SAFE FOOD AND WATER INITIATIVE

Executive Summary

Although Canada's food and water supplies are among the safest in the world, microbial contamination remains an important health issue. There are many reasons to resist complacency regarding the risks involved, including the emergence of new pathogens, changes in agricultural practices, and increased globalization. Canadian research in this area is strong and exists in many different sectors including technology, health, agriculture and environment. Given the limited resources available for research and the obvious overlap in priorities relevant to the microbial contamination of food and water, collaboration and partnership between stakeholders becomes essential.

The formation of the 17-member Canadian Research Coalition for Safe Food and Water in 2002 heralded the beginning of a new era of cooperation between federal departments, funding agencies and industry associations. Together the group identified national research priorities and developed a process for combining funds, resources and assets to jointly address this important health issue. To date, the major outcome of the Coalition has been the research initiative, launched on behalf of the group by CIHR, entitled "Microbial Contamination of Food and Water and Antimicrobial Resistance in the Food Chain - Phase II - Establishing a Framework".

Partners supporting the RFA
"Microbial Contamination of Food and Water and Antimicrobial Resistance in the Food Chain - Phase II - Establishing a Framework"

Agriculture and Agri-Food Canada
Canadian Food Inspection Agency
CIHR - Institute of Infection and Immunity
CIHR - Institute of Population and Public Health
Environment Canada
Health Canada
National Research Council Canada

This RFA was launched in partnership with Health Canada, prior to the creation of the Public Health Agency of Canada.

This initiative, supported by two Institutes of the Canadian Institutes for Health Research (CIHR) and five federal departments, resulted in the support of seven research teams each of which combined the expertise and resources of researchers from both university and government departments.

After just two years of funding, the teams have made remarkable progress both in research results achieved (many of which are already published), opportunities for commercialization (at least one biotech company spin off already), additional networking and partnership building and the formation of mutually advantageous linkages between government departments and universities. These seven teams serve as an excellent illustration of the power of collaboration and the advantages of combining expertise and resources towards a common goal, in this case protecting the safety of Canada's food and water supplies. Comments from the fifteen team members interviewed at the half-way mark reinforce the Coalition's decision to move ahead with a unified safe food and water initiative despite the administrative challenges that were encountered along the way. In today's financial climate, combining resources and linking research directly to policy seems to make eminent sense and the Safe Food and Water Initiative provides one example of how these goals can be met. It is anticipated that the teams will continue to pursue their research by applying to future funding opportunities at both CIHR and Natural Sciences and Engineering Research Council of Canada (NSERC). To facilitate this process, the Institute of Infection and Immunity is planning to host a workshop in September 2006 to bring together the team members and explore opportunities for future collaboration on research projects of mutual interest.

SAFE FOOD AND WATER INITIATIVE - 2006

Background

The Institute of Infection and Immunity (III) is one of the 13 Institutes of the Canadian Institutes of Health Research (CIHR). Created in June 2000, CIHR replaced the Medical Research Council as Canada's primary funding agency for health research. CIHR Institutes have a mandate to identify and address strategic research priorities within specific health domains. The Institutes strive to coordinate research efforts through partnership and collaboration and to enhance knowledge translation to ensure the rapid uptake of research results into practice. Institute interests span all areas of the health care continuum from prevention to palliation and encompass biomedical, clinical, health services and population level health research. The III mandate covers the entire fields of infection and immunity but has focused primarily on the nine strategic research priorities identified by the Institute Advisory Board (IAB), in consultation with the infection and immunity research communities. The Safe Food and Water Initiative was developed and launched to address two of these Institute priorities, Antimicrobial Resistance and Microbiologically Safe Food and Water.

Food- and water-borne illness represents a significant health threat for Canadians. In addition to the short- and long-term health effects of such illnesses, there is also a substantial cost to the Canadian economy in terms of work days lost and the potential impact of a contamination incident on international trade. These points have been well illustrated, in Canada, by outbreaks of water contamination such as the one that occurred in Walkerton, by several outbreaks of food-borne illness and by the original discovery of a single cow with bovine spongiform encephalitis (BSE), also known as 'mad cow disease'. It has been estimated that more than 200 diseases are caused by food- and/or water- borne transmission of pathogens or their toxins.

In reality, this number is likely much higher as the causative agent is often unidentified. A number of factors including changing demographics, globalization, new or emerging pathogens and antimicrobial use in agriculture, suggest that food- and/or water-borne illness will remain an important health issue. To safeguard our food and water supplies, evidence-based national food and water safety policies are required that are flexible enough to respond to changing conditions.

Prior to the creation of CIHR, a series of opportunity workshops were funded to provide research recommendations in priority areas likely to be of interest to the new Institutes. One of these, led by Dr. Brett Finlay of the University of British Columbia, focused on the microbial contamination of food and water and the use of antimicrobials in agriculture. Based on the recommendations from this workshop, III assumed a leadership role in the development of multiple partnerships with both the government and private sector to coordinate a national research agenda on microbiologically safe food and water. The result was the creation of what is currently the 17-member Canadian Research Coalition for Safe Food and Water.

Members of the Canadian Research Coalition for Safe Food and Water in 2006

Aquanet
Agriculture and Agri-Food Canada
Canadian Agri-Food Research Council
Canadian Aquaculture Industry Alliance
Canadian Cattlemen's Association
Canadian Food Inspection Agency
Canadian Institutes of Health Research
Canadian Pork Council
Canadian Veterinary Medical Association
Canadian Water Network
Chicken Farmers of Canada
Dairy Farmers of Canada
Environment Canada
Genome Canada
Health Canada
National Research Council Canada
Natural Sciences and Engineering Research Council

In May 2002, following a series of meetings, the Coalition launched its first Request for Applications (RFA), a Needs, Gaps and Opportunities Assessment (NGOA), funded by III, the Canadian Water Network and the Natural Sciences and Engineering Research Council (NSERC). The funded project, led by Dr. Mansell Griffiths of the University of Guelph, led to the publication of a comprehensive document entitled "Microbial Risk Assessment as a Foundation for Informed Decision Making", released in March 2004 and available through the III website.

In December 2002, III launched a second RFA entitled, "Microbial Contamination of Food and Water and Antimicrobial Resistance in the Food Chain - Phase II - Establishing a Framework", in partnership with the CIHR Institute of Population and Public Health (IPPH), Agriculture and Agri-food Canada, Environment Canada, the Canadian Food Inspection Agency, Health Canada and the National Research Council Canada. This RFA focused on common strategic research priorities identified by the group in a series of working group meetings.

Partners supporting the RFA
"Microbial Contamination of Food and Water and Antimicrobial Resistance in the Food Chain - Phase II - Establishing a Framework"

Agriculture and Agri-Food Canada
Canadian Food Inspection Agency
CIHR - Institute of Infection and Immunity
CIHR - Institute of Population and Public Health
Environment Canada
Health Canada
National Research Council Canada

This RFA was launched in partnership with Health Canada, prior to the creation of the Public Health Agency of Canada.

An important objective of this RFA was to promote the formation of new research teams, or to expand existing teams, that would bring together researchers working in university and federal department laboratories to combine their skills and resources in order to more efficiently and effectively address important research questions. To facilitate the creation of multi-sector research teams, III hosted an Application Development Workshop in December 2002 which was attended by more than 80 researchers from university laboratories and all five of the government departments supporting the RFA.

The RFA achieved its goal of bringing together researchers from these two very different worlds - university and government research laboratories. From the 24 full applications received, seven received funding in February 2004. Collectively, the seven teams are comprised of a mix of university and government scientists from more than twelve universities and five different government departments and the funded projects cover a wide range of topics within the theme of microbial contamination and antibiotic resistance. Full details of the composition of the research teams and the funding contributions from the six organizations supporting the RFA are given in Appendix 1. Each team received funding of up to $300,000 per year for up to three years to support operating costs, salaries for research personnel including graduate or postdoctoral students, technicians and administrative assistants, purchase of essential equipment, data collection, networking activities and dissemination of research findings.

Projects funded under the RFA *"Microbial Contamination of Food and Water and Antimicrobial Resistance in the Food Chain - Phase II - Establishing a Framework"*

Team Lead	*Research Institution*	*Title of Project*
Cashman, Neil R	University of British Columbia	The Canadian Prion Disease Network: Meeting the challenge
Isaac-Renton, Judith	University of British Columbia	Safe drinking water through source surveillance: Assessing impacts of environmental factors and microbial contamination of watersheds on community health
Karmali, Mohammed	University of Guelph	Comparative pathogenesis and public health significance of verocytotoxin-producing Escherichia coli serotypes
Louie, Marie	University of Calgary	Prospective multi-province surveillance for antimicrobial resistant Escherichia coli in drinking and recreational source waters: Impact on humans and the environment.
Mazumder, Asit	University of Victoria	Source tracking and environmental determinants of coliform bacteria in source water under various land-use in British Columbia
Sad, Subash	University of Ottawa	Modulation of immunity and development of therapeutics against *Salmonella*
Taylor, Diane	University of Alberta	Pathogenesis and antibiotic resistance in *Campylobacter*

In addition to these two RFAs, several members of the Coalition provided funds to the Canada Agriculture Museum for the development of a 1500 sq ft traveling Museum exhibit entitled "Food for Health". This exhibit, scheduled to open in March 2007, will reach thousands of Canadians from coast to coast with information on the relationship between food and health including safe food handling practices and the importance of a balanced diet and healthy lifestyle in the prevention of obesity and a number of chronic diseases.

The Outcomes

In 2005, as the projects funded under the second RFA reached their mid-point, III staff conducted a series of interviews, in person and by telephone, to assess the research progress and challenges encountered in managing the research teams. In total, 15 team members were interviewed from both university and government laboratories (indicated by an asterisk in Appendix 1). Team members involved in more than one team were asked to comment on all their projects individually. The interviews focused on research results and also on the operational successes and challenges of the teams program.

Application Process

Many interviewees credited the Application Development Workshop for providing the platform from which their team was formed. The workshop provided both valuable advice on the application process and an opportunity for networking between government and university researchers working in the field. In a few cases however, none of the team members were present at the workshop and their collaboration arose from existing relationships and connections that were extended and strengthened through this initiative. The management of the application process and peer review of applications was handled by CIHR with input from the federal partners on the composition of the peer review panel.

Funding

Challenges posed by regulations regarding disbursement of government funds required creative solutions on the part of the partners on this initiative. It was recognized at the outset that it would not be possible to pool financial resources in order to co-fund successful teams but that it would be necessary for each partner to contribute funds to their own researcher working as part of a team. Although somewhat cumbersome to administer, this system proved effective in providing the necessary financial and in-kind support to the teams. The partners continue to work together to explore alternative avenues to facilitate the joint financial support of research that encompasses overlapping interests. One issue that did emerge was that the value of in-kind contributions should not be underestimated as in many cases it was the sharing of expertise, infrastructure or resources between team members that had the greatest influence on the success of the project. Several team members made the comment that for future initiatives a five-year funding cycle would be more conducive to the training of graduate students.

Research Results

Despite an initial delay in the disbursement of funds, teams reported good progress during their first eighteen months and were close to being on track with most aspects of the proposed research. Even in this relatively short time period many teams have already produced results that have been presented at both national and international meetings or in some cases are in press or already published. Research highlights include the following:

- **The production of large amounts of recombinant prion proteins for chemical modification experiments - five candidates to date for mis-folded proteins suitable for antibody studies, development of new diagnostic techniques using epitope protection technology, a method with sufficient sensitivity to detect the presence of a single prion in buffer; and preliminary results on the conversion of material from Chronic Wasting Disease (Cashman);**

- **Collection of water samples and the creation of collaborations with provincial medical officers of health to establish health links; early surveillance of local outbreaks of water contamination in rural BC indicate water contamination (Isaac Renton);**

- **Identification of genomic regions that are predictive of virulence in verocytotoxin-producing *Escherichia coli* serotypes; preliminary results from tests in cows, mice, neonatal pigs and on human cells (Karmali);**

- **Preliminary data from laboratory surveillance of private well-water and recreational water sources indicates the presence of antimicrobial resistance bacteria in both these water sources; geospatial analysis of these data has been applied and is based on two approaches: a regional regression analysis focuses on contamination rates of wells among jurisdictions and their relationship to regional characteristics such as agricultural practices and livestock farming. A well-specific analysis focuses on the local land use characteristics that are associated with contamination such as soil types and geology. Together these analyses will shed light on both the regional and local conditions that contribute to total coliform, *E. coli* and resistant *E. coli* contamination. Further work is under way to determine the risk factors associated with well-water contamination with resistant *E. coli* using a case-control study design (Louie);**

- **Results from water sampling completed for year two have already led to a great example of knowledge translation. River water contamination has been significantly reduced by relocating cattle drinking containers away from the river and re-routing cattle movements by building bridges to discourage them from spending time in the river (Mazumder);**

- **Development of mutant strains of *Salmonella* based on an improved understanding of key virulence factors; positive preliminary results on the development of a vaccine for *Salmonella* in chickens and mice (Sad); and**

- **Antibiotic resistance and plasmid profiles are completed for over three hundred *C. jejuni* isolates (200 human and 100 animal) and associations have already been found between plasmid profiles and virulence in some cases; mechanisms of tetracycline and erythromycin resistance have been characterized; epidemiology and molecular analyses are in progress to trace how human infections are acquired (Taylor).**

Team Work

Without exception, the individuals interviewed confirmed the value of bringing together researchers from universities and government laboratories around a common research theme. In many cases the research projects would not have been feasible without the combination of expertise, resources and infrastructure made possible by the creation of these teams. Some examples include access to the large National Research Council Canada (NRC) fermenters for bacterial growth, the extensive *E. coli* strain library made available by Public Health Agency of Canada (PHAC) and the provision of tissue samples for prion studies by Canadian Food Inspection Agency (CFIA). In reality the in-kind contributions of the government departments have proven to be as valuable, if not more valuable, than their actual cash contributions and the involvement of several different departments has brought additional relevance to the projects in the form of policy driven research. Most teams credit their success to the strong leadership skills and commitment of the team lead and the organization of regular team meetings both by teleconference and in person. These meetings facilitate the coordination of tasks, encourage enthusiasm among students and technicians and promote strong links between team members. Many teams have also benefited from the training component of the projects with several students being shared between both university and government researchers. This initiative has enabled the formation of entirely new collaborations and allowed for the expansion of small pre-existing teams. Most teams hope to continue their association long beyond the termination of their projects and will no doubt continue to collaborate on future research initiatives.

Summary

The Safe Food and Water Initiative addressed a need for improved coordination of research efforts between government departments and universities on an important human health issue. Although not without its administrative challenges, the initiative appears to have surpassed expectations. Seven multidisciplinary, cross-sector teams were created in which extensive and varied expertise and resources were combined to address priority research questions. The effectiveness of these teams is illustrated by their early research results, their ability to attract additional partners to their projects and their success in recruiting large numbers of trainees. The formation of these teams has laid the foundation for extended networking and collaboration, forging links with other initiatives in the same field. For example the team led by Neil Cashman, "The Canadian Prion Disease Network: Meeting the Challenge" provided the impetus for the creation of a new Network Centres of Excellence (PrioNet Canada) focused on prion diseases. The initiative serves as an excellent example of the power of collaboration and the advantages of streamlining research efforts to avoid duplication, expedite research progress, and facilitate the uptake of research findings into policy and practice.

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Canadian Food Inspection Agency / Agence canadienne d'inspection des aliments

National Research Council Canada / Conseil national de recherches Canada

Health Canada / Santé Canada

Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

Environnement Canada / Environment Canada

Agriculture and Agri-Food Canada / Agriculture et Agroalimentaire Canada

canadian water network / réseau canadien de l'eau

Natural Sciences and Engineering Research Council of Canada / Conseil de recherches en sciences naturelles et en génie du Canada

Appendix I

Projects funded under the RFA "*Microbial Contamination of Food and Water and Antimicrobial Resistance in the Food Chain - Phase II - Establishing a Framework*"

** Asterisks indicate researchers interviewed by III staff*

This RFA was launched and funded before the creation of the Public Health Agency of Canada. The original partner was Health Canada, including the Office of the Chief Scientist and several additional departments..

The Canadian Prion Disease Network: Meeting the Challenge

Principal Applicants	Affiliation
Neil Cashman - team lead*	University of British Columbia
Michael Coulthart*	Public Health Agency of Canada
Avijit Chakrabartty	University of Toronto
Aru Balachandran*	Canadian Food Inspection Agency

Supported by:

Canadian Food Inspection Agency (CFIA)
Canadian Institutes of Health Research - Institute of Infection and Immunity (III)
Public Health Agency of Canada - National Microbiology Laboratory (NML)

Proposed Research:

Prion diseases are rapidly progressive, fatal and untreatable neurodegenerative syndromes that are neuropathologically characterized by microcavitation of the brain, neuronal loss, and accumulation of an abnormal amyloidogenic protein. The threat to the human food chain of newly emergent prion diseases - including bovine spongiform encephalopathy (BSE) and chronic wasting disease (CWD) - has created serious medical, veterinary, and economic challenges worldwide. The discovery in May 2003 of a case of BSE in Canada profoundly affected a broad range of industries related to cattle farming. Also of concern in Canada is CWD, which already afflicts captive and wild elk and deer, with potential spread to other cervid food animals (caribou and moose). There are no obvious natural biological or geographic barriers to prevent continent-wide spread of this disease within these cervid species, suggesting that CWD may ultimately produce the largest and most widespread reservoir of prion disease in human history. This project will focus on molecular risk assessment tools for prion transmission (Dr. Coulthart), new prion-selective epitope candidates (Dr. Chakrabartty) and ante-mortem diagnostics for prion infection (Dr. Cashman).

Safe Drinking Water through Source Surveillance: Assessing impacts of environmental factors and microbial contamination of watersheds on community health

Principal Applicants	Affiliation
Judith Isaac-Renton - team lead*	University of British Columbia
Hanspeter Schreier	University of British Columbia
Vic Gannon*	Public Health Agency of Canada
Paul Sockett*	Public Health Agency of Canada
Thomas Edge*	Environment Canada

Supported by:

Canadian Institutes of Health Research - Institute of Infection and Immunity (III) and Institute of Population and Public Health (IPPH)
Health Canada - Office of the Chief Scientist (OCS), Food Directorate (FD)
Public Health Agency of Canada - Department of Population and Public Health (DPPH) and Laboratory for Foodborne Zoonoses (LFZ)
Environment Canada (EC)

Proposed Research:

We have come to expect safe drinking water in Canada, but recent waterborne outbreaks can be perceived as evidence of an inability to provide it. New knowledge is urgently needed to improve surveillance methods and to guide health and water intervention strategies as well as policies and procedures. Currently, surveillance of drinking water is done after it has reached the community distribution system. The goal of this project is to expand on the present method of surveillance and use a continuous measurement of selected environmental parameters and water quality variables from "source to tap". The hypothesis is that this study will provide a more effective method of detecting microbial contamination events, thereby providing new information for improving drinking water quality. One of the specific objectives of this study will be to assess the link between environmental variables in source watershed, the water quality in distribution systems and human health.

Comparative pathogenesis and public health significance of verocytotoxin-producing Escherichia coli serotypes

Principal Applicants	Affiliation
Mohamed Karmali - team lead*	Public Health Agency of Canada
B. Brett Finlay*	University of British Columbia
Andrew Potter	University of Saskatchewan
Vic Gannon*	Public Health Agency of Canada
Philip Sherman	Hospital for Sick Children, Toronto

Supported by:

Canadian Institutes of Health Research - Institute of Infection and Immunity (III)
Health Canada - Office of the Chief Scientist (OCS)
Public Health Agency of Canada - Laboratory for Foodborne Zoonoses (LFZ)

Proposed Research:

Verocytotoxin-producing *E. coli* (VTEC) serotype O157:H7 is the food-borne pathogen that causes "hamburger" disease and also outbreaks of water-borne illness such as the one that occurred in Walkerton several years ago. Pathogenic VTEC strains are most commonly associated with cows, but recently have also been identified in other ruminants such as goats, sheep and deer. VTEC infections demonstrate a range of severity from mild diarrhea to severe disease complicated by the potentially fatal, hemolytic uremic syndrome (HUS) which is the leading cause of acute kidney failure in children. Over 200 different serotypes of VTEC have now been associated with human illness and their incidence appears to be rising. VTEC strains can be grouped into five categories ranging in virulence from those that always cause illness in humans to those that never do. It is not known why some VTEC are more virulent than others. The goal of this project is to understand the disease mechanisms and virulence factors among pathogenic strains of VTEC and distinguish VTEC that pose a serious risk to human health from those that do not. This will be accomplished by identifying the critical virulence factors that are associated with disease through the comparison of the genomes and proteins of virulent and non-virulent VTEC strains. The virulence of any protein that appears to be unique to strains causing outbreaks and HUS will be confirmed in animal models of disease.

Prospective multi-province surveillance for antimicrobial-resistant Escherichia coli in drinking and recreational source waters: Impact on humans and the environment

Principal Applicants	Affiliation
Marie Louie - team lead*	Université de Calgary
Rebecca Irwin	Public Health Agency of Canada
Patrick Levallois	Laval University
Scott McEwen	University of Guelph
Allison McGeer	University of Toronto
Norman Newmann	University of Calgary

Supported by:

Canadian Institutes of Health Research - Institute of Population and Public Health (IPPH)
Health Canada - Office of the Chief Scientist (OCS)
Public Health Agency of Canada - Laboratory for Foodborne Zoonoses (LFZ)

Proposed Research:

Antimicrobial resistance has rapidly increased in the last few years and has become a major public health threat. There is no doubt that the widespread use of antimicrobial agents in agriculture, veterinary practices, and food animal production can select for resistant bacteria, which can then be transmitted between animals to the surrounding environment and water sources. What is not well known is the extent of antibiotic resistant bacteria in water. This team of researchers will conduct a surveillance study to determine the occurrence of antibiotic resistant *E. coli* (AR-*E. coli*) in water samples from private drinking water in Alberta and southern Ontario and recreational/beach water sources in Alberta, Ontario and Quebec. The study will use the existing infrastructure in provincial and private water-testing laboratories in those particular provinces. Another objective of the study will be to assess whether AR-*E. coli* are clustered geographically to areas with high food animal/agriculture intensity or high human population density or both. This exciting new exploration will identify areas of significant spatial clustering in AR-*E. coli* and produce maps to educate public health officials and water purveyors. In addition, the project will also conduct a case-control study to identify the risk factors for contamination of private drinking water supplies with AR- *E. coli* and determine their impact on human health.

Source tracking and environmental determinants of coliform bacteria in source water under various land-use in British Columbia

Principal Applicants	Affiliation
Asit Mazumder - team lead*	University of Victoria
Jeff Aramini	Public Health Agency of Canada
Klaas Broersma*	Agriculture and Agri-Food Canada
Julian Davies	University of British Columbia
Réal Roy	University of Victoria
Mansour Samadpour	University of Washington

Supported by:

Canadian Institutes of Health Research - Institute of Infection and Immunity (III) and Institute of Population and Public Health (IPPH)
Health Canada - Office of the Chief Scientist (OCS)
Public Health Agency of Canada - Laboratory for Foodborne Zoonoses (LFZ)
Agriculture and Agri-Food Canada (AAFC)
Environment Canada (EC)

Proposed Research:

The major health risk with drinking water is caused by contamination of source water of unknown origin. With increasing exposure of Canadian community watersheds to various land-use (e.g., livestock farming, manure application, agriculture, recreation, sewage, septic and manure inputs), the risks of water contamination with fecal bacteria (especially *E. coli*) is increasing rapidly. Standard methods for monitoring fecal bacterial contamination of water do not identify the source of contamination, thereby making it difficult to remedy the problem and prevent reoccurrence of contamination. The goal of this project is to reduce health risks caused by bacterial pathogens in drinking water by assessing the impact of various land-use activities in fecal contamination of source water; developing and validating the robustness of different methods in tracking the sources of *E. coli* contamination; and assessing and modeling how different environmental factors regulate the transport, viability and outbreak potentials of *E. coli*.

Modulation of immunity and development of therapeutics against *Salmonella*

Principal Applicant	Affiliation
Subash Sad - team lead*	National Research Council Canada
Robert Hancock	University of British Columbia
B. Brett Finlay*	University of British Columbia
Lakshmi Krishnan*	National Research Council of Canada
Andrew Potter	University of Saskatchewan

Supported by:

Canadian Institutes of Health Research - Institute of Infection and Immunity (III)
National Research Council Canada (NRC)

Proposed Research:

Salmonella in an important health threat and is the causative agent of gastroenteritis and typhoid fever in humans. Outbreaks of infections can have significant impact on health (particularly in aged, immunocompromised individuals, and pregnant women), and on the economy (losses due to affected livestock can be considerable). While scientists are beginning to understand the mechanisms of virulence of *Salmonella* on tissue culture cells in vitro, relatively little is known about which mechanisms of virulence and immune evasion strategies operate in vivo. Consequently, we have not been able to create any satisfactory vaccine approaches against *Salmonella*. With the advent of modern genomic approaches that can methodically evaluate the key virulence and immune mechanisms of bacterial pathogenesis, in combination with the use of novel delivery technologies, it is now possible to design effective protective strategies for disease control. The goal of this project is to evaluate *Salmonella* pathogenesis and devise effective preventative strategies through a rational understanding of host immune modulation. By using modern genomic and immunological approaches the team will methodically decipher the key virulence and immune mechanisms of bacterial pathogenesis. This will lead to rational selection of immunotherapy targets. The results will lead to the creation of therapeutics that can then be formulated in potent delivery vehicles, and tailored to be effective in all hosts irrespective of immune status, with minimal side-effect. Such vaccines against *Salmonella* will be more important for humans who are at a higher risk, such as aged or pregnant individuals. As an alternative, vaccination of livestock could curtail transmission at the source.

Pathogenesis and antibiotic resistance in *Campylobacter*

Principal Applicant	Affiliation
Diane Taylor - team lead*	University of Alberta
Monika Keelan	University of Alberta
Vic Gannon*	Public Health Agency of Canada
Lai-King Ng	Public Health Agency of Canada
Kris Rahn	Public Health Agency of Canada
John Nash	National Research Council Canada

Supported by:

Canadian Institutes of Health Research - Institute of Infection and Immunity (III)
Health Canada - Office of the Chief Scientist (OCS)
National Research Council Canada (NRC)
Public Health Agency of Canada - Laboratory for Foodborne Zoonoses (LFZ)
Public Health Agency of Canada - National Microbiology Laboratory (NML)

Proposed Research:

Campylobacter bacteria are commonly found in the environment, and exist as part of the normal intestinal flora of many birds and mammals (chickens and cattle). *Campylobacter* infection in humans is associated with acute gastroenteritis. The illness is usually self-limiting and deaths are rare, although occasionally, complications of *C. jejuni* infection result in the development of more severe neurological and autoimmune illnesses such as Guillain-Barré, Miller-Fisher and Reiter's syndromes. The factors determining the clinical outcome of infection with *C. jejuni* are likely dependent upon the infecting strains as well as the susceptibility of the host, but the mechanisms of pathogenesis are still unclear. The objective of this project is to better understand the mechanism of spread of antibiotic resistance in *C. jejuni*, as well as the pathogenic mechanism involved in the disease process. The team will determine the frequency of antibiotic resistance and resistance plasmids in *C. jejuni* strains from humans, chickens, and cattle. The bacteria involved will then be tested for their ability to invade cells in culture. This project will also assess the relationships among the three strain populations (human, poultry, beef) using various typing methodologies to determine if and how antibiotic resistance moves from animals to humans. DNA micro-array chips will be used to find the genes responsible for causing disease in humans in order to better understand the origin of antibiotic resistance in *C. jejuni* infecting humans.