Infections of the GI Tract

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Research Goal 1

Develop tools to identify etiologies of intestinal infections.

Alternate Research Goal 1

Elucidate the etiology, epidemiology, and pathogenesis of intestinal infections and improve diagnostic tests.

Research Goal 1 Objectives

- Understand the pathogenic mechanisms for viruses, parasites and bacteria causing intestinal infection.

- Understand how microorganisms interact with their environment to reach critical numbers capable of human infection and to express pathogenic factors in the intestine.

- Conduct epidemiologic investigations using modern tools to define infectious etiologies, establish the incidence of known and novel etiologic agents of diarrheal disease and the health impact of acute and persistent enteric infection in distinct subgroups of hosts including normal, and immune compromised populations, e.g., solid organ transplant, bone marrow transplant, oncology patients.

Research Goal 1
Objectives (continued)

- Develop new point-of-care diagnostics to easily and rapidly detect known microbial enteric pathogens.
- Discern correlates of protective immunity for enteric infections.
- Develop animal models to manipulate the microbial community in the gut.
- Establish easily accessible systems for all medical professionals to assist in the interruption of food and waterborne transmission of enteric infections. (?)

Research Goal 2

Improve the prevention and treatment of intestinal infections.

Research Goal 2 Objectives

- Define how common conditions such as age, malnutrition, or diabetes mellitus modify mucosal innate and adaptive immunity and physiology, altering susceptibility to enteric illnesses, and vice versa.
- Understand the role of host genetics in the response to GI infections.
- Understand the mechanisms of action of probiotics and prebiotics.
- Conduct appropriately designed and powered large-scale, placebo-controlled, randomized double blind clinical trials to demonstrate safety and efficacy and substantiate the potential for novel interventions to treat or prevent enteric infections.

Research Goal 2
Objectives (continued)

- Promote strategies to reduce nosocomial enteric infection, including handwashing.
- Investigate and promote novel strategies to reduce and treat *C. difficile* infection.
- Advance vaccine strategies for appropriate pathogens to reduce morbidity and mortality of enteric infection. Integrate measures to control enteric parasitic infections including vaccine distribution and potential mass treatment protocols (e.g., wide-scale de-worming, preventive chemotherapy agents).

Research Goal 3

Understand and modulate the long-term intestinal and non-intestinal consequences of GI infection.

Research Goal 3 Objectives

- Understand the short-term (and long-term) burden and impact of enteric infections on cognition, development and health. Comprehensive outcome measurements should be developed to guide and standardize assessments in different populations.
- Identify biomarkers to predict the development of systemic diseases secondary to the exposure to enteric pathogens.
- Attenuate host response to specific human infections.

Research Goal 3
Objectives (continued)

- Define the relationship between intestinal infection and chronic GI (IBS, IBD) and non-GI diseases.
- Study the feasibility of developing vaccines or other agents against “non-pathogenic” bacteria that might trigger pathologic intestinal inflammation.
- Identify the consequences of reducing the burden of intestinal infection and/or altering the microbiome (e.g., the hygiene hypothesis).

Research Goal 4

Understand the human microbiome in health and disease and modulate it for beneficial effects.

Research Goal 4 Objectives

- Augment microbial “censusing” capacities of the intestinal microbiota. Develop a comprehensive understanding of the intestinal microbiome and the effect of the host genome on microbial colonization. Understand the consequences of interactions between GI pathogens and normal gut flora on GI function.

- Develop and make accessible computational approaches and tools to assay the microbiome in the gut in a variety of disease states.

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Research Goal 4
Objectives (continued)

- Determine if the microbiota is altered under pathophysiologic, i.e., infectious diarrhea, IBS, IBD, obesity, in models and in people.

- Modulate the gastrointestinal microbiota to prevent systemic and intestinal disease.

- Determine if genetically modified organisms can deliver therapeutic molecules.

Major Challenges/Steps To Achieve Goals

- Technologies to study intestinal infection
- Therapeutic development for intestinal infection
- Resources for intestinal infection research
- Methods to modulate the human microbiome

Major Challenges/Steps To Achieve Goals

Technologies To Study Intestinal Infection

- Efforts that replace archaic enteric pathogen detection technology to identify agents across taxa
- Rapid, sensitive point-of-care diagnostics to detect all known enteric pathogens
- Genetic and replication tools to study viral pathogens and resources to study viral pathogens in human challenge models
- Small mammal models and an artificial intestine or *in vitro* models to study intestinal physiology, mucosal immunity, and microbial-host interactions and provide fundamental insights prior to clinical trials
- New *in vivo* imaging systems for animal models and humans to study pathogenesis of infectious agents.

Major Challenges/Steps To Achieve Goals

Therapeutic Development for Intestinal Infections

- Correlates of protective immunity for GI pathogens to eliminate the need to challenges or field trials to study efficacy and speed development of licensed candidate vaccines

Major Challenges/Steps To Achieve Goals

Resources for Intestinal Infection Research

- Repositories for human biological samples, research reagents, and animal models
- New databases, communication networks, and scientific resources to develop and sustain longitudinal, large population field studies and productive international collaborations
- Infrastructure and improved technology to more promptly identify infected patients to understand the epidemiology of foodborne diseases

Major Challenges/Steps To Achieve Goals

Methods To Modulate the Human Microbiome

- Fill the pipeline for new investigators
- Understand how to segregate the important variables in the massive data sets to be generated by research on the microbiome
- Adequate bioinformatic/computational power limit
- Multidisciplinary teams of researchers in human studies to incorporate immune function, transcriptome, microbiology, and clinical responses