

*Cancers of the
Digestive System*

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Research Goal 1

Develop population-based strategies for screening and prevention of digestive tract cancers.

Research Goal 1

Objectives

- Understand the major risks factors for digestive tract cancers.
- Develop risk modeling and stratification to identify high risk populations for digestive tract cancers.

Research Goal 1

Objectives (continued)

- Conduct large-scale trials of screening modalities to determine efficacy and cost effectiveness, and integrate effective strategies into practice.



Research Goal 2

Ascertain the importance, detection, and natural history of pre-malignant conditions progressing to digestive tract cancer.

Research Goal 2

Objectives

- Characterize cancer syndromes for genetic defects and clinical behavior that predispose to digestive tract cancers.
- Develop and study preclinical *in vitro* and *in vivo* models of digestive tract cancers to recapitulate the natural history seen in humans.



Research Goal 2

Objectives (continued)

- Determine the natural history of premalignant lesions in the development of digestive tract cancer.
- Define the role of inflammation in digestive tract cancer development.
- Determine the role of the microbiome in the initiation or propagation of digestive tract cancers.

Research Goal 3

Evaluate disparities in digestive tract cancer etiology, risk, treatment management, and outcomes.

Research Goal 3

Objectives

- Conduct clinical studies on access, utilization, treatment, and outcomes of patients with digestive tract cancers who belong to diverse ethnic, racial, or high risk groups.
- Understand the influence of genetic factors on cancer risk, prognosis and response to therapy.

Research Goal 4

Develop biomarkers to predict presence, target therapy and evaluate therapeutic response in digestive tract cancers.

Research Goal 4

Objectives

- Develop improved population-based assessment of risk for digestive tract cancers that can be detected in blood.
- Utilize preclinical *in vitro* and *in vivo* models of digestive tract cancers to ascertain biomarkers that predict tumor behavior and response to therapy.

Research Goal 5

Evaluate nutraceutical, probiotic, chemopreventive, and targeted therapies in digestive tract cancers.

Research Goal 5

Objectives

- Utilize preclinical *in vitro* and *in vivo* models of digestive tract cancers to ascertain potential effectiveness and mechanisms of preventive agents and small molecules.
- Conduct large scale randomized clinical trials utilizing agents or targeted therapies to determine effectiveness in prevention or treatment of digestive tract cancers.

Research Goal 6

Understand the molecular and cellular mechanisms common to all digestive cancers.

Research Goal 6

Objectives

- Define genetic and epigenetic mechanisms that characterize digestive tract cancers.
- Characterize digestive tract cancer stem cells, and the local environment niche that supports and propagates the cancer.



Research Goal 6

Objectives (continued)

- Ascertain molecular signatures and presence of commensal flora (microbiome) for evaluation of linkage with population-based risk for digestive tract cancers. Determine the role of infection or host integration of microbes with risk for digestive tract cancers.

Research Goal 7

Identify genetic risk factors for esophageal cancer and use that information to develop new tools for detection, diagnosis, and treatment.

Research Goal 7

Objectives

- Perform comprehensive genetic analyses of esophageal squamous cell carcinoma and adenocarcinoma.
- Develop non- or minimally invasive imaging and/or molecular techniques for pre-malignant changes in esophageal cancer.



Research Goal 7

Objectives (continued)

- Determine biomarkers for predicting disease and evaluating therapeutic response in esophageal cancers.

Research Goal 8

Understand the molecular profiles of various types of gastric cancer to improve risk stratification, prevention and treatment.

Research Goal 8

Objectives

- Ascertain a complete molecular profiling of the histological types of gastric cancers from different locations within the stomach.
- Develop a molecular roadmap for gastric cancer development that mirrors the known phenotypes.



Research Goal 8

Objectives (continued)

- Develop better tools to conduct transgenic animal studies to further our understanding of gastric mucosal biology.
- Refine risk stratification for screening and surveillance of gastric cancers.

Research Goal 9

Define the genetics, familial inheritance patterns, detection and treatment of pancreatic cancer.

Research Goal 9

Objectives

- Accelerate research into the genetics, familial inheritance patterns, and molecularly determined individual therapeutic options.
- Improve imaging technologies to detect early malignant pancreatic cancers.
- Facilitate collection of biospecimens linked to clinical data.

Research Goal 10

Identify genetic factors for risk stratification, and expand primary prevention and screening strategies for colorectal cancer.

Research Goal 10

Objectives

- Evaluate chemopreventive and other primary prevention strategies.
- Improve means to identify patients, colons, or pre-malignant lesions that give rise to the greatest risk for colorectal cancer.



Research Goal 10

Objectives (continued)

- Determine strategies to expand the use of colorectal cancer screening in clinical practice.
- Determine the natural history of small colorectal adenomatous polyps.

Research Goal 11

Understand the etiology, natural history, prevention and management of rare GI cancers.

Research Goal 11

Objectives

- Improve imaging technologies and therapeutic options to detect and remove small intestinal cancers.



Research Goal 11

Objectives (continued)

- Determine predictive factors or biomarkers that more accurately predict patient outcome, such as with MALT lymphoma and *H. pylori* eradication, anal carcinoma and immunosuppression or human papilloma virus infection, or the development and behavior of intra-abdominal desmoids in familial adenomatous polyposis.

Major Challenges/Steps To Achieve Goals

- Collaborative research and centralized resources
- Technology development
- Animal models

Major Challenges/Steps To Achieve Goals

Collaborative Research and Centralized Resources

- Mechanisms for collaborative research
- Multi-institutional repositories of samples and data from well-characterized patients for research on disparities among ethnic, racial, or high-risk groups
- Facilities to complement the Cancer Genomic Anatomy Project (CGAP)
- Centers to collect and maintain clinical information and epidemiological data linked to a repository of biological specimens and other data
- High-throughput genomic and proteomic facilities to profile digestive tract cancers and their subtypes
- High-throughput drug discovery programs based on targeted approaches to cancer biology as an opportunity for collaboration with industry

Major Challenges/Steps To Achieve Goals

Technology Development

- Advanced non- or minimally invasive imaging or molecular techniques for detection of premalignant changes in digestive tract cancers

Animal Models

- New transgenic animal models that replicate sporadic human cancer