

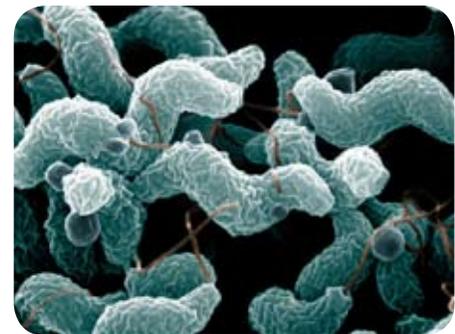
# Canadian Microbiome Initiative

## **BACKGROUND**

The human body plays host to trillions of microbes, including bacteria, viruses and protists. These microbes constitute the “Human Microbiome” that resides both on the surface and deep within numerous sites in our bodies. It is estimated that the number of microbial cells outnumbers host cells by a factor of at least 10:1 and that they encode approximately 100-fold more genetic information than the human genome. It has been recognized that microbes play an important role in human health, not just as pathogens, or as benign communities that keep pathogens at bay, but also in association with a number of chronic health conditions including gastrointestinal diseases, obesity, autoimmune diseases, diabetes, cancer, arthritis, asthma and cardiovascular disease. Perturbations in the normal microbiome have also been associated with certain neurological and behavioural changes. Until recently the task of studying the human microbiota was daunting, not only because of the sheer number of organisms colonizing the human body, but also because of the difficulties involved in studying colonies of microbes, and the interactions between them in their natural environment. However, with the emergence of the field of metagenomics and the availability of a new generation of genome sequencing platforms, it is now possible to sequence, analyze and characterize complex microbial communities fast and efficiently. These cutting-edge genomic and bioinformatics technologies open the door for biological studies on the complex relationships between microbes and humans.



*Escherichia coli (E. coli)*



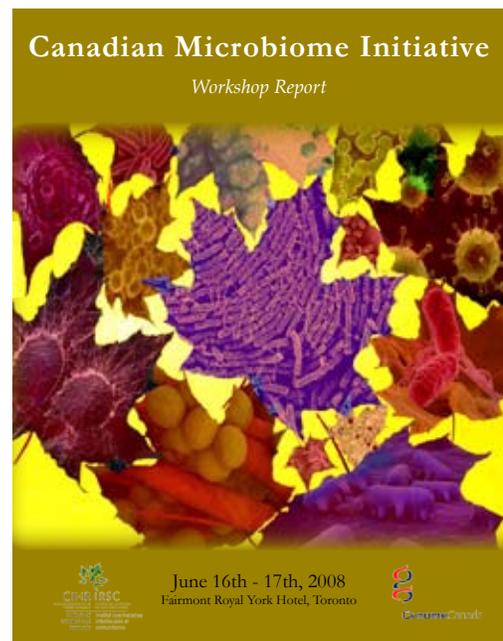
*Campilobacter*

The National Institutes of Health (NIH), through the Human Microbiome Project (HMP), plan to sequence and analyse the genomes of the human microbiome in selected body sites in order to determine whether there is a core set of microbiota shared by all humans. Using this reference database, it is hoped to be able to predict the genetic capabilities of unknown

species on the basis of similarities with known genes and to assess the role of the human microflora in health and disease. Much of the initial sequencing work is being undertaken by the HMP, but the vast amounts of data required calls for a coordinated international approach in which common techniques are used to collect samples, extract DNA and annotate data - hence the recent creation of the International Human Microbiome Consortium (IHMC). IHMC will coordinate the microbiome initiatives around the world including those in the EU, China, Japan, Singapore, Australia and Canada.

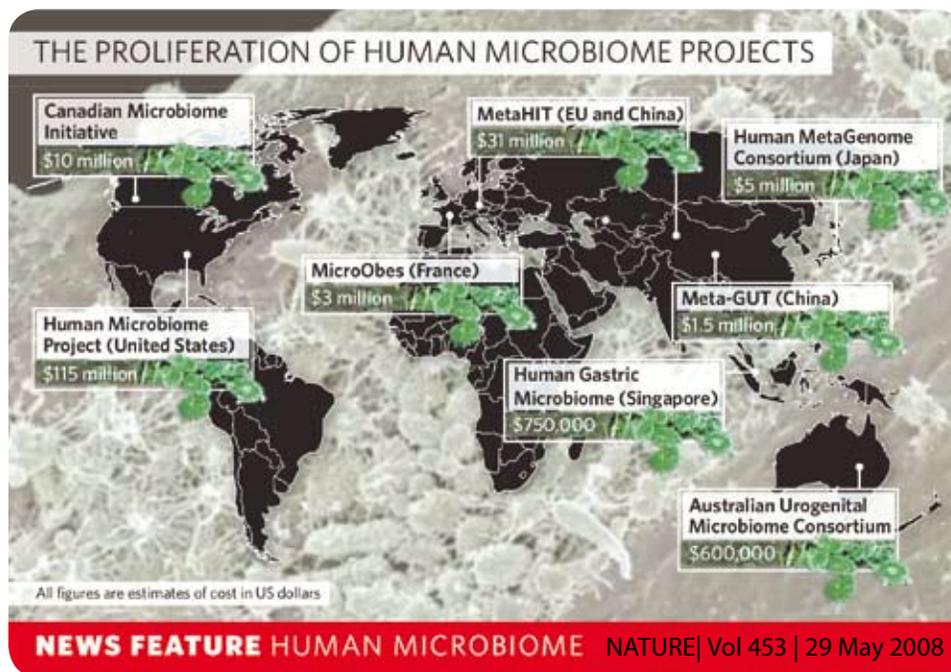
## ***CANADIAN MICROBIOME INITIATIVE***

Canada is well placed to take advantage of these ongoing initiatives due to research strengths in fields of gastroenterology, neuroimmunology, virology and infectious diseases and also our collaborative research culture and publicly-funded health care system. On behalf of CIHR, the Institute of Infections and Immunity (III) has championed the development of a conceptual framework for a Canadian microbiome strategy and engaged Canadian researchers in establishing research strategies and priorities related to the HMP. In September 2007, III initiated the Canadian Microbiome Initiative (CMI) to align with the HMP and to help Canadian researchers take a leading role in the IHMC. In June 2008, III and Genome Canada co-hosted the Canadian Microbiome Workshop, which brought together Canada's leading microbiome researchers to explore and develop strategies and priorities for the CMI and explore the research areas in which Canada can make unique contributions. III has already secured significant funds in support of CMI and developed strong national partnerships to support a strong Canadian presence in the field of microbiome research.



## ***THE INTERNATIONAL HUMAN MICROBIOME CONSORTIUM***

The Scientific Director of Ill serves as the Canadian representative on the International Human Microbiome Consortium (IHMC). (<http://www.nih.gov/news/health/oct2008/nhgri-16.htm> ). IHMC's initial focus will be to coordinate research efforts internationally and generate a shared comprehensive data resource available to investigators working in this area. The goals of the IHMC are to: generate a shared resource of human microbiome data and protocols; coordinate international efforts to reduce redundancy; and provide a venue for exchange of results and strategies. Currently, US\$250 million has been committed to the IHMC from around the globe, including \$10 million from Canada.



### **Current participants in the IHMC include:**

Australia: Commonwealth Scientific and Industrial Research Organization  
Canada: Canadian Institutes of Health Research  
China: Human Gut Microbiome and Infections  
China: Ministry of Science and Technology  
Europe: European Commission  
France: National Agency for Research (INRA)  
Ireland: the DAFF/HRB elderly gut metagenomics project ELDERMET  
Japan: Human Metagenome Consortium Japan (HMGJ)  
South Korea: Ministry for Health, Welfare and Family Affairs  
United States: National Institutes of Health

## ***THE CIHR-III CATALYST GRANT IN HUMAN MICROBIOME RESEARCH***

In June 2008, III, in partnership with the CIHR Institute of Nutrition, Metabolism and Diabetes (INMD), launched a Human Microbiome Catalyst Grant competition to support one-year grants of up to \$100,000 that will enable Canadian researchers to make a contribution to the creation of new knowledge in the area of the human microbiome and its translation into an understanding of how the microbes in the human body affect both the normal healthy and disease states. This catalyst grant funding opportunity garnered a great deal of interest from the research community and attracted 21 applications. With funding support from the CIHR Institute of Circulatory and Respiratory Health (ICRH), the CIHR Institute of Gender and Health (IGH), INMD, and the CIHR Ethics Office, the following 12 projects received one year funding to support individual researchers working in the area of the human microbiome to begin forming teams as an initial step towards the pursuit of additional funding opportunities in the national and international realms.

### **Researchers funded in the CIHR-III Microbiome Catalyst Grant competition**

<b>Principal Investigator</b>	<b>Institution</b>	<b>Project Title</b>
Allen-Vercoe, Emma	University of Guelph	Investigating the potential effects of host-derived stress hormones on the human gut microflora
Finlay, Barton	University of British Columbia	The Role of the Gastrointestinal Microbiota in Asthma
Holt, Rob	BC Cancer Research Centre	Linking Infectious Agents to Cancer: A Metagenomics Approach
Hwang, David	University Health Network	Assessing the impact of polymicrobial pulmonary infections in cystic fibrosis via metagenomics
Kozyrskyj, Anita	University of Alberta	The impact of antibiotics on intestinal microbiota of infants
Manges, Amee	McGill University	Microbial metagenomics of the intestinal microbiota and the etiology of Clostridium difficile-associated disease in hospitalized patients
Money, Deborah	University of British Columbia	Metagenomic characterization of the human vaginal microbiome
Neufeld, Josh	University of Waterloo	Establishing a complete taxonomic baseline for the human microbiome
O'Doherty, Kieran	University of British Columbia	Developing Ethical and Regulatory Guidelines for Research on the Human Microbiome and its Applications: Speaking to the Experts and Stakeholders
Rioux, Kevin	University of Calgary	Characterizing the fecal microbiome and bacteria-derived volatile organic compounds in patients with non-alcoholic fatty liver disease (NAFLD)
Stintzi, Alain	University of Ottawa	Role of the gut microbiome in Pediatric Gastrointestinal Illnesses
Surette, Michael	University of Calgary	Elusive respiratory pathogens in the oropharyngeal flora

## Research Descriptions of the projects funded in the CIHR-III Microbiome Catalyst Grant competition

**Dr. Holt** is analysing RNA samples from early stage **tumours** with the intention of determining if an infectious agent is detectable in these neoplasms using a method called Whole Transcriptome Shotgun Sequencing.

**Dr. Surette** is tracking down the elusive pathogens in the **oral cavity and upper respiratory tract** that are unidentifiable and are currently escaping detection by conventional clinical microbiology.

**Dr. Hwang** is trying to show that the lungs of **CF** patients harbour dozens of bacterial species, and that the composition of the bacterial community in the lung affects the severity of the disease and the effectiveness of different treatments.

**Dr. Neufled** is comprehensively profiling the phylogenetic diversity of the human gut and oral microbiome by pioneering a newly developed high-throughput sequencing technique and developing **novel bioinformatic tools** for subsequent data analysis.

**Dr. Finlay** is determining whether shifts in resident gastrointestinal microbiota play a role in developing atopic diseases such as **asthma** (i.e. testing the so-called "hygiene hypothesis").

**Dr. Allen-Vercoe** is exploring the effects of host-derived **stress hormones** on the human gut microbiota and to show that these stress hormones exert a direct effect on the population balance of the gut's microflora.

**Dr. Rioux** is examining previously unexplored links between compositional and functional changes in the intestinal microbiota and the pathogenesis of **liver disease** (NAFLD), possibly identifying novel therapeutic targets in the prevention and management of this disease.

**Dr. Manges** is investigating the etiology of **C. difficile**-associated disease in order to test and compare three alternate models of pathogenesis.

**Dr. Kozyrskyj** is measuring the effect of **antibiotic use** during infancy on the composition of intestinal microbiota and whether it is associated with the development of atopic disease in children.

**Dr. Money** is looking to determine whether healthy reproductive-aged women share a core **vaginal microbiome**, with variations that can be clearly defined and correlated with health and disease.

**Dr. Stintzi** is performing a comprehensive analysis of the gastrointestinal tract microbiome in children with **IBD** in order to test the hypothesis that the composition of the gut microbiota is uniquely associated with either Crohn's disease and/or ulcerative colitis.

**Dr. O'Doherty** is undertaking the challenge of collating and critically analysing the diversity of views and positions on human microbiome research and develop and understanding of how the human microbiome project is likely to shape **public understanding** of health and the human body.

## **EMERGING TEAM GRANTS**

In July, 2009, The CIHR Institute of Infection and Immunity announced the launch of the Emerging Team Grant: Canadian Microbiome Initiative (CMI). This initiative will provide an opportunity for multidisciplinary teams of Canadian researchers to analyze and characterize the microbes that colonize the human body in order to: understand of the composition and distribution of the microbial flora in different body sites; gain new insights on the function of the normal flora in healthy individuals; and probe the links between the human microflora and disease.. It is expected that successful teams will take advantage of the international microbiome research database where appropriate.

Total amount available for this initiative is **\$13.275 million**, with the possibility of increased funding through additional partnerships.

Letters of Intent are due **November 2nd, 2009** and funding is set to being in September 2010.

***This funding opportunity is supported by:***



## ***EMERGING TEAM GRANTS***

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The specific objectives of this funding opportunity are:

- To characterize communities of microbes found in different body sites in healthy individuals to determine if individuals share a common microbiome;
- To explore the interactions between microbes and determine how perturbations at one site can affect microbes at another body site;
- To investigate the role the microbiota play in human health and to probe the associations between the human microbiome and a variety of diseases and health conditions;
- To establish links and collaborations between researchers with expertise in different fields e.g. genomics, proteomics, bioinformatics, immunology, physiology, microbial ecology, ethics;
- To establish links and collaborations between research teams currently studying microbes at different body sites e.g. oral, gastrointestinal, respiratory tract;
- To promote research that utilizes existing Canadian infrastructures such as large-scale genomics and bioinformatics platforms and cohort studies;
- To create competitive Canadian teams that are able to contribute to, and benefit from, the work of the IHMC and other international opportunities;
- To identify and address potential ethical and legal issues associated with microbiome research and the emerging technologies as an integral part of research teams.

For information about this funding opportunity, please visit:

**[www.researchnet-recherchenet.ca/rnr16/vwOpprtntyDtls.do?prog=793&tag=1](http://www.researchnet-recherchenet.ca/rnr16/vwOpprtntyDtls.do?prog=793&tag=1)**

or contact

Judith Bray

CIHR Institute of Infection and Immunity

[judith.bray@cihr-irsc.gc.ca](mailto:judith.bray@cihr-irsc.gc.ca)

613-954-7223