A Canada-UK Workshop: "Beating the Bugs"

CIHR IRSC
Institut des maladies infectieuses et immunitaires
Institute of Infection and Immunity

MRC Medical Research Council
Leading science for better health

Canada

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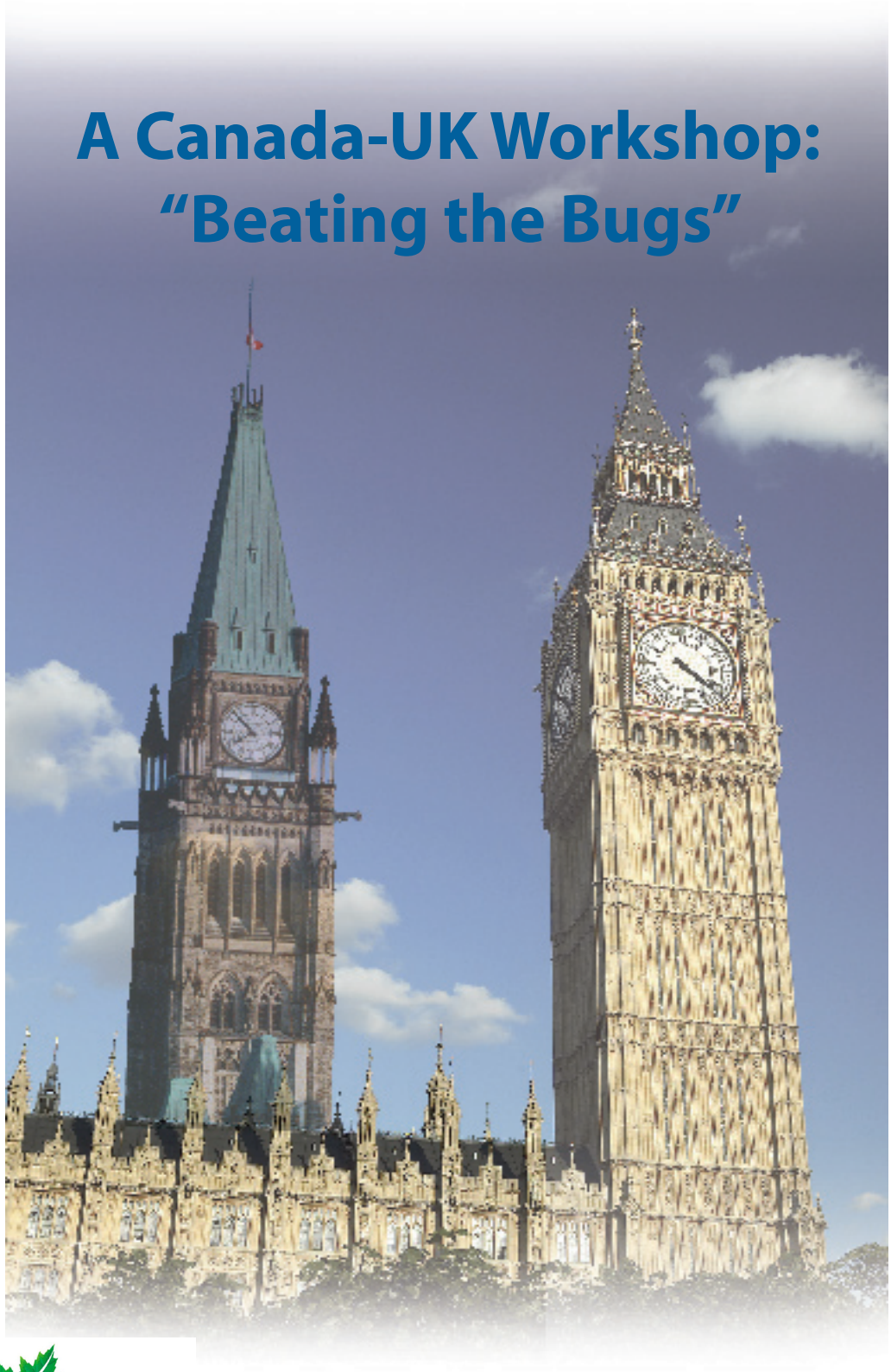

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Executive Summary

Antibiotic resistance is a key factor in the hospital and community acquired multi-drug resistant infections that are posing an increasing threat to global health. The complacency of the last fifty years is rapidly being replaced by mounting concern that we may soon have no defences against the common pathogens previously controlled by antibiotics. Both the UK and Canada are battling similar problems with resistant organisms and both countries are investing in research to address the issue.

In an attempt to fast track the outcomes of this research, an invitational workshop was hosted by the Canadian High Commission to bring together the leading researchers from both countries to explore opportunities for partnerships that would capitalize on complementary areas of expertise to advance the research at an accelerated pace. The workshop, held at Canada House, London, on February 6th and 7th 2008, brought together over 40 Canadian and UK researchers who were given the task of identifying specific research areas/topics that would benefit from a UK/Canada collaboration and of convincing their respective funding agencies (the UK Medical Research Council - UK MRC and the Canadian Institutes of Health Research Institute of Infection and Immunity - CIHR-III) that there would be a genuine value gained through collaboration.

Over the course of a day and a half, researchers listened to state of the art scientific presentations and participated in small group brainstorming sessions aimed at identifying potential areas for collaboration. By the end

of the workshop it was clear that there was a genuine need and a desire among the participants to create UK/Canada teams or consortia to combine research strengths in the two countries. The following four broad topic areas were identified as being likely to benefit the most from collaboration:

- ***Systems biology approaches to antibiotic action and resistance*** – *would take advantage of unique bacterial strains in Canada and the UK to develop novel therapeutic approaches and new drug modalities and combinations*
- ***Bacterial cell wall analysis*** – *a systematic development of a toolbox for cell wall analysis leading to the development of new therapeutics targeting cell wall biosynthesis*
- ***Immunomodulators for controlling antibiotic resistant infections*** – *evaluation of novel small molecular immunomodulators to reduce the global burden of infectious disease*
- ***Preventing resistant infections*** – *preventing the emergence of antibiotic resistance through an improved understanding of the epidemiology, ecology and routes of transmission of resistant pathogens leading to improved infection control*

The UK MRC and CIHR-III are now in discussions on how best to move the research agenda forward and jointly support collaborative funding opportunities to build on the recommendations coming out of the workshop. It is anticipated that competitive opportunities will be created to support successful UK/Canadian teams of researchers able to demonstrate the value-added component of their combined research activities.

A Canada-UK Workshop: "Beating the Bugs"

Workshop Report[1]

INTRODUCTION

Antibiotic resistance is becoming a global health problem of increasing severity as more and more microbes become resistant to many, if not all, currently available antibiotics. The promise of antibiotics in the 1950s, as the 'cure all' for bacterial infections, began to pale almost as soon as they were in widespread use, with rapidly dividing microbial populations easily acquiring mechanisms to evade their action. In recent years the pace of acquired resistance has accelerated(1) and there are real fears that we could return to a "pre-antibiotic" era in which we have few defences against common bacterial infections(2). Concomitant with the rise in antibiotic resistance, the large pharmaceutical companies which produced our current armamentarium of drugs are producing few new antibacterial products and for those that do actually make it to market, resistance is rapidly acquired. Both hospital and community acquired resistant "superbugs" are increasingly documented in the media, popular press and science journals, raising alarm amongst front-line clinicians, researchers and the population at large. New approaches in the prevention and treatment of bacterial infections will be needed if we are to avert the looming health crisis.

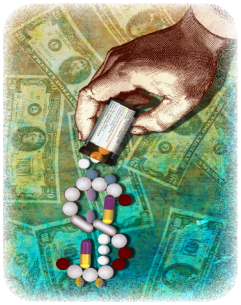
1. The opinions recorded in this report reflect those expressed by participants or other authoritative sources and unless otherwise stated do not represent formal positions of the organising institutions.

(1) Infectious Diseases Society of America. *Bad Bugs No Drugs. As antibiotic discovery stagnates a public health crisis brews* [online], <http://www.idsociety.org/pa/IDSA_Paper4_final_web. pdf>(2004).

(2) *Drugs for bad bugs: confronting the challenges of antibacterial discovery* David J. Payne, Michael N. Gwynn, David J. Holmes, David L. Pompliano *Nature Reviews Drug Discovery* **6**, 29 - 40 (08 Dec 2006), doi: 10.1038/nrd2201, Review.

Background

Antibiotic resistant bacteria do not observe geographical boundaries and many countries are struggling to deal with outbreaks of a variety of "superbugs." Both the UK and Canada have strong academic and clinical research strengths in this area and both countries have recently turned their attention to the control of infectious diseases. In the UK, the major funders of infection research have combined to form the UK Clinical Research Collaboration (UK CRC), which recently launched the first of two rounds of a joint initiative in translational infection research, coordinated by the Medical Research Council (UK MRC). In Canada, the Canadian Institutes of Health Research, Institute of Infection and Immunity (III) has just announced more than $10 million in funding for the Novel Alternatives to Antibiotics initiative which was launched in partnership with many private and public sector partners to explore novel approaches in the fight against bacterial infections. In addition, both countries fund excellent basic and clinical research focused on infection control through their regular granting programs. It is therefore anticipated that UK/Canada research partnerships combining the research strengths in both countries could move the science forward at an accelerated pace.



Goals and Objectives of the Workshop

A Canada/UK workshop, organised by UK MRC, III, and the Canadian High Commission took place over a day and a half at Canada House in Trafalgar Square, London on February 6th and 7th, 2008. More than 40 participants were invited from the UK and Canada (see Appendix 1). Participants were invited on the basis of their scientific calibre, their specific area of expertise and existing UK/Canada collaborations. The purpose of the workshop was to bring together researchers with different perspectives on the problem of antibiotic resistance in order to address topics such as immune modulation, molecular determinants of resistance, clinical aspects, and systems biology approaches. The objective was to assess whether there would be genuine gains through facilitating the creation and support of UK/Canadian partnerships between researchers with complementary expertise and whether such collaborations would result in improved mechanisms to address the problem of antibiotic resistance. The workshop participants were tasked with the job of convincing the research funders that any potential financial investment would be strategic, timely and productive and that the sum of any collaborative research projects would be greater than the parts.

DAY 1

KEYNOTE SPEAKERS

The workshop began with a number of keynote addresses from senior researchers working across a broad spectrum of research themes. The purpose of the presentations was to provide an overview of different research areas and establish an initial forum for discussion among participants. What follows is a brief synopsis of the salient points of each presentation.

"Setting the Scene: Public Health Perspectives – Canada" – *Dr. Michael Mulvey, Chief, Antimicrobial Resistance and Nosocomial Infections, National Microbiology Laboratory, Canada.*

Dr. Mulvey gave a brief overview of antimicrobial resistance activities in the Public Health Agency of Canada (PHAC), including a description of PHAC's organizational structure, surveillance activities, research facilities and educational/outreach programs. This was followed by surveillance data for a number of the more problematic antibiotic resistant bacteria such as MRSA, VRE and *C. difficile*. Canadian surveillance data show a steady increase, particularly in the last five years, in the infection and colonization rates for nosocomial and community acquired MRSA, VRE, and ciprofloxacin resistant *N. gonorrhoeae*, but an overall levelling off for *C. difficile* and tuberculosis (although the overall pattern of TB drug resistance has increased). PHAC is also involved in studies on the links between antibiotic use in agriculture and the emergence of resistance in humans. One study in particular demonstrated a significant drop in ceftiofur resistance among several bacterial species once its use in the Quebec poultry industry ceased. Of note was the emergence of new infections e.g. multi-drug resistant *acinetobacter* introduced to Canada primarily by soldiers returning from service in Afghanistan and the rising antibiotic resistance rates seen in northern communities, particularly among aboriginal populations. In terms of overall antibiotic prescribing practices, Canada falls at about the mid-range (slightly above the UK) when compared with 24 European countries with Greece being at the high end and the Netherlands at the low end. Recommendations included the development of rapid diagnostics, improved surveillance and prescribing practices with better integration of data between hospitals, government departments and agricultural practices and more in depth studies on the actual economic costs of antimicrobial resistance.

"Setting the Scene: Public Health Perspectives –UK" – *Professor Brian Duerden, Inspector of Microbiology and Infection Control, Department of Health, UK.*

Professor Duerden reported a similar situation [to Dr. Mulvey] in the UK, with increasing numbers of community and hospital acquired infections resistant to an ever increasing number of antibiotics. As in Canada, an emphasis has been placed on making better use of existing antibiotics through more prudent prescribing practices and on educational programs for health professionals and the lay public, including children, to reduce the demands for and misuse of antibiotics in situations where they are ineffective e.g. most common respiratory illnesses.

Some of the major concerns about antibiotic resistance are treatment failures, clinical costs to patients (e.g. prolonged illness, long-term disability or even death), the requirement for increasingly toxic and broad spectrum antibiotics, and the potential side effects they cause and the overall cost to the economy in terms of working days lost, extended health care needs and drug costs.

The UK has a long history, dating back 40 years, of documenting antibiotic resistance and setting forth recommendations for a UK strategy to combat the problem. Some of these recommendations have resulted in actions, such as the support for antimicrobial pharmacists; national prescribing policies; a statutory code of practice that includes annual inspections; and health checks with unannounced spot checks. The antibiotic policy framework released in 2007 includes additional recommendations for restricting the use of broad spectrum antibiotics, documentation of the reasons for prescribing and the stop dates, and the restriction of prophylactic antibiotics (e.g. before surgery) generally to a single dose. The UK has also set specific targets for reducing MRSA and *C. difficile* infection rates.

"Finding the Bug: Controlling resistance through rapid DNA-based diagnostics" – *Dr. Michel G. Bergeron, Professor and Chairman, Division of Microbiology and Centre de recherche en infectioilogie, Université Laval, Canada.*

The presentation focused on the role of rapid diagnostics in the prevention and treatment of antibiotic resistant infections. In the early days of microbiology, and even today, it still takes from two days to two weeks to diagnose an infection and identify the causative agent. Much of this time is spent doing culture and phenotypic identification using chemical reactions. While waiting for the results patients are often prescribed inappropriate treatments or suffer unnecessary morbidity or even mortality. During the last two decades there has been a revolution in molecular technologies, which now makes it possible to use DNA-based assays to identify microbes in record times.

The ability to begin adequate initial antibiotic therapy based on a definitive diagnosis could dramatically reduce the mortality rates from a number of serious bacterial infections. Rapid diagnostics also permit pre-admission screening for resistant organisms, reducing the likelihood of transmission.

Dr. Bergeron described three rapid diagnostic tests developed by his transdisciplinary team that are now approved for use in Canada, the US and the EU and which provide a means to prevent meningitis in newborns, hospital infections such as MRSA, and the dissemination of microbial resistance. The latest technology coming out of Dr. Bergeron's lab combines genomics, DNA microarrays, innovative biosensors, microfluidics, and nano-technologies. These "lab on a chip" devices can be mounted on a single CD and will enable rapid point-of-care tests administered by attending health professionals. Diagnostics, a neglected area in the past, now offers the promise of tremendous savings in both health care costs and patient morbidity. With an estimated 89% of hospitalised influenza patients still being prescribed antibiotics, there is a huge market for accurate and sensitive rapid diagnostic tests which lead to more precise treatments, improved control of resistance, better control of epidemics/bioterrorism attacks, and a safer environment (e.g. detection of contaminated food and water).

"Bug Meets Drug: Everything you need to know about antibiotic resistance in 25 minutes!" – *Professor Laura Piddock, University of Birmingham, UK.*

Professor Piddock's presentation focused on the mechanisms involved in the development of antibiotic resistance and how resistance, once acquired, is transferred and disseminated between bacteria. There are at least four known targets for antibacterial action: cell wall synthesis; cell membrane permeability; nucleic acid synthesis; and protein synthesis. Bacteria, however, can rapidly develop defence mechanisms such as: enzyme synthesis to inactivate the drug; prevention of access for the drug through altered membrane permeability; efflux pumps; changes in the target binding site; and manufacture of new targets that bypass existing ones.

Antibiotic resistance is a genetic phenomenon mediated through a variety of mechanisms such as spontaneous chromosomal mutation and acquisition of resistance genes transferred by plasmids, transposons and integrons. Expansion of resistant clones occurs through a process of environmental pressure (although resistance can persist in the absence of the antibiotic) and natural selection and, although some resistant bacteria initially carry a fitness burden, this can be overcome. Once acquired, single and multi-drug resistance can be easily and rapidly transferred between bacterial populations by clonal spread (e.g. chromosome mutations) or gene transfer (e.g. transmissible plasmids). There is also bacterial movement between ecosystems such as the farm to fork continuum; between health care facilities and the community at large; and even between humans and their pets. Globally there is significant variation in the incidence and specificity of antibiotic resistance in that a pathogen causing a major health problem in one country might be almost non-existent in another. Of particular concern is the emergence of highly virulent and/or multi-drug resistant bacterial strains such as *C. difficile* 027, MDR and XDR tuberculosis and acinetobacter.

In order to control the development and spread of antibiotic resistance it is necessary to understand how the antibiotic works, the resistance mechanism(s), the species of bacterium and the host. Promising avenues for future discovery include antibacterial peptides, fatty acid inhibitors, efflux inhibitors, inhibitors of metal-lactamases, phage therapy and antisense molecules.

"Bug Meets Immunity: Prospects for novel vaccines and immunotherapies" – *Dr. Lorne Babiuk, VP research, University of Alberta, Canada.*

The presentation focused on the role of vaccines and immune modulation in the control and prevention of infectious diseases. Exposure to the foreign antigens of an invading pathogen can trigger an immediate (within hours) innate immune response and/or a longer term (in days) acquired immune response as the immune system attempts to eliminate the infectious agent. The type of response generated, e.g. humoral or cellular, is critical in determining disease course and can be modified by immune modulators such as CpG, host defence peptides and polyphosphazenes. CpG, for example, has been shown to significantly protect chickens from *E. coli* infection using a single dose over a one microgram threshold. Similarly, CpG has been shown to protect lambs against parainfluenza-3 virus infection and can also be used as an adjuvant in cattle to improve vaccine effectiveness. In studies using CpG as an adjuvant in vaccines to protect against Respiratory Syncytial Virus in mice and calf model systems, it was shown that the addition of CpG modulated the ratio between the IgG1 and IgG2 responses (a good indicator of a T-cell response) and reduced the IgE response, reducing the potential for adverse side effects.

Polyphosphazenes are an example of a novel delivery model and are active in soluble and microsphere form with a wide range of antigens in humans and animals. They dramatically reduce the antigen dose required, stimulate a long lasting immune response and have been proven to be safe and well tolerated in humans. The mode of action is through cytokine secretion, specifically among the interleukins and interferons.

By combining CpG and Polyphosphazenes a synergistic response is generated that enhances the immune response more than a hundredfold. By using polyphosphazene microspheres, the response can be further enhanced and broad mucosal immunity can be induced, via an increase in antibody-secreting cells. By combining cationic peptides with CpG and Polyphosphazenes in a triple combination of adjuvants and formulation the potential exists for single dose protection.

"Bug Genome Meets Human: Susceptibility, virulence and pathogenesis" – *Professor Gadi Frankel, Department of Biochemistry, Imperial College, UK.*

Dr. Frankel gave a detailed account of his research on enteropathogenic (EPEC) and enterohaemorrhagic (EHEC) *E. coli* and the relationship between attaching and effacing lesion formation and actin polymerization. *E. coli* was first discovered in Germany in 1885 and in 1945 strain *E. coli* 0111 was determined to be the cause of an infantile diarrhoeal outbreak in the UK. From that point, the term EPEC was used to describe *E. coli* serotypes associated with diarrhoeal outbreaks and it was eventually discovered that EPEC colonization of the small bowel produced characteristic histopathological attaching and effacing (A/E) lesions. In 1989, a fluorescent actin staining test was developed as a diagnostic for EPEC following the discovery that actin polymerisation is an integral part of the cell-adhering process.

In the last 20 years evolving molecular technologies have enabled entire genome sequencing and a detailed analysis of the pathogenesis of EPEC and EHEC infection and colonization, including highly virulent strains such as *E. coli* 0157. In recent years much research has focused on actin polymerization and the host cell cytoskeletal rearrangements resulting in the formation of a pedestal beneath the adherent bacterium and localized destruction of microvilli. The capacity to form A/E lesions is encoded mainly by the locus of the enterocyte effacement (LEE) pathogenicity island and its distribution suggests that it was acquired multiple times during the evolution of these pathogens.

The research presented demonstrated an extremely sophisticated understanding of the pathogenic processes in these bacteria which has resulted in a challenge to the accepted dogma of EHEC induced actin polymerization. Despite decades of study on actin polymerization there are still significant gaps in our understanding of how it relates to lesion formation and it is becoming clear that cultured epithelial cells represent a poor model for the infection of mucosal surfaces in vivo. Continued research in appropriate animal mode systems will hopefully provide the answers.

"Beating the Bug: Novel approaches to treating infections" – *Dr. Bob Hancock, University of British Columbia, Canada.*

Cationic peptides are a naturally-occurring defence mechanism in bacteria, insects, plants, fish, birds, amphibians, crustaceans and mammals (including humans), and demonstrate both antimicrobial and non-antimicrobial activities. In nature, most antibacterial peptides are small, and broad spectrum although many demonstrate only weak direct antimicrobial activity. For example, peptides isolated from the Horseshoe Crab demonstrate excellent activity against a wide range of bacteria, including *E. coli*, *Salmonella typhimurium*, *Pseudomonas aeruginosa*, MRSA, the fungus *Candida albicans* and even the HIV virus, while small bovine peptides have the same range of activities but are much weaker. A bovine derived peptide with activity against catheter-associated infections is already in Phase III clinical trials. Faced with increasing antibiotic resistance and declining production of new antibiotics (only two new classes in the last 44 years), cationic peptides represent a promising avenue for improving on nature's own response. By taking a small peptide (e.g. 8 amino acids) and substituting one amino acid at a time it is possible to build more potent peptides. To date, thousands of peptides have been built and used to further design peptides with excellent broad spectrum activity against most superbugs using artificial intelligence methods. Research shows these peptides can prevent infection. In addition to these direct activities, peptides can also selectively modulate the innate immune response causing up-regulation of protective innate immunity, while down-regulating potentially harmful inflammation. A bovine-derived peptide IDR-1, which lacks direct antibacterial activity was shown to reduce or eliminate infections in mice to a variety of bacteria (including MRSA and VRE), if administered up to 48 hours before infection or up to 6 hours after infection via a variety of routes, with no apparent harmful side effects.

These results offer promise for the role of peptides as potent immune modulators either on their own or as an adjunct to sub-optimal doses of traditional antibiotics. Using sophisticated visualization strategies to examine complex innate immunity networks it is possible to gain an understanding of the mechanisms in play and the many contributing pathways. Selective boosting of innate immunity represents a promising new therapeutic approach to treating infections.

Keynote Address: A Canada-UK Workshop – Beating the Bug – *Sir Leszek Borysiewicz, Chief Executive, Medical Research Council, UK.*

Sir Leszek's presentation gave participants, especially the Canadians, some insight into the UK MRC, the status of health research in the UK, the funding mechanisms in place and the potential opportunities for UK/Canada collaborations. The UK MRC and CIHR, both of which are funded by tax-payers dollars, have many commonalities, including a mandate to fund excellent science likely to lead to improvements in human health; a focus on both chronic and infectious diseases; a need to constantly evaluate research progress and the translation of this knowledge into improved practices; and the flexibility to respond rapidly to change. Change in the UK has been largely driven by a series of comprehensive reports, ending with the recent "Cooksey Review" released in 2006, which examined the state of the health care system and the role that health research plays in addressing key issues. Many of the recommendations in the "Cooksey Review" are the same as those coming out of the CIHR five-year international review – namely to continue the support of basic research while at the same time placing more emphasis on: knowledge translation and applied research; strategic coordination between organizations; and improved models for drug development. Following the release of the "Cooksey Review," the Office for Strategic Co-ordination of Health Research (OSCHR) was created to bridge the gap between discovery and delivery through the development of multidisciplinary strategic teams able to address translation gaps and the creation of joint review panels with other government departments. UK MRC funding for 2007/08 is just over £500 million (Can $1 billion) and is expected to increase by 30% by 2010/11. Of this funding, roughly half supports intramural research in UK MRC's institutes and units, and half supports extramural research including £40 million (Can$80 million) to respond to new strategic initiatives from the research community.

The UK MRC has already worked with CIHR particularly in addressing global health issues and chronic diseases such as cancer, cardiovascular disease, respiratory diseases and Type 2 diabetes. One of the key focus areas is prevention strategies and behaviour change, which would include behaviour changes required in antibiotic prescribing practices and public demand. Sir Leszek encouraged the UK and Canadian researchers to learn from each other and promote interactions through

new collaborations and partnerships. The final message was that if our researchers come together in innovative projects likely to make an impact on the global stage and that clearly demonstrate the value of collaboration, strategic funding may be possible.

Breakout Session 1

Participants were assigned to one of four teams, each with an equal balance of UK and Canadian researchers, and asked to identify two or three themes that might be appropriate for UK/Canada collaborations. Each team was encouraged not to limit themselves to the expertise in the group but to also consider additional researchers in both countries who they felt could make a valuable contribution. The aim of the exercise was to generate a maximum of 12 potential research themes that could be condensed to three or four overarching topics for further discussion on day 2. Each team was provided with an electronic reporting template and asked to identify a different presenter for each of their chosen themes. In total the following twelve themes were identified:

- ***Disarming the pathogen*** – *modifying virulence and antibiotic resistance using peptides, small molecule inhibitors, novel immune modulators, vaccines*
- ***Elucidating pathogen-host systems*** – *create infrastructure for systems biology approaches e.g. databases; perturb the system with pathogens and examine the influence of antibiotics; correlates of protection; create, test and refine models*
- ***Antibiotic adjuvants*** - *does not require new antibiotics and may improve use of existing ones; natural produce may sensitize bacteria to existing antibiotics; combinations of small molecule drugs with antibiotics*

- ***Immune modulators*** *– peptides and other immunomodulatory molecules; probiotics; vaccine adjuvants to improve existing vaccines*

- ***Phage as alternatives to antibiotics*** *– phage adapts quickly and works on XDR strains; can use phage products of whole phage; diagnostic applications; basic questions need to be addressed*

- ***Systems biology of antibiotic action and resistance*** *– poorly understood beyond single gene level; antibiotics are metabolic inhibitors and possible coordination molecules; biofilms; global regulatory networks*

- ***TB – A paradigm for novel interventions*** *– biology of disease; diagnostics; treatment and management; pharmacology; therapeutic vaccines; novel therapies*

- ***Control and investigation of emerging resistance across the Atlantic*** *– preventing spread of resistance through education and behaviour change; epidemiology; management; rapid diagnosis; new treatments; optimising antibiotic use; new therapies; new vaccines*

- ***Transmission and persistence – infection control*** *– clinical and societal; rapid, quantitative diagnostics and mol. Epi; superspreaders (patients and bacteria); antimicrobial use and policy; colonization and decolonization; biofilms*

- ***A multidisciplinary approach to sepsis*** *– resistance in gram negative bacteria; reduction of incidence in targeted populations; epidemiology of resistance; diagnosis, antibiotic prescribing; novel treatments*

- ***Basic Biology*** *– mode of action, novel targets; physiology, metabolism and virulence; intrinsic and acquired resistance; experimental evolution; biofilms*

- ***Novel Therapies*** *- phage and phage derived therapies; vaccines, therapeutic antibodies; combinational approaches; new agents including immunomodulators; anti-virulence targeting e.g. biofilms*

During the reception and dinner, workshop participants were asked to sign up for the topic of greatest interest to them. Based on the sign-up sheets and the overlap between topics and taking into account the requirement for both UK and Canadian representation in each group, the themes were condensed into four broad groups (Red, Blue, Yellow and Green) for the breakout session on Day 2. Participants were allowed to change groups if they were not happy with their final placement.

DAY 2

PRESENTATIONS

The day began with four short presentations from CIHR, UK MRC, Wellcome Trust and the UK CRC to describe existing funding opportunities.

CIHR – *Dr. Bhagi Singh, Scientific Director of the CIHR Institute of Infection and Immunity.*

Dr. Singh described the CIHR mandate which includes developing strategic research agendas in collaboration with national and international partners. The Institute of Infection and Immunity (III), one of thirteen virtual Institutes, develops and supports strategic research programs to combat infectious and immune-based disease. III has five strategic priority areas: Emerging Infections and Microbial Resistance; HIV/AIDS; Immunotherapy; Pandemic Influenza Preparedness; and Vaccines of the 21st Century. III also supports strategic training programs associated with these five areas and Letters of Intent are due on April 1st 2008 for the next CIHR-wide competition. This program might be an appropriate vehicle for Canada/UK collaborations and workshop participants were advised to check the CIHR website for further details (*www.cihr-irsc.gc.ca*). The Canadian research environment is already highly collaborative with many ongoing national and international partnerships and there is a strong research base in microbiology. In addition, III has recently committed Can$10 million in support of a large strategic initiative entitled "Novel Alternatives to Antibiotics" which included a focus on immune modulation, novel bacterial agents, probiotics and bacteriophage therapy. Many of the researchers leading the projects funded under this initiative were present at the workshop.

UK MRC – *Dr. Peter Dukes, Head Infections and Immunity Board, MRC.*

As information regarding the UK MRC was presented in the earlier talk by Sir Leszek Borysiewicz, Dr. Dukes gave a very brief presentation, highlighting the funding currently supporting research into bacteriology, which resides primarily in the extramural program. Typically UK MRC grants in bacteriology are for three years but the community is being urged to consider larger scale, five-year multidisciplinary program grants which offer increased stability. Recent strategic priorities identified by the UK MRC include translational research, vaccine research, and clinical research collaborations. Additional funds are also available for influenza and global health research. With the new leadership at the UK MRC has come a reshaping of the budget and a push for big strategic ideas that are "outside of the box." UK/Canada partnerships in the area of antibiotic resistance may fit well into this category.

Wellcome Trust – *Rick Davis, Business development, Technology transfer Division, Wellcome Trust.*

The Wellcome Trust, established in 1936 with an endowment of £14 billion (making it second only to the Gates Foundation), is an independent research-funding charity with strong international presence and interests that range from science to the history of medicine. Wellcome Trust funds creative research through projects, programs, equipment and fellowship support and also technology transfer. Eligibility generally requires that the centre of gravity, i.e. the lead researcher, be based in the UK, but international collaborations are encouraged. In the technology transfer division, researchers from Europe, the US and India are eligible to apply in certain strategic areas. Under technology transfer, funding is provided to move technology or ideas forward to a point where further investment can be raised from external sources. Wellcome Trust has already invested in antimicrobial research by seeding drug discovery and encouraging commercial

application. Funded areas include rapid diagnostics; a vaccine for typhoid; antibiotics for *C. difficile*; bacterial cell wall inhibitors for MRSA; and, in partnership with GlaxoSmithKilne, a large program focused on drug resistant hospital infections. Wellcome Trust operates on a philosophy of being open to ideas from everyone in areas that are considered important - so workshop participants were encouraged to approach Wellcome Trust with innovative ideas and partnerships.

UK Clinical Research Collaboration (UKCRC) – *Dr. Jo Dekkers, Program Manager, UK CRC.*

UK CRC, a collaboration between the major funders of infection research in the UK, launched an initiative in translational infection research. In 2007 the initiative will provide up to £16.5 million (Can$33 million) for the support of Consortium Grants and Strategy Development Grants (SDG). In the first round of the launch, five SDG were funded and three Consortium grants were short-listed. The second round of the launch will be in January 2009 and there is the potential to involve Canadian collaborators in the Consortium Grant applications, which might represent another possible avenue for funding. The deadline for Consortia outlines is March 2009.

Breakout Session 2

In breakout session 2, each of the four groups was asked to identify specific opportunities within their chosen theme that would clearly benefit from a Canada/UK collaboration and then choose one of these topics as the basis for a hypothetical grant proposal. To help with the development of the proposal, each group was given the same set of questions to guide them and an electronic template of three PowerPoint slides to use for their report-back. The questions included: aim of the proposal; strategic/scientific rationale; potential impact; added value; the research plan; participants and their resources; required funding; and outputs and measures of success. After each group had presented their research proposal, everyone was asked to vote (by show of hands) for the project they considered to be the best and most likely to succeed. The presentations are summarized below.

Systems Biology of Antibiotic Action and Resistance – *Yellow Group*

This project aimed to use a systems biology approach to define the resistome of *E. coli* under specific environmental conditions in order to understand:

- *how multi-resistant strains emerge*
- *what happens upon the acquisition of mobile genetic elements*
- *how regulatory networks respond to antibiotic exposure*
- *how does the resistome vary between strains and between planktonic*
- *biofilm modes of growth*

Improved understanding of the mode of action of antibiotics is expected to generate novel targets/receptors. In addition, unique strains are available in the UK and Canada, so identifying the commonalities and differences leading to resistances may lead to novel therapeutic approaches and new drug modalities and combinations. The research plan included the assembly of the *E. coli* resistome in three characterized strains – UK specific, Canada specific and one common to both countries; sequencing of genomes, with and without plasmids; and the application of proteomics, transcriptomics, bioinformatics and metabolomics technologies to study the effects of various antibiotics. The group identified numerous collaborators in the UK and Canada, and identified industry, the Gates Foundation and the Wellcome Trust as potential partners. Funding requested was $2 million per year for five years.

The Ultimate Network: the bacterial cell wall – *Blue Group*

The aim of this project was to undertake the systematic development of a community toolbox for cell wall analysis (from assay development for individual enzymes to the analysis of intact bacteria) that will lead to new understanding and eventual drug development. The cell wall is a validated and universal target with many facets, including an immune modulation role, that have been poorly exploited due to lack of basic information. Expertise is fragmented both in Canada and the UK, so a collaborative venture would:

- *harness the synergy*
- *address neglected areas of research*
- *identify new connections among systems*
- *validate a model system for systems biology that can be perturbed by small molecules*

The group identified numerous potential collaborators both in Canada and the UK, with a wide range of complementary expertise and resources. The project would make a quantum leap in our basic understanding leading to new therapeutics targeting cell wall biosynthesis. Resources requested included:

- *Network support for activities including an international meeting for peptidoglycan aficionados*
- *Collaborative grants (UK and Canada with capacity to integrate) and funding for face-to-face catch ups*
- *Training grants and mobility resources to bring more trainees into the field*
- *Support for centralized facilities to create, develop and distribute reagents and to provide highly skilled analytical services*

Immunomodulators for Controlling Antibiotic Resistant Infections – Green Group

Given that antibiotics are failing and, even when effective, do not address the inflammatory component associated with infection, this group proposed to create a network for the evaluation of novel small molecular immunomodulators. A consortium style approach was proposed, which would build on existing synergies between Canada and the UK, avoiding duplication and leverage ideas and funds. Such a consortium would:

- *Dramatically reduce the burden of infectious disease*
- *Lead to the development of low cost delivery of therapeutics for developing countries*

- *Circumvent therapeutic failures due to antibiotic resistance.*
- *Change medical practices*

The first steps would be to identify additional participants, inventory assets and organize a workshop to determine focus (e.g. organisms, types of immunomodulators, animal models, translation strategy and key deliverables). Many participants from both countries were identified. Funds requested were $2-5 million per year for five years and outputs were described as innovative therapeutics, leverage of expertise and resources, sustainable collaborations and linkages with commercial partners and foundations.

Global Challenge: Preventing resistant infections – Red Group

This group proposed moving from reactive to predictive models which would have a major impact on preventing the emergence of antibiotic resistance (saving lives and costs), and would likely be of great interest to policy makers. To accomplish this aim, the group planned to:

- *Address the knowledge gap - current knowledge is hospital based*
- *Characterize the epidemiology and ecology of resistant pathogens*
- *Identify reservoirs and routes of transmission – environment, community and healthcare*
- *Establish robust sampling frames in Canada, the UK and globally*
- *Develop the basis for effective intervention strategies*

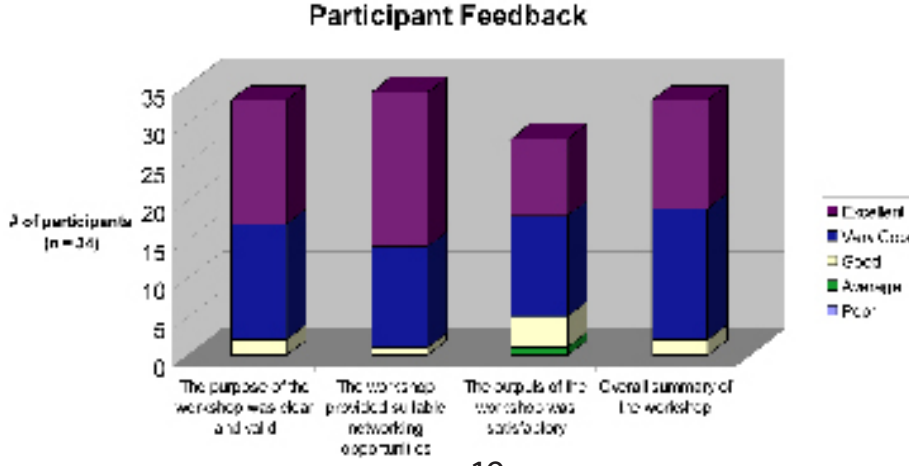
The project would take advantage of complementary expertise to provide better information for infection control, leading to better use of antibiotics in both countries and developing new, standardized technologies to improve health. The first step would be to further develop a strategy and identify one or two exemplar projects within the program.

Summary and Path Forward

The workshop provided a mechanism with which to explore the potential for UK/Canada collaborations in the field of antibiotic resistance. Participants embraced the opportunity to meet new colleagues and learn from each other of potential opportunities for partnership. There appeared to be a genuine desire to proceed to the next step and build on the collaborations formed at the workshop to include additional interested researchers with complementary expertise and resources. Many participants were already discussing the opportunities presented during the workshop and were anxious to investigate existing funding opportunities. Several research themes were identified, with strengths in both countries, that participants felt would benefit from UK/Canada collaborations. At the end of the workshop, the funders met briefly to discuss possible next steps and to plan a course of action that would build on the momentum created by the workshop to facilitate the creation of a UK/Canada funding opportunity of benefit to both countries. Details will be forthcoming in the near future.

Workshop Evaluation

Before leaving, participants were asked to fill in an evaluation form to assist the organizers in assessing the success of the workshop, identifying areas of strengths and weakness, and to inform the planning of similar workshops in the future. The workshop evaluation was overwhelmingly positive, with 31 of 34 respondents indicating their overall satisfaction with the workshop as 'very good' or 'excellent.' Participants indicated that the workshop was a great opportunity for networking, that the workshop's purpose was clear and valid, and that the desired outputs of the workshop were achieved to a satisfactory level. Many participants also highlighted the strong possibility for collaboration arising from the workshop. In one participant's words: "*This workshop provided an excellent opportunity to meet people with related interests. I believe useful collaborations will arise from this.*"

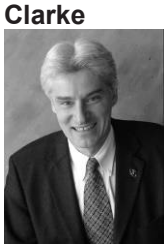


Appendix 1

Canada/UK Participants List – February 6-7, 2008

Canadian participants

Name	Affiliation	Area of Research	Theme
Yossef Av-Gay 	University of British Columbia Division of Infectious Diseases Room 440D HP East 2733 Heather St. Vancouver, BC V5Z 3J5 604-603-1806 yossi@interchange.ubc.ca	Genetics, TB; Mycobacterium tuberculosis (Mtb); novel methods to identify inhibitors by screening large numbers of compounds to identify those that make Mtb antibiotic sensitive; Protein Kinases as novel drug targets for TB Therapeutics, innate resistance provided by Mycothiol.	Resistance: Molecular Determinants
Lorne Babiuk 	University of Alberta 3-7 University Hall Edmonton, AB T6G 2J9 780-492-5353 lorne.babiuk@ualberta.ca	Vaccines, innate immunity, novel vaccine development, infectious diseases	Immune systems
Michel G. Bergeron 	Université Laval Centre de recherche en infectiologie du CHUL 2705, boul. Laurier Québec City, QC G1V 4G2 418-654-2705 Michel.G.Bergeron@crchul.ulaval.ca	Rapid DNA diagnostic tests for the detection of microbes; Development of compact disc (CD) which can detect nucleic acids (Point-of-care test); Microbicides (Invisible Condom®); Immunotargeting of HIV in lymph mode.	Resistance: Molecular Determinants
Edith Blondel-Hill 	British Columbia Children's Hospital Department of Laboratory Medicine 2G5 4500 Oak Street Vancouver, BC V6H 3N1 604-875-2345 ext 7649 ebhill@cw.bc.ca	Antimicrobial utilization; guideline and policy development for antibiotic use and prescribing; mechanisms of resistance; susceptibility testing.	Resistance and infection control: Clinical and Social Determinants

Name	Affiliation	Area of Research	Theme
Judith Bray 	CIHR – Institute of Infection and Immunity (III) Room 97, 160 Elgin Street Address Locator: 4809A Ottawa, ON K1A 0W9 613-954-7223 jbray@cihr-irsc.gc.ca	The CIHR Institute of Infection and Immunity (III) supports research and helps to build research capacity in the areas of infectious disease and the body's immune system. Through the Institute's programs, researchers address a wide range of health concerns related to infection and immunity including disease mechanisms, disease prevention and treatment, and health promotion through public policy.	Organizing Committee
Lori Burrows 	McMaster University Dept. of Biochemistry and Biomedical Sciences 4H18 Health Sciences Centre 1200 Main Street West, Hamilton, ON L8N 3Z5 905-525-9140 ext. 22029 burrowl@mcmaster.ca	Type IV pili and type II secretion systems in Pseudomonas aeruginosa; the role of peptidoglycan structure in expression of secretion and motility systems; biofilm formation and prevention; and development of novel antimicrobial compounds.	Novel Therapies
Anthony Clarke 	University of Guelph Science Complex Guelph, ON N1G 2W1 519-824-4120 ext. 53362 aclarke@uoguelph.ca	Enzymology of peptidoglycan metabolism; mechanism of action of penicillin-binding proteins; pathways for O-acetylation and de-O-acetylation of peptidoglycan; structure-function relationship and mechanism of action of lytic transglycosylases; bacterial resistance to beta lactam antibiotics; broad spectrum beta lactamase inhibitors; interaction of beta lactamases with beta lactam antibiotics and with inhibitors.	Resistance: Molecular Determinants
Alan Davidson 	University of Toronto Department of Biochemistry, and Dept. of Molecular Genetics Medical Sciences Building Room 4285 1 King's College Circle Medical Sciences Building Room 5207 Toronto, ON M5S 1A8 416-978-0332 alan.davidson@utoronto.ca	Antibiotic resistance; bacteriophage therapy, specialized phage-tail structures called pyocins that are produced by Pseudomonas bacteria; novel antibacterial therapies for the pathogens Pseudomonas aeruginosa and Staphylococcus aureus.	Novel Therapies
Julian Davies 	University of British Columbia (Professor Emeritas) Department of Microbiology and Immunology Life Sciences Institute 2350 Health Sciences Mall Vancouver, BC V6T 1Z3 604-822-5856 jed@interchange.ubc.ca	Microbial ecology; origins and mechanisms of antibiotic resistance in bacteria; gene capture and horizontal gene transfer; degradation pathways of xenobiotics and lignin-derived products by streptomycetes; non-cultivable bacterial species; genes for antibiotic biosynthetic pathways; isolation of novel secondary metabolites for pharmaceutical application; novel antibiotics; resistance mechanisms; xenobiotic degradation; the biology of antibiotics (discovery, production, function, and resistance); mechanisms of horizontal gene transfer and environmental microbiology.	Resistance: Molecular Determinants

Name	Affiliation	Area of Research	Theme
Jonathan Dennis 	University of Alberta Department of Biological Sciences CW 405, Biological Sciences Centre M 354, Biological Sciences Bldg. Edmonton, AB T6G 2E9 780-492-2529 jon.dennis@ualberta.ca	Bacteriophages; Burkholderia cepacia complex and their phages; Phage aerosols; Efflux pumps; Antibiotic resistance and solvent tolerance; Mobile genetic elements; Plasmids.	Novel Therapies
Jennifer Gardy 	University of British Columbia CMDR - Room 222A 2259 Lower Mall Vancouver, V6T 1Z4 604-827-4005 jennifer@cmdr.ubc.ca	Pathogenesis of innate immunity; host defence peptides; database creation – key genes, proteins and interactions; systems biology; computational modelling, perturbations of innate immune networks.	Immune Systems
Bob Hancock 	University of British Columbia Centre for Microbial Diseases and Immunity Research Lower Mall Research Station, UBC Room 232 - 2259 Lower Mall Vancouver, BC V6T 1Z4 604-822-2682 bob@cmdr.ubc.ca	Gram-negative bacterial surfaces; antibiotic uptake and resistance; host defence (antimicrobial) peptides (a component of the immune system that kills bacteria); genetics/genomics of P. aeruginosa; selective modulation of the innate immune response; novel therapeutics based on the immunomodulatory and antibiotic activities of host defence peptides; regulation of resistance and virulence.	Novel Therapies
David Heinrichs 	University of Western Ontario Room 215 Sieben's Centre London, ON N6A 5C1 519-661-3984 deh@uwo.ca	Novel anti-infective therapeutics that can both treat and prevent S. aureus (particularly MRSA) infections: S. aureus pathogenicity; identification and validation of highly selective targets that are essential in the acquisition of iron, the critical nutrient for S. aureus, from the infected host; development and validation of therapeutic antibodies against these iron acquisition targets that will prevent the pathogen's ability to survive in the host.	Novel Therapies
Walid Houry 	University of Toronto 1 King's College Circle Medical Sciences Building, Room 5308 Program in Proteomics and Bioinformatics Department of Biochemistry Toronto, ON M5S 1A8 416-946-7141 walid.houry@utoronto.ca	Molecular chaperones; proteases; self-compartmentalizing cylindrical serine protease - ClpP; activators of cylindrical proteases (ACP) as a novel class of antibiotics.	Novel Therapies

Name	Affiliation	Area of Research	Theme
Allison McGeer 	Mount Sinai Hospital, Toronto Department of Microbiology Room 210 600 University Ave Toronto, ON M5G 1X5 416-586-3118 amcgeer@mtsinai.on.ca	Prevention of serious bacterial and viral infections in adults; use of surveillance to answer research questions and change practice;. Prevention, diagnosis and treatment of infectious diseases; Clostridium difficile associated diarrhea (CDAD); creation of prediction rules for severe CDAD and also relapsing CDAD; definition of a group of high risk patients; new therapeutic strategies.	Resistance and Infection Control: Clinical and Social Determinants
Michael Mulvey 	University of Manitoba, Public Health Agency of Canada National Microbiology Laboratory Winnipeg, MB R3E 3R2 204-789-2133 michael_mulvey@phac-aspc.gc.ca	Monitoring the emergence of antimicrobial resistant organisms (AROs) in our hospitals and communities including MRSA, C. difficile, VRE. ESBLs, multidrug resistant (MDR) Acinetobacter, Salmonella and S. pneumoniae, and Neisseria gonorrhoeae; AROs in northern communities including antimicrobial prescribing patterns; molecular epidemiology of AROs; development of an educational programs aimed at both health care providers and individuals in the community in an attempt to reduce the prevalence of AROs; proteomics and genomics studies involving epidemic MRSA, C. difficile, and Salmonella Typhimurium DT104.	Resistance and Infection Control: Clinical and Social Determinants
Marc Ouellette 	Université Laval Centre de recherche en infectiologie CHUQ-pavillon CHUL 2705 bou. Laurier Québec City, QC G1V 4G2 418-654-2705 Marc.Ouellette@crchul.ulaval.ca	Antimicrobial resistance; mechanisms of resistance in the parasite, Leishmania and the bacteria Streptococcus pneumoniae; development of new tools to diagnose resistance and novel targets for new drugs; novel pathways; potential therapeutic and diagnostic targets; phage therapy; Whole genome analysis.	Novel Therapies
Subash Sad 	National Research Council – University of Ottawa Research Officer, Immunomodulation NRC Institute for Biological Sciences (IBS) 1200 Montreal Road, Bldg. M-54, Room 127 Ottawa, ON K1A 0R6 613-993-6015 subash.sad@nrc-cnrc.gc.ca	Innate immune mechanisms, cytokine biology, immune regulation, immune evasion, control of intracellular pathogens, novel lipid-based alternatives to antibiotics, adaptive immune mechanisms, novel vaccine delivery vehicles, cellular immunology, genomics, lipid chemistry.	Immune Systems

Name	Affiliation	Area of Research	Theme
Bhagi Singh 	Scientific Director – CIHR Institute of Infection and Immunity (III) University of Western Ontario The Siebens-Drake Research Institute 1400 Western Road, Room #224 London, ON N6G 2V4 519-661-3228 bsingh@uwo.ca	The CIHR Institute of Infection and Immunity (III) supports research and helps to build research capacity in the areas of infectious disease and the body's immune system. Through the Institute's programs, researchers address a wide range of health concerns related to infection and immunity including disease mechanisms, disease prevention and treatment, and health promotion through public policy.	Funder - CIHR
David Speert 	University of British Columbia Rm 377 Res Ctr 950 W 28th Av Vancouver, BC V5Z 4H4 604-875-2438 dspeert@cw.bc.ca	Innate host defenses; microbial determinants of pulmonary pathogenesis; lung infections in patients with cystic fibrosis; Pathogenesis of Pseudomonas aeruginosa; pathogenesis of Burkholderia cepacia complex; innate host defense mechanisms, particularly of the lung; molecular epidemiology of bacterial infection; role of macrophages, polymorphonuclear leukocytes and dendritic cells; the role of specific receptor-ligand interactions; biofilm formation/quorum sensing; molecular epidemiology.	Immune Systems
Donald Weaver 	Dalhousie University Departments of Medicine (Neurology) and Chemistry Halifax, NS B3H 4J3 902-494-7183 donald.weaver@dal.ca	Drugs which can be prescribed in combination with antibiotics to better fight infections; gram-negative bacteria, compounds that interfere with the upkeep of the outer membrane; overcoming resistance.	Resistance and Infection Control: Clinical and Social Determinants
Gillian Wu 	York University Lumbers Building 4700 Keele St. Toronto, ON M3J 1P3 1-416-7362100 (23070) gillwu@yorku.ca UK Contact: Visiting Fellow, Clare Hall, University of Cambridge Herschel Road, Cambridge CB3 9AL, UK Ph (from North America) 011 44 1223 332374	Generation of lymphoid diversity; polymporphisms in the immune system, especially in autoimmune diseases such as arthritis; determination of variations in responses to antigens including microbial and self antigens.	Immune Systems

UK participants

Name	Affiliation	Area of Research	Theme
Mike Barer 	University of Leicester mrb19@le.ac.uk	Clinical Microbiology; Tuberculosis; Chemotherapy of stressed and non--replicating bacteria; Mycobacterial lipid metabolism.	Susceptibility, Virulence and Pathogenicity
Weng Chan 	University of Nottingham weng.chan@nottingham.ac.uk	Quorum sensing modulators; virulence modulators; anti-infective agents; Gram-positive pathogens; Staphylococcus aureus; peptidomimetics; peptide chemical biology.	Novel Therapies
Derrick Crook 	University of Oxford derrick.crook@ndcls.ox.ac.uk	Adult infectious diseases and clinical microbiology and specialist training; bacterial infections caused by Streptococcus pneumoniae, Streptococcus agalactiae, Haemophilus influenzae and Staphylococcal species; epidemiology; population biology; antibiotic resistance elements; host genetic susceptibility.	Susceptibility, Virulence and Pathogenicity
Jo Dekkers 	Medical Research Council jo.dekkers@headoffice.mrc.ac.uk	Programme Manager for Infections and Immunity Board.	Funder
Brian Duerden 	Department of Health	Inspector of Microbiology and Infection Control at the Department of Health. Responsible for ensuring the quality and consistency of clinical and public health microbiology services.	Policy and Funder

Name	Affiliation	Area of Research	Theme
Peter Dukes 	Medical Research Council peter.dukes@headoffice.mrc.ac.uk	Board Programme Manager for Infections and Immunity Board	Funder
Chris Dowson 	University of Warwick c.g.dowson@warwick.ac.uk	Antibiotic resistance; bacterial pathogenicity; population genetics; molecular basis for the evolution of antibiotic resistance; chemotherapeutic agents or vaccination; regulation of the resistant phenotype, due to the acquisition of resistance determinants or cell physiology.	Novel Therapies
Mark Enright 	Imperial College London m.c.enright@imperial.ac.uk	Epidemiology of infections caused by bacteria; development of genetic tools to track 'superbugs' MRSA as they spread in human populations; evolution of antibiotic resistance.	Antibiotic Resistance
Gadi Frankel 	Imperial College London g.frankel@imperial.ac.uk	Host pathogen interaction and transmission, focusing on *E. coli* O157 and enteropathogenic *E. coli* (EPEC). Combining novel infection models and imagining methods to study type III secretion system (apparatus and effectors) and infection dynamics, mechanisms of bacterial attachment, colonisation and subversion of cell signalling.	Susceptibility, Virulence and Pathogenicity
Stephen Gillespie 	University College London s.gillespie@medsch.ucl.ac.uk	Tuberculosis; drug development; clinical trials; mathematical modelling of treatment effects; diagnostics for clinical trials.	Immunity, Vaccines and Immunotherapy

Name	Affiliation	Area of Research	Theme
Peter Hawkey 	Heart of England NHS Foundation Trust hawkeyp@heartsol.wmids.nhs.uk	Molecular evolution of lactamases, aminoglycoside inactivating enzymes and the TET(M) family of transposons; molecular typing methods and the molecular epidemiology of nosocomial bacteria.	Antibiotic Resistance
Andrew Hayward 	University College London a.hayward@pcps.ucl.ac.uk	Antimicrobial prescribing; antimicrobial resistance; primary care; acute respiratory infection.	Immunity, Vaccines and Immunotherapy
Ian Henderson 	University of Birmingham i.r.henderson@bham.ac.uk	Bacterial pathogens; class of virulence determinants; secreted virulence proteins; type V secretion.	Susceptibility, Virulence and Pathogenicity
Robin Howe 	University of Cardiff howera@cardiff.ac.uk		
Claire Kidgell 	Wellcome Trust	Science Programme Officer, Immunology and Infectious Disease.	Funder
Doug Lowrie 	NIMR dlowrie@nimr.mrc.ac.uk	The location and form of persister TB bacteria in murine models; the capacity of the bacteria that cause tuberculosis to persist in tissues; sensitive molecular probe technologies and mouse models of persistent infection.	Susceptibility, Virulence and Pathogenicity

Name	Affiliation	Area of Research	Theme
Alasdair MacGowan 	University of Bristol	Research focuses on infectious and immunological disease, in studies concerned with antibacterial resistance. The research is concerned with research on basic mechanisms of drug action and resistance, optimising the use of antibodies to reduce the likelihood of emergence of resistance, resistance epidemiology.	Antibiotic Resistance
Dietrich Mach 	University of Swansea d.mack@swansea.ac.uk	Staphylococcus epidermidis; medical biofilm disease; intravascular catheters or joint prostheses; S. epidermidis in surface adherent biofilms; polysaccharide intercellular adhesin (PIA); homoglycan of b -1,6 -linked N- acetylglucosamine residues; isogenic biofilm-negative icaA-insertion mutants expression of PIA and biofilm formation; essential virulence factors of S. epidermidis in foreign body infection models; isogenic biofilm -negative mutants with regulatory defects in transcription of icaADBC; allelic gene replacement analysis of regulatory gene loci.	Novel Therapies
William Maton-Howarth 	Department of Health William.maton-howarth@dh.gsi.gov.uk		
Laura Piddock 	University of Birmingham l.j.v.piddock@bham.ac.uk	Antibiotic resistance in enteric bacteria (Salmonella, Campylobacter, Escherichia coli); efflux pumps in both antibiotic resistance and pathogenicity.	Antibiotic Resistance
David Roper 	University of Warwick	Structural and molecular enzymology of antibiotic resistance mechanisms particularly in respect of Vancomycin and beta-lactam resistance. Biosynthesis of peptidoglycan in Gram positive and negative pathogens.	Antibiotic Resistance

Name	Affiliation	Area of Research	Theme
Peter Taylor 	London School of Pharmacy Peter.taylor@pharmacy.ac.uk	Novel Antibacterial Therapies; Natural Products with Antibacterial Activity; Overcoming Resistance to Antibiotics; MRSA; Complement; Bacterial Neonatal Meningitis; Bacteriophage Enzymes as Therapeutics; *Escherichia coli.*	Novel Therapies
Liz Wellington 	University of Warwick e.m.h.wellington@warwick.ac.uk	Characterisation of bacterial and fungal microorganisms in soil; analysis of bacterial gene expression; detection, quantification and activity of specific bacterial and fungal communities; pathogen survival in soil; analysis of soil microbial communities	Antibiotic Resistance
Paul Williams 	University of Nottingham paul.williams@nottingham.ac.uk	Bacterial cell-to-cell communication (quorum sensing), gene regulatory networks and the control of virulence and biofilm gene expression; post-transcriptional gene regulation; quorum sensing systems as antibacterial targets; discovery and development of novel antibacterial agents.	Novel Therapies
Neil Woodford 	Health Protection Agency	Reference bacteriology; resistance mechanisms; molecular epidemiology; susceptibility testing; antisense antibacterials.	Novel Therapies
Brendan Wren 	London School of Hygiene and Tropical Medicine brendan.wren@lshtm.ac.uk	Evolution of bacterial virulence; development of novel conjugate vaccines using protein glycan coupling technology; application of systems biology to understand host pathogen interactions.	Immunity, Vaccines and Immunotherapy
Wilma Ziebuhr 	Queen's University Belfast	Epidemiology of heathcare-associated biofilm-forming, multiresistant Staphylococci; mechanisms of genome flexibility and horizontal gene transfer; effect of subinhibitory antibiotic concentrations on gene expression and metabolism; novel antimicrobial compounds.	Antibiotic Resistance

Appendix 2

MRC Medical Research Council Leading science for better health

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

A Canada-UK Workshop: "Beating the Bugs"

A promotion of research collaborations on the themes of early identification of resistance and novel biological alternatives to today's antibiotics

February 6th and 7th, 2008

Hosted by: the Canadian High Commission in London
Canada House, Trafalgar Square, London, UK

AGENDA

Day 1 - Wednesday, February 6th

Time	Agenda Item	Presenter
9.00	**Registration and coffee**	
9.30	Welcome	James Wright, Canadian High Commissioner
9.35	Introductions and Objectives of the Workshop	Peter Dukes, UK MRC; Judy Bray, III
9.45	"Setting the Scene: Public Health Perspectives –Canada"	Michael Mulvey, Public Health Agency of Canada
10.05	"Setting the Scene: Public Health Perspectives – UK"	Brian Duerdan, UK Department of Health
10.25	"Finding the Bug: Controlling resistance through rapid (<1h) DNA-based diagnostics	Michel Bergeron, Canada
10.55	**Health Break**	
11.15	"Bug Meets Drug: Antibiotic resistance"	Laura Piddock, UK
11.45	"Bug Meets Immunity: Prospects for novel vaccines and immunotherapies"	Lorne Babiuk, Canada
12.15	"Bug Genome Meets Human: Susceptibility, virulence and pathogenesis"	Gordon Dougan, UK
12.45	"Beating the Bug: Novel Approaches to Treating Infections"	Bob Hancock, Canada
13.15	**Lunch – Networking Opportunity**	**All**

Day 1 - Wednesday, February 6th (continued)

Time	Agenda Item	Presenter
14.00	Breakout Session 1 – four groups according to theme	All
15.30	**Health Break**	
16.00	Report back from breakout groups and discussion	All
17.00	Keynote Address	Sir Leszek Borysiewicz, MRC
17.45	**Networking reception**	All
18.30	**Group Dinner** **After Dinner Talk: "Wonder Drugs and Super Bugs" - A Historical Perspective of Antibiotic Resistance**	**All** **Julian Davies, Canada**

Day 2 - Thursday, February 7th

Time	Agenda Item	Presenter
9.00	Welcome and re-cap of Day 1	Judy Bray, Canada; Peter Dukes, UK
9.15	Breakout Session 2	All
11.00	**Health Break**	**All**
11.30	Report back from four breakout groups, presentation of projects and vote for "best" project	All
12.50	Summary, Path forward and adjournment	Peter Dukes, UK; Judy Bray, Canada
13.00	**Lunch – Final Networking Opportunity**	**All**
14.00	**Private Meeting of Funding Agencies**	