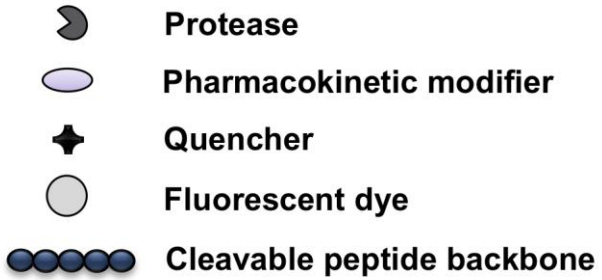


Novel advanced imaging

LUM015 for NIR Imaging in Human GI Cancers

(DF/HCC IRB: 13-415; clinicaltrials.gov *NCT02584244)*

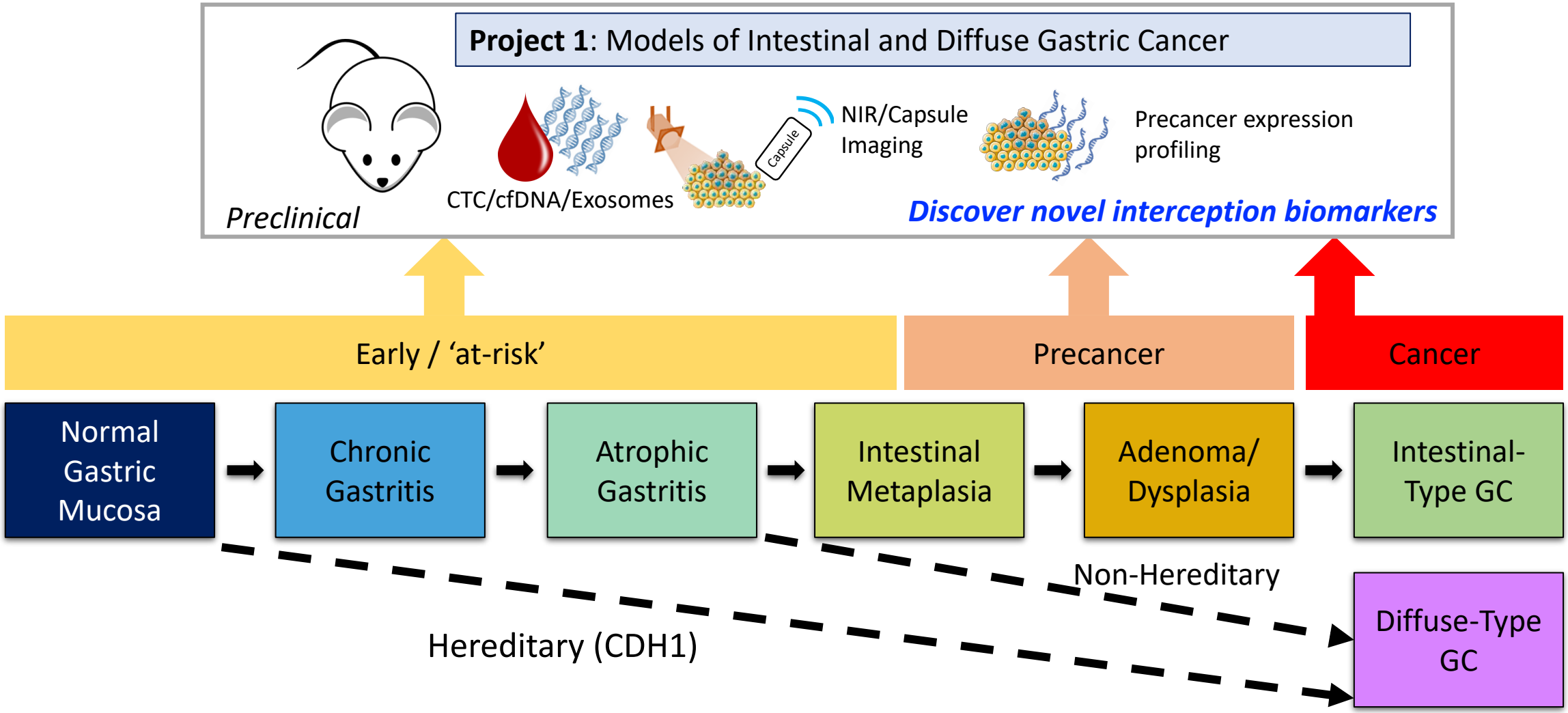




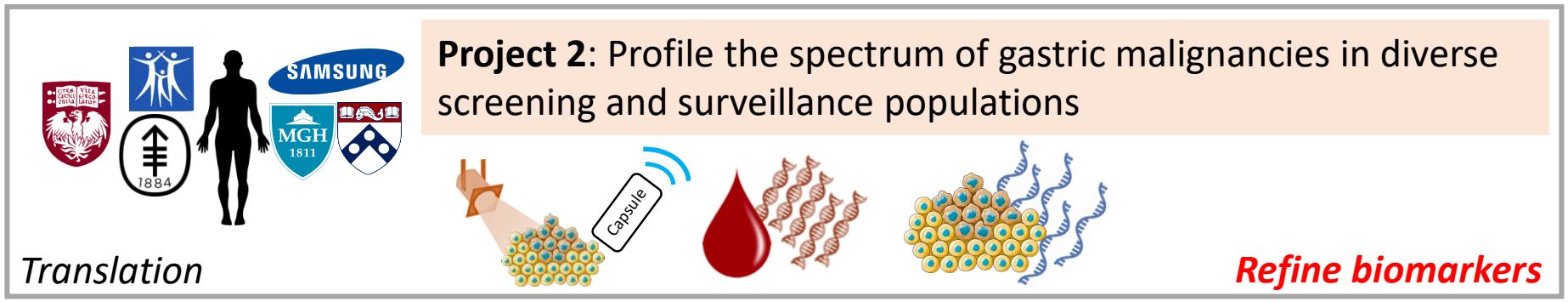
LUMICELL

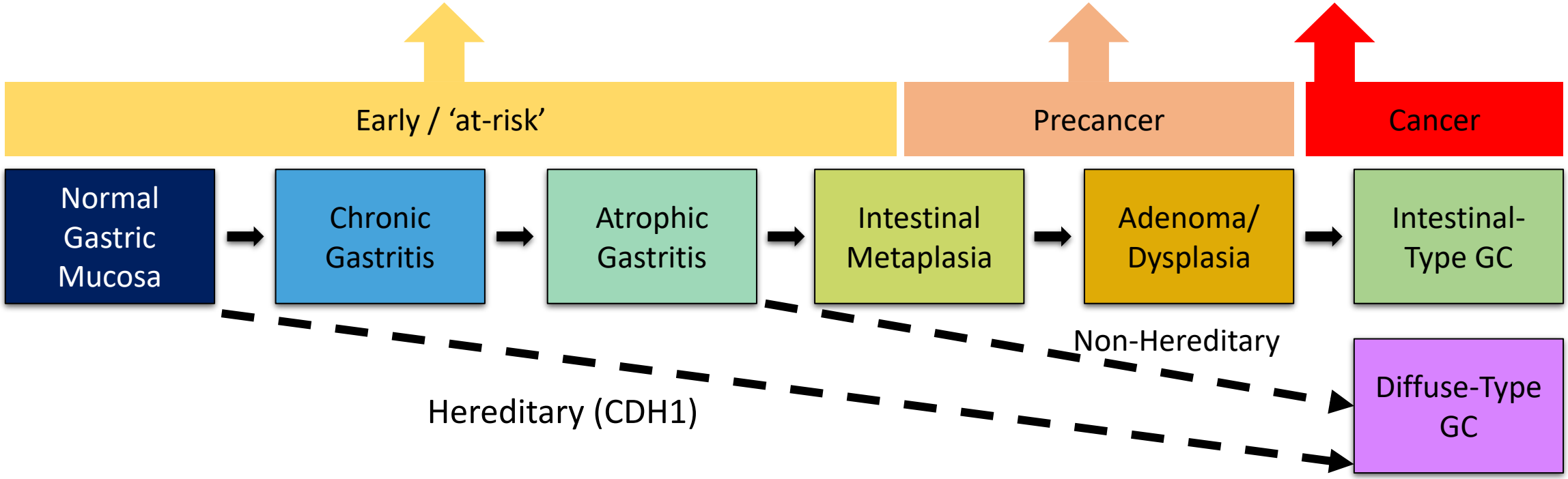
Drew et al. DDW, 2018

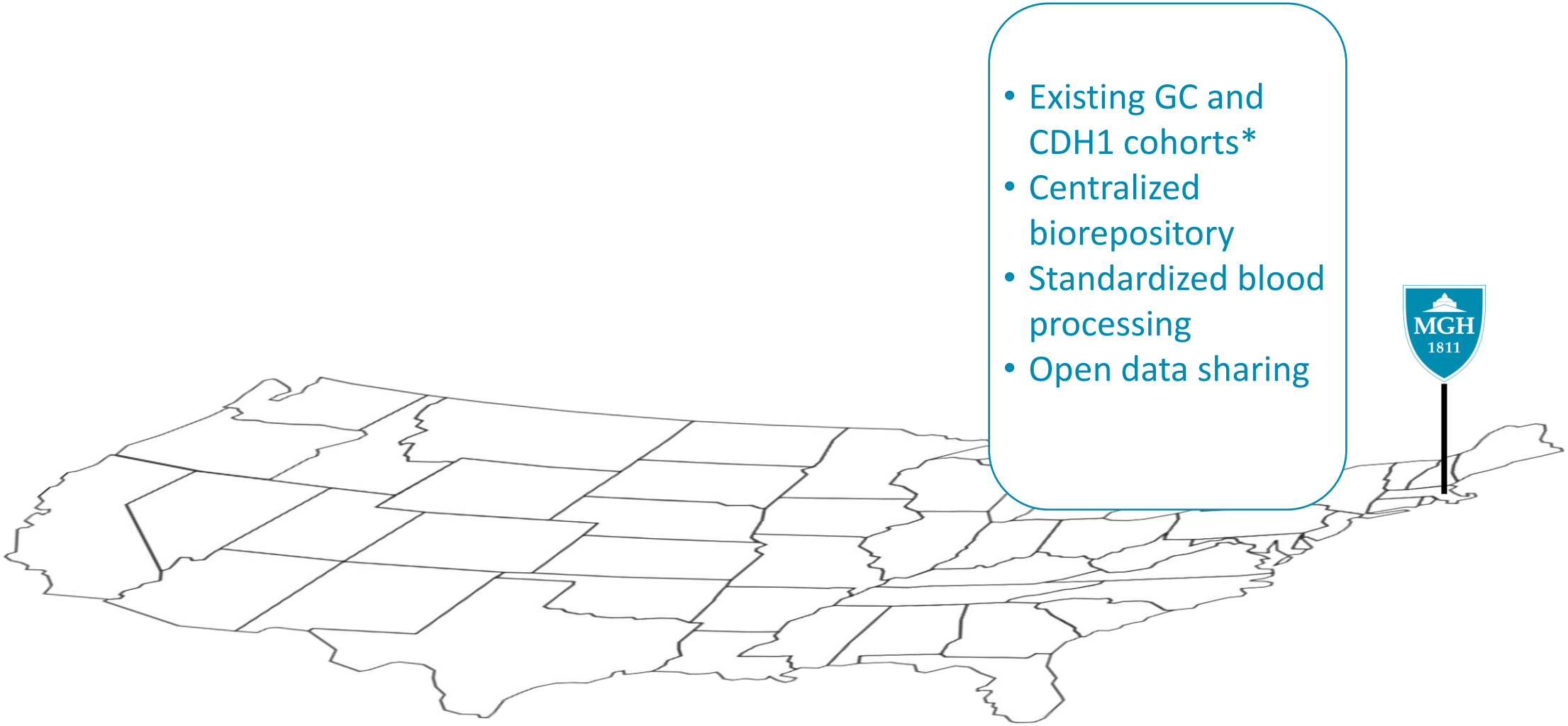
1 Novel preclinical models of diffuse and intestinal GC



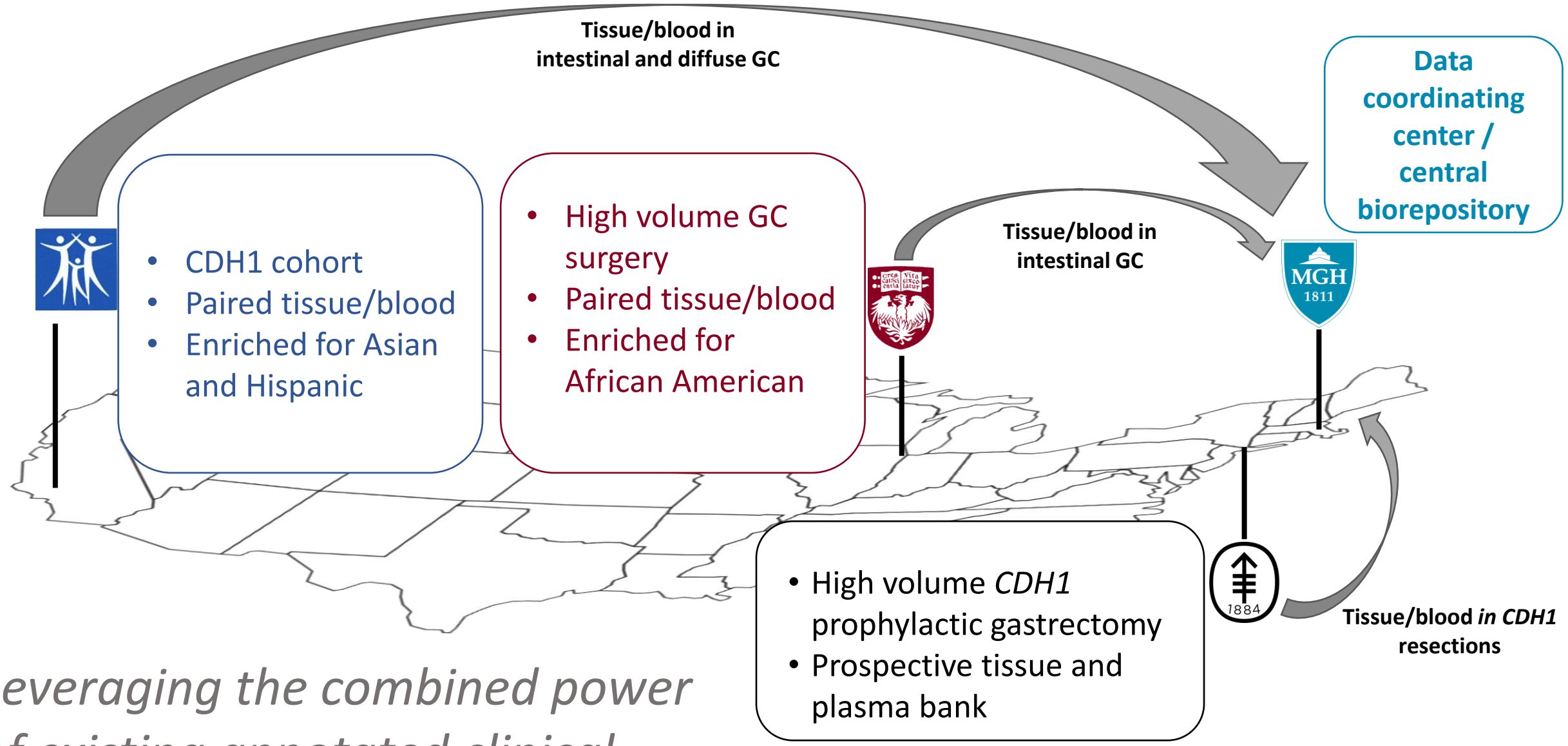
2 Translating preclinical findings to patient populations





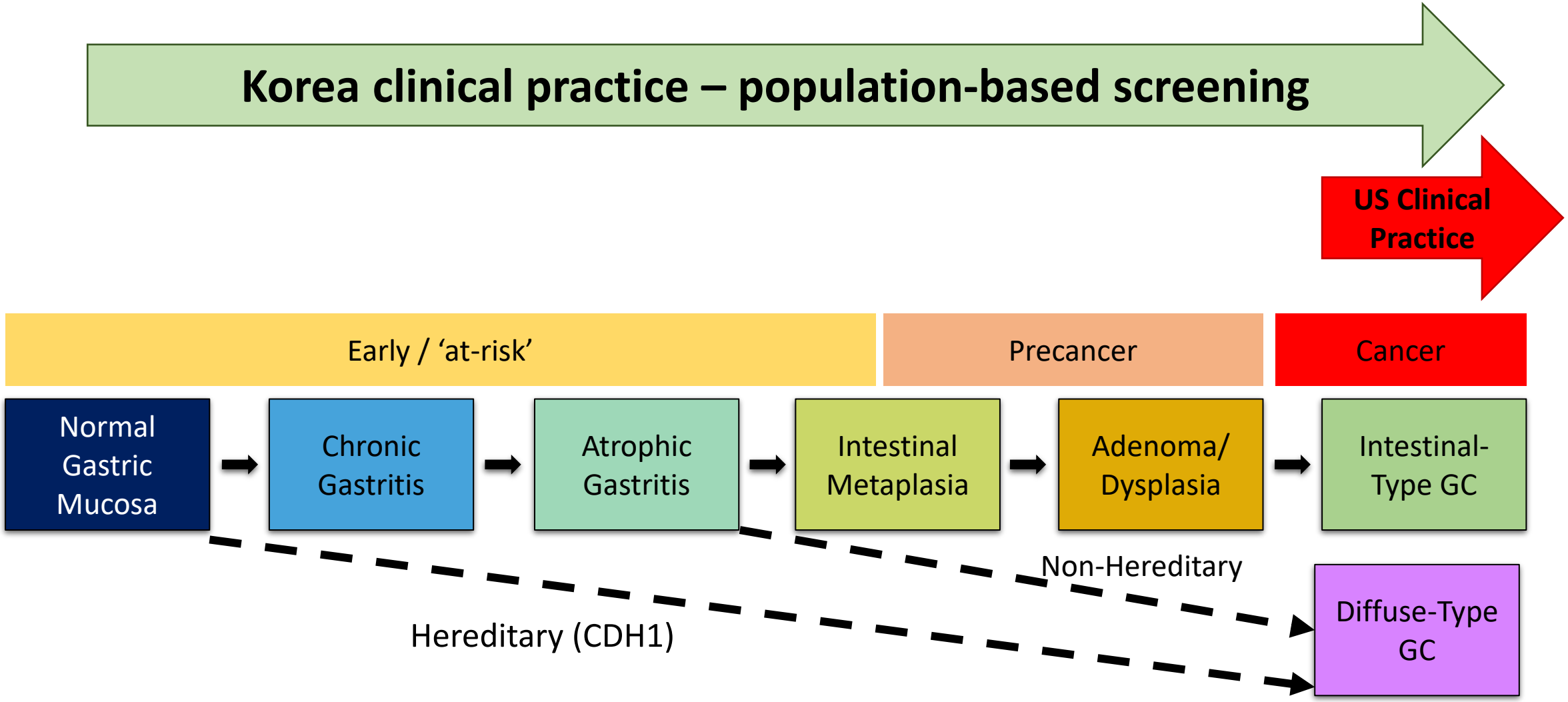


Friedman M et al. *Clin Gastroenterol Hepatol*, 2019



Leveraging the combined power of existing annotated clinical biorepositories across the US

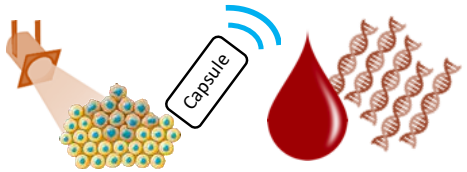
Learning from the world's largest gastric screening program



3 Prospective validation in a GC trial for rapid clinical translation

Project 3: Proof-of-principle for biomarkers/ imaging modalities in GC patients

NAPOX Trial



Validate biomarkers

Early / 'at-risk' | Precancer | Cancer

Normal Gastric Mucosa → Chronic Gastritis → Atrophic Gastritis → Intestinal Metaplasia → Adenoma/ Dysplasia → Intestinal-Type GC

Non-Hereditary

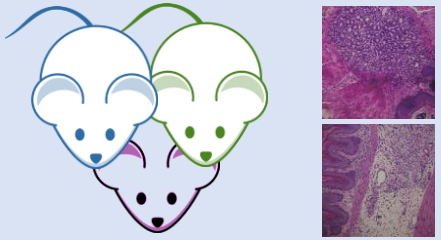
Hereditary (CDH1)

Diffuse-Type GC

PRECISION PREVENTION AND INTERCEPTION

1 PRECLINICAL MODELS

Models of gastric cancer TCGA subtypes mimicking human biology

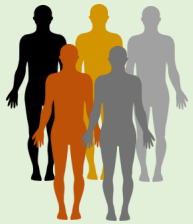


Directly translatable GC Findings

Translation of putative markers to humans

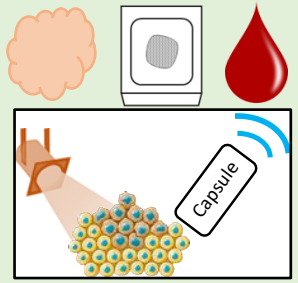
3 VALIDATION IN A GC TRIAL

N=25-50



Gastric cancer patients

Standardized sample collection

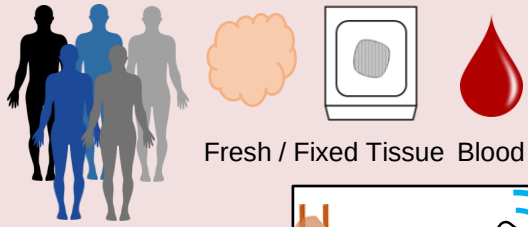


Refine, Validate, and Extend Human Findings in GC Models

Validation of Biomarkers/Imaging

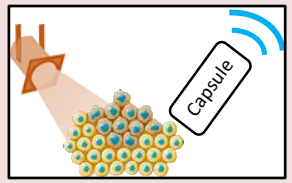
2 SCREENING/SURVEILLANCE COHORTS

N=100s



Fresh / Fixed Tissue Blood

Multi-center early gastric cancer/ precancer patient population



Clinically-actionable Biomarkers for Early Detection/Interception

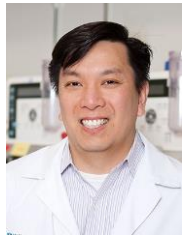
An international, interdisciplinary team of experts in gastric cancer, advanced imaging, & molecular biomarkers

Massachusetts General Hospital
Boston, MA

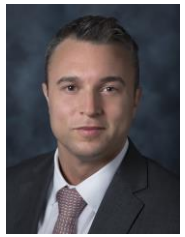
LEADER

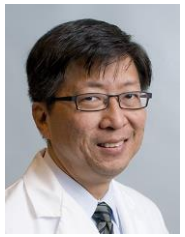
Andrew Chan

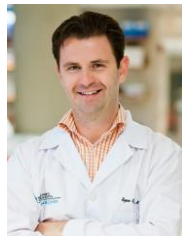
Gary Tearney


David Ting

Theodore Hong


Samuel Klempner


Daniel Chung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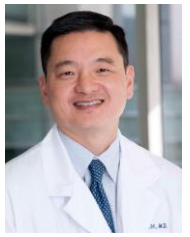
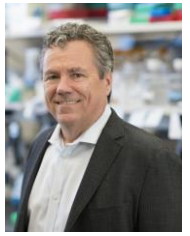

Sam Yoon


Scott Lowe

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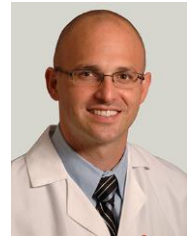
Jeeyun Lee

Hyuk Lee

University of Chicago
Chicago, IL


Principal
Daniel Catenacci

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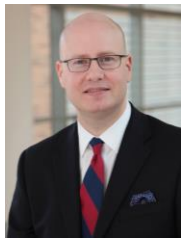
Jeremy Davis