18th Annual Infectious Diseases Research Day

&

5th Annual Canadian Center for Vaccinology Symposium

April 15, 16, 2013

Halifax

Sponsored by

Canadian Center for Vaccinology

Dalhousie Divisions of Infectious Diseases
of the Departments of Pediatrics and Medicine

Dalhousie Infectious Diseases Research Alliance

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Welcome

Lynn Johnston MD,FRCPC
Chief, Div of Infectious Diseases,
Dept of Medicine, Dalhousie U

Scott Halperin MD,FRCPC
Director
Canadian Center for Vaccinology

Rafael Garduño PhD
Director,
Dalhousie Infectious Diseases
Research Alliance

Welcome to the 18th Annual Infectious Diseases Research Day and 5th Annual CCfV Symposium.

We are very pleased to again offer a variety of speakers from faraway parts of Canada and also right here in Halifax. Our goal, as always, is to highlight Canadian research by established investigators and emerging new talent. The presentations you will see and hear cover bench research at a molecular level, through evaluation of treatments and products, to the essential translation of research into practice and programs that improve the health of Canadians. It is a celebration of research, the people who are inspired by research, and those who translate the evidence into front line practice.

A special note of appreciation to our longstanding corporate partners in research who have provided educational grants to this essential educational event. Their assistance ensures we can assemble renowned speakers, together with trainees and practitioners, to learn and better serve our communities.

As you watch and listen over the next two half days, we encourage you to ask questions of the presenters and share your new knowledge and insights with colleagues and friends. Let us know what you gained from this event, and how we can improve it in the future.

With thanks to….

This program was supported in part by educational grants provided by:

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Shelly McNeil
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Program

Monday April 15

1:00 – 2:00pm	Presentation – Brett Finlay PhD *E. coli O157: Why the XL foods recall should never have happened*	IWK Health Centre O.E. Smith auditorium
2:00 – 2:30pm	Presentation – Shelly McNeil MD *Monitoring influenza vaccine effectiveness: Experience of the PCIRN Serious Outcomes Surveillance Network*	
2:30 – 3:00pm	Presentation – Jason LeBlanc PhD *Targeting toxin: New strategies against Clostridium difficile*	
3:00 – 4:30pm	Poster judging (posters on display 1:00 – 5:30)	IWK Health Centre Gallery
4:30 – 5:30pm	Public presentation – Anna Taddio PhD *The 4 P's of managing needle pain in children*	IWK Health Centre O.E. Smith auditorium
5:45 – 7:00pm	Reception and presentation by Tom Marrie MD *Q fever: Lessons learned from Alberta*	Tupper Link Theatre A

Tuesday April 16

8:00 – 9:00am	TJ Marrie Lecture (Grand Rounds) – Brett Finlay PhD *Diarrhea, asthma, and the microbiota*	Halifax Infirmary RB Theatre
9:20 – 12:30pm	Oral Presentations (10)	1613 A-B Veterans' Hospital
12:30 – 2:00pm	Buffet lunch and presentation by Anna Taddio PhD *Developing a clinical practice guideline: the good, the bad and the ugly*	1613 A-B Veterans' Hospital

Speakers

Brett Finlay PhD

Dr. B. Brett Finlay is a Professor in the Michael Smith Laboratories, and the Departments of Biochemistry and Molecular Biology, and Microbiology and Immunology at the University of British Columbia. He obtained a B.Sc. (Honors) in Biochemistry at the University of Alberta, where he also did his Ph.D. (1986) in Biochemistry under Dr. William Paranchych, studying F-like plasmid conjugation. His post-doctoral studies were performed with Dr. Stanley Falkow at the Department of Medical Microbiology and Immunology at Stanford University School of Medicine, where he studied Salmonella invasion into host cells. In 1989, he joined UBC as an Assistant Professor in the Biotechnology Laboratory. Dr. Finlay's research interests are focused on host-pathogen interactions, at the molecular level. By combining cell biology with microbiology, he has been at the forefront of the emerging field called Cellular Microbiology, making several fundamental discoveries in this field, and publishing over 400 papers. His laboratory studies several pathogenic bacteria, with Salmonella and pathogenic E. coli interactions with host cells being the primary focus. He is well recognized internationally for his work, and has won several prestigious awards including the E.W.R. Steacie Prize, the CSM Fisher Scientific Award, CSM Roche Award, a MRC Scientist, five Howard Hughes International Research Scholar Awards, a CIHR Distinguished Investigator, BC Biotech Innovation Award, the Michael Smith Health Research Prize, the IDSA Squibb award, the Jacob Biely Prize, the prestigious Canadian Killam Health Sciences Prize, the Flavelle Medal of the Royal Society, the Queen Elizabeth II Diamond Jubilee Medal, is a Fellow of the Royal Society of Canada and the Canadian Academy of Health Sciences, is a Member of the German National Academy of Sciences, and is the UBC Peter Wall Distinguished Professor. He is an Officer of the Order of Canada and Order of British Columbia. He is a cofounder of Inimex Pharmaceuticals, Inc., and Director of the SARS Accelerated Vaccine Initiative. He also serves on several editorial and advisory boards, and is a strong supporter of communicating science to the public.

Anna Taddio PhD

Anna Taddio studied pharmacy at the University of Toronto and performed her doctoral research training in clinical pharmacology at The Hospital for Sick Children. Her research interests include the short-term and long-term effects of pain and pain management in infants and children undergoing painful medical procedures. Dr. Taddio has authored > 100 peer-reviewed articles and book chapters. She was recipient of a number of awards recognizing her achievements including a New Investigator Award from CIHR (2003), the Early Career Award by the Canadian Pain Society (2005), the Young Investigator Award by the International Association for the Study of Pain Special Interest Group on Pain in Childhood (2006), the Piafsky Young Investigator Award by the Canadian Society for Clinical Pharmacology (2006), the Mayday Fund Fellowship Award (2008) and the Noni MacDonald Award by the Canadian Paediatric Society (2012). Recently, she has been leading a national working group, the Help ELiminate Pain in KIDS Team (HELPinKIDS), studying and promoting effective pain management strategies during childhood vaccination. The HELPinKIDS Team has received awards by the Canadian Society for Pharmacology and Therapeutics (2011) and the Canadian Pain Society (2012) for scientific contributions and knowledge translation efforts related to childhood vaccination pain management. Dr. Taddio currently holds the positions of Associate Professor at the University of Toronto Leslie Dan Faculty of Pharmacy and Senior Associate Scientist at The Hospital for Sick Children in Toronto.

Shelly McNeil MD

Shelly McNeil is currently a Professor of Medicine and Pediatrics and an adult Infectious Diseases Consultant at the QEII Health Sciences Centre in Halifax, Nova Scotia, Canada. Dr. McNeil completed her medical education at Dalhousie University followed by a three-year residency in Internal Medicine at Dalhousie and a three-year fellowship in Infectious Diseases at the University of Michigan in Ann Arbor. Dr. McNeil returned to Dalhousie as an Assistant Professor of Medicine in 2000 and is currently cross-appointed as an Associate Professor of Pediatrics. She was promoted to Professor of Medicine effective July 1, 2012. Dr. McNeil is a Clinician Scientist at the Canadian Centre for Vaccinology, Halifax where her research focuses on immunization policy and program evaluation, the evaluation of the epidemiology of vaccine-preventable diseases in adults with a focus on the elderly and pregnant women, assessment of the effectiveness of vaccines in the prevention of serious outcomes in adults and clinical trials of new vaccines targeted at adolescent and adult populations. She is the Principal Investigator of the Serious Outcomes Surveillance Network of the Public Health Agency of Canada/Canadian Institutes of Health Research Influenza Research Network (PCIRN). Dr. McNeil was awarded the Dalhousie University Faculty of Medicine Clinical Research Scholar Award for the period 2005-2010. She is a member of the National Advisory Committee on Immunization (NACI), the Nova Scotia Infectious Diseases Expert Advisory Committee and the HPV and Rotavirus Working Groups of the Canadian Immunization Committee and Vice Chair of Immunize Canada.

Jason LeBlanc PhD

Dr. Jason LeBlanc received his B.S. and M.S. degrees in Biochemistry at the University of Moncton. His early training involved isolation of immunomodulatory peptides from *Lactobacillus*-fermented milk ("probiotics") to prevent pathogenic *E. coli* O157:H7 infection. In 2006, he earned his Ph.D. from the Department of Microbiology and Immunology at Dalhousie University, where he studied the molecular mechanisms regulating oxidative stress responses in *Legionella pneumophila*. After completing his Ph.D., Dr. LeBlanc continued his training in clinical microbiology earned certifications as a Fellow of the Canadian College of Microbiologists and the American Board of Medical Microbiology. He currently holds the position of co-Director of Immunology, Virology, and Molecular Epidemiology in the Division of Microbiology at Capital Health. Dr. LeBlanc is an Assistant Professor in Department of Pathology and is appointed in the Departments of Medicine and Microbiology and Immunology, Faculty of Medicine, Dalhousie University.

Dr. LeBlanc's laboratory uses molecular engineering and structural mimicry to identify peptides capable of inhibiting toxins, such as toxins TcdA and TcdB of *Clostridium difficile*. Since current antibiotic therapy favors recurrences, and the emergence of hypervirulent strains associated with more severe disease, toxin-neutralizing peptides could lead to non-antibiotic based therapies or new prevention strategies against *C. difficile*.

Poster Presentations

(Presenter's name underlined)

Oral Presentations

(Presenter's name underlined) *Abstract* *Page*

9:30-9:45: *Marianne Stanford*[*†], Alecia MacKay[†], Valarmathy Kaliaperumal[†], Bithika Ray[†],Tara Quinton[†], Lisa MacDonald[†], Marc Mansour[†]. "Formulation in Depovax[tm] enhances the immunogenicity of recombinant protein based anthrax vaccines" 29 42

9:45-10:00: *Andrew M. Leidal*[1], David P. Cyr[1], Richard J. Hill[1], Patrick W.K. Lee[1,2] and Craig McCormick[1]. "Subversion of Autophagy by Kaposi's Sarcoma-Associated Herpesvirus Impairs Oncogene-Induced Senescence" 30 43

10:00-10:15: *Cara S. MacRae*, Sarah M. McAlpine, Michelle Warhuus, Todd F. Hatchette. "A Genetic Analysis of the Mouse Adaptation of Human Pandemic H1N1 (A/CALIFORNIA/07/09)" 31 44

10:15-10:30: *N.W. Whelan*[1], A. Steenbeek[1], R. Martin-Misener[1], J. Scott[2], H. D'Angelo-Scott[3], and B. Smith. "A Retrospective Review of the School-Based Human Papillomavirus (HPV) Immunization Program: Evaluating the Effects of Public Health Nursing Engagement Strategies With Schools, Parents and Youth on HPV Vaccine Uptake in Greater Halifax" 32 45

10:30-10:45: *Shelly McNeil, MD*[1,2], Simon RM Dobson, MD[3], Marc Dionne[4], Meena Dawar, MD[3], Gina Ogilvie, MD[3,5], Mel Krajden, MD, PhD[3,5], Chantal Sauvageau , MD[4] , David W Scheifele, MD[3], Tobias R Kollmann, MD, PhD[3], Scott A Halperin, MD[1], Joanne M Langley, MD[1], Julie A Bettinger, PhD[3], Joel Singer, PhD[3], Deborah Money, MD[3], Dianne Miller, MD[3,6], Monika Naus, MD[3,5], Fawziah Marra, Pharm D[3.5], Eric Young, MD[81]Canadian Center for Vaccinology, IWK Health Centre and Capital Health, Dalhousie University, [2]Dept. of Medicine, Capital Health, [3]Vaccine Evaluation Centre, University of British Columbia, [4]Centre de Recherche du CHUL (CHUQ), [5]British Columbia Centre for Disease Control, [6]BC Cancer Agency, [7]British Columbia Ministry of Health. "Responding to Public Health Need: A Multicentre Canadian Trial to Assess the Immunogenicity of a 2 Dose Schedule of Human Papillomavirus Vaccine in Young Adolescents Compared to 3 Doses in Young Women" 33 46

10:45-11:00 Refreshment Break

Abstracts

1. *Shigella flexineri* effector OspG affects mortality in a murine model of infection

Angela Daurie, John Rohde

Affiliation: Dalhousie University, Halifax

The author requests that this abstract not be published

2. Characterization of the Viable but Non-Culturable *Legionella Pneumophila* in Water and the Role of 3-Hydroxybutyrate Dehydrogenase in its Formation

B. Al-Bana[1], M. Haddad[1], A. Cohen[4], S. Lee[1,3,5], R. Garduño[1,2]

Affiliation: Dalhousie University, Department of Microbiology & Immunology[1], Department of Medicine[2], Department of Paediatrics[3], Proteomics Core Facility[4], Canadian Centre for Vaccinology[5]

Introduction: *Legionella pneumophila* (*Lp*), the causative agent of Legionnaires' disease (LD), is an intracellular pathogen of freshwater protozoa. *Lp* has many morphological forms that fit within a developmental cycle. In water, *Lp* enters into a viable but non-culturable (VBNC) state, which is largely uncharacterized. VBNC *Lp* is suspected to be infectious to humans and to play a role in transmission of LD.

Methods: VBNC cells were produced from two developmental *Lp* forms, stationary phase forms (SPFs) and mature infectious forms (MIFs) by suspension in double deionized (dd) or tap water at 45°C. VBNC morphology was examined by electron microscopy and their ability to regain culturability was assessed by co-culturing with amoeba. VBNCs' environmental fitness was examined by testing their resistance to lysis by SDS and digestion by the ciliate *Tetrahymena*. The effect of added salts to dd water on *Lp* culturability was monitored. The protein profile of VBNCs was studied by SDS-PAGE and shotgun proteomics.

Results: Results showed that VBNCs have a unique morphology and that in tap water they lose their poly-β-hydroxybutyrate inclusion bodies. Both SPFs and MIFs lost culturability faster in dd than in tap water and addition of salts to dd water prolonged *Lp* culturability. However, MIFs retained higher viability in dd and tap water (85% and 51%, respectively) than SPFs (5% and 20%, respectively). Moreover, only ~1 cell out of 10^6 VBNCs from tap water regained culturability. VBNCs, except for those produced from SPFs in dd water, resisted digestion inside *Tetrahymena* and lysis by SDS. Proteomic analysis results showed that VBNC has an increased level of 3-hydroxybutyrate dehydrogenase (BdhA), which catalyses the oxidation of β-hydroxybutyrate to acetoacetate. BdhA role in VBNC formation was studied using *bdhA::km* mutant resulting in an early loss of culturability and a dramatic decrease in viability.

Conclusions: VBNC has a distinct morphology and physiology that varies with the developmental stage and the environmental conditions used. VBNCs have a different protein profile than the culturable *Lp*, suggesting a correlation with their unique physiology and adaptation. Moreover, BdhA seems to influence *Lp* survival and hence VBNC formation. These results provide a better understanding of *Lp* VBNC form and the factors influencing its formation.

3. Identification of peptide antagonists targeting toxins in clostridium difficile

B.-L. Rooney, J. Leblanc

Affiliation: Dalhousie University/Capital District Health Authority

Introduction: Pathogenesis of *C. difficile* is mediated by toxins TcdA and TcdB. This study aimed to identify toxin-neutralizing peptides.

Methods: Peptide libraries were synthesized to mimic the sequences of the receptor binding domains (RBD) of TcdA and TcdB from historical and hypervirulent strains of *C. difficile* (630 and Nap1, respectively). Each peptide was evaluated using cell culture cytotoxicity neutralization assays (CCCNA). Briefly, toxins were purified from broth-culture supernatants toxin-deficient mutants (TcdA+B- or TcdA-B+, respectively) or 630 and Nap1 parent strains (TcdA+TcdB+). Double mutants (TcdA-B-) were used as controls. Normalized toxins amounts were added to FSK or HT29 cells in presence or absence of each peptide. Cells were counted (n=1000) and cytopathic effect (CPE) was expressed as a percentage ± S.D. for triplicate values obtained in three independent experiments.

Results: In a dose-dependent manner, two peptides prevented TcdB-induced CPE. These had identical sequences and were derived from distinct libraries. On FSK cells, the peptides completely inhibited toxins derived from TcdA- mutants or the parent strains. On HT29 cells (TcdA-sensitive), toxin inhibition was only observed with TcdB derived from the TcdA- mutants. Partial inhibition was observed with toxins from the parent strains. The residual CPE activity was attributed to TcdA since it was blocked with anti-TcdA antibody. No peptides were identified that could inhibit TcdA on FSK cells. However, the quantity of TcdA required to achieve CPE on FSK cells was ~10,000-fold more than TcdB, suggesting that a TcdA-sensitive cell line (i.e. HT29) or higher concentrations of peptides may be required. This hypothesis is currently being evaluated.

Conclusions: This study identified a peptide capable of inhibiting *C. difficile* TcdB *in vitro*. The use of peptide antagonists is a novel avenue of research that could lead to new adjunct therapies against *C. difficile* infection.

5. Regulation of host gene expression by ns1 protein of influenza a virus

Denys A. Khaperskyy[1], Todd F. Hatchette[2], and Craig McCormick[1]

Affiliation: [1]Department of Microbiology and Immunology, Dalhousie University, Halifax; [2]Department of Pathology and Laboratory Medicine, QE II Health Science Centre, Halifax

The author requests that this abstract not be published

6. Exploring Parental Acceptability of Rotavirus vaccine: Maritime Universal Rotavirus Vaccination Project

D.MacDougall[1,2], B.Halperin[1,3,5], K.Webber[1,4], P.Publicouver-Brouwer[1], S.Halperin[1,5,6,7]

Affiliation: 1. Canadian Center for Vaccinology, Dalhousie University, IWK Health Centre, Capital Health 2. St. Francis Xavier University, School of Nursing 3. Dalhousie University, School of Nursing 4. School of Health and Human Performance, Dalhousie University 5. Department of Pediatrics, Dalhousie University, IWK Health Centre 6. Department of Medicine, Dalhousie University, Capital Health 7. Department of Microbiology and Immunology, Dalhousie University,Halifax

Introduction: The National Advisory Committee on Immunization (NACI) recommends that all infants receive rotavirus vaccine (RV); but not all provinces/territories provide RV in universal, publicly funded programs. In a demonstration project, we compared public knowledge, attitudes, and beliefs (KAB) in a province with a public health (PH) nurse-delivered, universally funded, rotavirus vaccination program (URVP) (Prince Edward Island [PEI]) to a province with a physician–delivered URVP (Halifax metropolitan area, NS [H-NS])

Methods: Information about KAB of parents whose children were eligible for the URVP were collected through the use of two validated surveys distributed in public health clinics and physician's offices.

Results: After year 1, vaccine coverage for the first dose was over 90% in PEI (1372 live births) and approximately 25% in H-NS (4853 live births). Surveys were completed by 216 PEI and 170 H-NS parents of infants eligible for the URVP. Demographics were similar except for a more rural predominance in PEI and urban predominance in H-NS. 85.6% of PEI and 48.2% of H-NS respondents reported their infants received the RV. More PEI parents were aware of the NACI recommendation, were aware of the URVP, and reported that their health care provider discussed rotavirus infection and vaccine with them. Knowledge scores for both jurisdictions ranged from 50-70% correct for RV vaccine questions and over 70% for RV illness questions. Attitudes were similar in both jurisdictions but there was less concern with vaccine safety (74.5% vrs.65.8%) in PEI.

Conclusions: In general, attitudes and knowledge were similar in PEI and H-NS; however, more PEI respondents felt that their province was doing a good job providing information about the URVP and were comfortable about making a decision to receive the vaccine. Publicly funded vaccination programs are an important determinant of the public's perception of the importance of a vaccine.

7. Mechanistic target of rapamycin complex 1 regulation during Kaposi's sarcoma-associated herpesvirus lytic replication

Pringle, E.S., Leidal, A.M., McCormick, C

Affiliation: Department of Microbiology and Immunology, Dalhousie University

The author requests that this abstract not be published

8. Peptidoglycan deacetylase SFPGDA is involved in regulation of invasion and type three secretion in *Shigella flexneri*

Haila Kottwitz, Saima Sidik, Julie Ryu, John Rohde

Affiliation: Department of Microbiology and Immunology, Dalhousie University

The author requests that this abstract not be published.

9. AmyA is a Soluble Amylase Responsible for Starch-degrading Activity of *Legionella pneumophila* but not Essential for its Intracellular Differentiation

Hany Abdelhady[1], Peter Robertson[1], Rafael Garduño[1,2]

Affiliation: Department of Microbiology and Immunology[1], and Department of Medicine[2], Dalhousie University, Halifax

Introduction: *L. pneumophila* survives in freshwater habitats inside amoebae where it replicates and then differentiates into the highly virulent mature infectious forms (MIFs), and can accidentally infect human macrophages causing the non-communicable Legionnaires' disease (LD). It is known that *L. pneumophila* utilizes amino acids as primary energy and carbon sources for replication. However, it has been recently reported that it is also able to metabolize carbohydrates. Microarray studies have shown that the *lpg1669* (*amyA*) gene, which encodes an amylase (AmyA), is upregulated following *L. pneumophila* infections of amoebae, but not human macrophages. Here we test the hypothesis that *amyA* contributes to the full differentiation of *L. pneumophila* into MIFs in its natural environment.

Methods: An *L. pneumophila amyA* mutant (allelic replacement) was constructed and the transcription (RT- PCR) and the expression (western blot) of *amyA* gene in both wild-type and the *amyA* mutant were studied. The changes in *amyA* expression following *L. pneumophila* infections of the amoeba *Acanthamoeba castellanii*, the ciliate *Tetrahymena tropicalis*, and U937-derived human macrophages were quantified (quantitative RT-PCR). The morphology (electron microscopy) and the infectivity (intracellular growth) of both wild-type and the *amyA* mutant following amoebae and human macrophage infections were examined.

Results: *amyA* was not part of an operon and was not transcribed or expressed in the *amyA* mutant. *amyA* was upregulated inside amoebae and *T. tropicalis* but not human macrophages, suggesting a role in the full differentiation of *L. pneumophila* into MIFs. AmyA is secreted into the growth medium and is able to hydrolyse starch and dextrin. *amyA* mutant showed neither different morphological features nor growth defects *in vitro* (BYE broth), following infections of amoebae and human macrophages, or feeding of *Tetrahymena* ciliates.

Conclusions: Although not essential for *L. pneumophila* extracellular or intracellular growth or differentiation, *amyA* is expressed and upregulated during the intracellular replication of *L. pneumophila* in freshwater protozoa. Together, these findings show that *L. pneumophila* is able to utilize carbohydrates as an energy source.

10. Directed Trafficking Through the ER/Golgi Pathway to the Plasma Membrane by a Novel Polybasic Motif in the Reovirus p14 FAST Protein

H. B. Parmar, C. Barry, F.B. Kai and R. Duncan

Affiliation: Dalhousie University

Introduction: The reovirus fusion-associated small transmembrane (FAST) proteins are the smallest known membranefusion proteins. All FAST proteins are single-pass transmembrane proteins that traffic through the ER-Golgi pathway to the cell surface where they induce cell-cell membrane fusion. Protein traffic to the plasma membrane has important implications on human disease and virus replication, and the pathways and signals involved remain unclear. Here, we have investigated the role of the polybasic motif in the endodomain of the p14 FAST protein in terms of its functionality and trafficking properties. It is now clear that the p14 polybasic motif contains novel sorting signals required for Golgi export to the plasma membrane, one of the least understood steps in cellular protein trafficking.

Methods: Various p14 polybasic mutant proteins were created by site-directed mutagenesis and PCR based overlap- extension method. The fusion activity of all constructs was analyzed by syncytia formation assays, and cell surface expression was determined by flow cytometry. Subcellular localization of these p14 constructs was determined by confocal microscopy and endoglycosidase assays.

Results: Alanine substitution of the p14 polybasic motif led to a loss of plasma membrane localization and p14 accumulation in the trans-Golgi network (TGN), indicating the polybasic motif acts as a Golgi export signal. Further extensive mutagenesis of the polybasic motif indicated that the numbers of basic residues present in the polybasic motif are important for Golgi export. Also, membrane proximal polybasic motif act as a Golgi export signal while membrane distal polybasic motif act as an ER retention signal. Moreover, insertion of the membrane proximal polybasic motif into a Golgi resident protein mediated protein export from the Golgi to the plasma membrane suggesting universal role of the polybasic motif for Golgi export.

Conclusions: The p14 polybasic motif is involved in protein export from the Golgi complex to the plasma membrane and requires minimum of three basic residues for efficient export. This is the first example of such basic sorting signals, which presumably interact with cellular trafficking machinery to mediate protein export from the Golgi to the cell surface.

11. Infecting bone-marrow derived dendritic cells with *Shigella flexneri* causes down-regulation of CD40

Jessica Pickrem

Affiliation: Dalhousie University

Introduction: *Shigella flexneri* is a member of the Enterobacteriaceae family of Gram-negative bacilli, and is the causative agent of Shigellosis, or bacillary dysentery. Upon infection, *Shigella* invades the host colonic epithelium using a type III secretion system (T3SS) that is encoded by a large virulence plasmid. This secretion system injects protein virulence determinants, or "effectors" directly into the host cytosol where they interfere with host immune surveillance systems. The innate immune response to *Shigella* infection has been the subject of intense research. By comparison, there is little known about how *Shigella* may affect the adaptive immune system.

Methods: To investigate the interaction between *Shigella*-infected antigen presenting cells and adaptive immune cells, I used flow cytometry to monitor expression levels of surface molecules on *Shigella*-infected bone-marrow derived dendritic cells.

Results: I observed that wild-type *Shigella* down-regulated the surface expression of CD40, which is required for formation of the immunological synapse and dendritic cell activation. Avirulent *Shigella,* lacking the virulence plasmid, did not down-regulate CD40, nor did a mutant lacking the type III secretion apparatus. A third mutant deleted for *mxiE*, a major transcriptional regulator of T3SS substrates, also did not down-regulate CD40 levels.

Conclusions: Taken together, these data indicate that *Shigella* uses one or more substrates of the T3SS that are under control of MxiE to down-regulate CD40. These results pave the way toward understanding the adaptive immune response to *Shigella* and may prove useful in the search for a vaccine against Shigellosis.

12. The reovirus fast proteins subvert host exosome biogenesis to enhance cell-cell fusion

Jolene Read and Roy Duncan

Affiliation: Microbiology & Immunology Dept., Dalhousie University

Introduction: Exosomes are secreted membrane vesicles that carry payloads functioning in cell-cell communication. They can be distinguished from other extracellular vesicles by their endocytic origin, being released upon fusion of a multivesicular body with the cell membrane. Many enveloped viruses have evolved to hijack this pathway to mediate viral budding and egress. Non-enveloped viruses do not acquire host membrane and often exit cells via lysis, therefore it is unknown if they also exploit this pathway. Our research focuses on the non-enveloped, fusogenic reoviruses, which encode the Fusion-Associated Small Transmembrane (FAST) proteins, whose only function is to cause cell fusion. Since FAST proteins contain many hallmarks of proteins targeted to exosomes, we hypothesize that FAST proteins subvert the exosome pathway. Furthermore, we hypothesize that exosomes may play a functional role in cell fusion.

Methods: Extracellular vesicles were isolated from conditioned media from cells transfected with various FAST proteins via ultracentrifugation. The vesicles were characterized by western blotting and their role in cell fusion was determined by treating cells with purified vesicles.

Results: FAST proteins were found to be present in exosome-like vesicles in an N_{exo}/C_{endo} topology and were constitutively secreted throughout cell fusion. Isolated exosomal fractions, when added directly to naïve cells, induced cell fusion. Furthermore, treatment of fusing cells with dimethyl amiloride, an inhibitor of exosome-release, decreased overall fusion, while treatment with A23187, a potentiator of exosome-release, enhanced fusion, further suggesting a role for exosomes in cell fusion.

Conclusions: Taken together, we suggest that the FAST proteins are the first example of a protein from a non-enveloped virus to exploit exosome biogenesis. We propose the release of FAST proteins into the extracellular space via exosomes plays an important role in cell fusion. (1,984 characters)

13. Examining the Role of IpaH9.8 During Shigella Infection

Kaitlyn Tanner and John Rohde

Affiliation: Dalhousie University

The author requests that this abstract not be published.

14. Cost effective real-time PCR for the detection of varicella zoster virus

K. Binkhamis, T. Alsiyabi, T. Hatchette, J. Leblanc

Introduction: Molecular assays such as real-time PCR have become gold standard for the detection of viruses; however, their cost is far more expensive than virus culture. The major contributors to cost are the nucleic acid extraction (NAE) and the PCR reagents. Here, a low cost in-house real-time PCR for varicella zoster virus (VZV) was evaluated and the traditional NAE was replaced with a crude mechanical lysis: homogenization and heat treatment.

Methods: Using replicates of 10-fold serial dilutions (n=12), the limit of detection (LoD) and inter- and intra-assay variations were calculated for virus culture and direct immunofluorescence, real-time PCR following NAE, and the same real-time PCR following homogenization and heat treatment. Specificity was assessed using various organisms including herpes viruses. To assess the clinical performance of each method, 200 clinical specimens were compared to a modified gold standard (defined as 2 of 3 concordant results). Discordant results were resolved by second DNA extraction and using commercial quantitative real-time PCR. A cost analysis was also performed for all 3 methods.

Results: The real-time PCR assay was highly sensitive and specific for VZV. Using the NAE-based protocol, the LoD was between 3 and 18 copies per reaction, and for homogenization was ~18 copies per reaction. The LoD for virus culture was ~10,000-fold less sensitive than either molecular method. The clinical sensitivity for the real-time PCR following NAE was 100%, and 97.2% following homogenization. Virus culture was significantly less sensitive at 54.8%. All methods were highly specific.

Conclusion: While slightly less sensitive than NAE, homogenization coupled to an in-house real-time PCR provides a cost effective method for the detection of VZV, with performance characteristics far exceeding traditional virus culture and immunofluorescence.

15. Functional analysis of paralogous thiol disulphide oxidoreductases in *Streptococcus gordonii*

L. E. Davey, S. A. Halperin, S. F. Lee

Affiliation: Department of Microbiology and Immunology, Dalhousie University; Canadian Center for Vaccinology, IWK Health Centre

Introduction: Disulphide bonds are important for the folding and stability of many extracellular proteins, including bacterial virulence factors. Their formation is catalyzed by thiol-disulphide oxidoreductases (TDORs), a process that has been characterized in Gram-negative bacteria, but is poorly understood in Gram-positive species.

Methods: *Streptococcus gordonii*, a commensal bacterium of the human oral cavity, was used as a model organism to study disulphide bond formation. Five putative TDORs were identified from the sequenced *S. gordonii* genome and each gene was insertionally inactivated with an erythromycin resistance cassette. The mutants were analyzed for autolysis, eDNA release, biofilm formation, bacteriocin production, and genetic competence. One TDOR was selected for additional characterization and identification of natural substrates.

Results: Phenotypic analysis of the TDOR mutants revealed a single enzyme, Sgo.2006, that was involved in biofilm formation, eDNA release, bacteriocin production, genetic competence, and autolysis. Based on these results, the Sgo.2006 mutant was selected for additional investigation. An *in silico* screen for secreted proteins with ≥2 cysteines was used to generate a list of 36 potential substrates, including the autolysin AtlS. Western blotting revealed that AtlS was produced as a single 130 kDa band in the Sgo.2006 mutant, in contrast to the doublet observed in the parent (130 and 90 kDa). Functional analysis by zymography showed that AtlS was inactive in the Sgo.2006 mutant, suggesting that AtlS may be a natural substrate. Finally, we used a foreign protein known to contain two disulphide bonds to test disulphide bond formation. Alkylation experiments showed that the test protein lacked disulphide bonds when expressed in the Sgo.2006 mutant, supporting the hypothesis that Sgo.2006 is a TDOR.

Conclusions: Taken together, our results show that Sgo.2006 is critical to disulphide bond formation in *S. gordonii*, and suggest that this enzyme may represent a novel type of oxidoreductase in Gram-positive bacteria.

16. Depovax[tm] formulated vaccine to RSV targets novel mechanism of action

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The author requests that this abstract not be published

17. Validation of real-time Reverse Transcriptase Polymerase Chain Reaction (rRT-PCR) assays for the detection and characterization of Influenza strains

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Introduction: The turnaround time and simplicity of real-time Reverse Transcriptase Polymerase Chain Reaction (rRT-PCR) assays are placing them as essential tools for Influenza vaccine effectiveness (VE) studies. Specimens are tested for the presence or absence of Influenza A or B strains, and further characterization of subtype or lineage allows for VE measurement against vaccine matched or mismatched strains, in addition to calculation of strain-specific disease burden.

Methods: Singleplex rRT-PCR assays were selected and their specificity verified by *"in silico"* analysis of the primers and probes using Basic Local Alignment Search Tool (BLAST) analysis. Cycling conditions were optimized from the original conditions for multiplexing, to decrease time and cost. The primary screening rRT-PCR assay targets the Matrix (M) for the detection of Influenza A or B viruses, followed by a secondary assay targeting the HA gene to subtype the virus. Subtyping involves two separate reactions, either to identify influenza A virus subtypes pH1N1, sH3N2, or to determine the B virus lineages (Victoria and Yamagata). Four virus strains, one of each subtype or lineage detectable in the secondary assays, were tested as follows: 24 replicas made from six 10-fold dilution points (24 X 6) per virus were tested across four experiment days, where each experiment was equally split in the hands of two operators. The Limit of Detection (LoD) was defined as the Cp (Crossing point) value where 95% (23/24) of replicas were detected and was calculated using a probit analysis for each of the detectors. Assay specificity was further evaluated by testing a panel of nucleic acid extracted from other common respiratory organisms and viruses.

Results: No significant unexpected similarities were observed with any of the primer and probe sequences throughout the National Center for Biotechnology Information (NCBI) database, nor were there any primer/probe dimer formations detected using BLAST. The Cp cut off values, at 95% detection rate, fell between 34.5 and 38.9 for all six probes; while %CV for intra- and inter-assay precision was <6% for Cp values that were above the LoD. No cross-reactivity was observed with other respiratory pathogens, indicating an analytical specificity of 100%.

Conclusions: This validation enhances our ability to serve as the central laboratory for the PCIRN Serious Outcomes Surveillance Network, and provides essential infrastructure for ongoing assessment of strain-specific effectiveness of Canadian influenza immunization programs.

18. Effectiveness of 2011/12 and 2012/13 Seasonal Influenza Vaccines in the Prevention of Influenza-related Hospitalization in Canadian Adults: A PCIRN Serious Outcomes Surveillance (SOS) Network Study

Shelly McNeil, Ardith Ambrose, Melissa Andrew, Guy Boivin, Bill Bowie, Ayman Chit, May ElSherif, Karen Green, Francois Haguinet, Todd Hatchette, Barbara Ibarguchi, Jennie Johnstone, Kevin Katz, Jason LeBlanc, Mark Loeb, Donna MacKinnon-Cameron, Anne McCarthy, Allison McGeer, Jeff Powis, David Richardson, Makeda Semret, Vivek Shinde, Grant Stiver, Sylvie Trottier, Louis Valiquette, Hongyue Wang, Duncan Webster, Lingyun Ye, on behalf of the Public Health Agency of Canada/Canadian Institutes of Health Research Influenza Research Network (PCIRN) Serious Outcomes Surveillance Network and the Toronto Invasive Bacterial Diseases Network (TIBDN)

Introduction: Annual influenza vaccination is recommended for adults aged 65 years and older and younger adults with medical co-morbidities putting them at increased risk of severe disease. The goal of the Canadian influenza immunization program is prevention of influenza-associated hospitalization and death but little data is available to assess the effectiveness of seasonal influenza vaccination in the prevention of serious outcomes.

Methods: In 2011/12 and 2012/13, the PCIRN SOS Network conducted active surveillance for influenza among hospitalized adults from 15Oct to 30April in 40 acute care facilities in 7 Provinces, encompassing ~18,000 beds. A nasopharyngeal swab for influenza PCR was obtained from all patients admitted with community-acquired pneumonia, exacerbation of COPD/asthma, unexplained sepsis, any respiratory diagnosis or symptom, and, on one day per week, acute coronary syndrome, stroke, or other cardiac diagnoses with triage temperature ≥37.5C. Up to two test-negative controls matched for date, site of enrolment and age of the case (≥ 65y vs <65y) were enrolled for calculation of vaccine effectiveness (VE). Crude VE estimates were adjusted using multivariable logistic regression with stepwise backward selection of covariates with a p-value of <0.1 in the univariate analysis. VE was estimated as (1-OR) X 100.

Results: In 2011/12**,** 538 cases and 673 controls were enrolled; in 2012/13 over 1000 cases and 1500 controls were enrolled. In 2011/12, 312 (58%) of cases were ≥65 years (mean age 79.7y; range 65-104y) and 93% had one or more comorbidity. 266 (49.8%) of cases and 417 (63.1%) of controls had received an influenza vaccine ≥ 2 weeks prior to onset of symptoms. The overall, unadjusted VE for the prevention of hospitalization in adults was 45.9% (95% CI: 29.1-58.7); among persons ≥ 65y, unadjusted VE was 47.3% (25.7-62.6) and among those < 65y, unadjusted VE was 43.4% (12.2-63.5). Overall adjusted VE in adults was 50.5% (34.7-62.4); VE in adults ≥ 65y adjusted for age, admission from LTCF, obesity, smoking and medications prior to admission was 53.9% (34.7-67.4). VE in adults <65y adjusted for age and pregnancy was 42.1% (5.8-64.5). VE for the 2012/13 season will also be presented.

Conclusions: In 2011/12, the seasonal influenza vaccines used in Canada were moderately effective in the prevention of hospitalization of adults due to lab-confirmed influenza. VE was not significantly different in those ≥ 65y than in those <65y.

19. Safety, Immunogenicity and Tolerability of Three Influenza Vaccines for Older Adults: Results of a Randomized, Controlled Comparison

Shelly McNeil, Todd Hatchette, Scott A. Halperin, David W. Scheifele on behalf of the PHAC/CIHR Influenza Research Network

Introduction: Several new trivalent inactivated influenza vaccines (TIVs) reportedly increase immune responses of older adults. We assessed safety, tolerability and immunogenicity of 2 new vaccines in Canadian seniors.

Methods: A multi-center, randomized, controlled, parallel group design was used, with evaluator blinding. Participants were community-dwelling adults ≥65 years old, who had received routine TIV within 2 years. Vaccines included intradermal (Intanza15, Sanofi Pasteur) (IDV), adjuvanted (Fluad, Novartis) (ADV) and subunit (Agriflu, Novartis) (TIV) formulations for 2011-2012. Blood was obtained before (V1), 21-28 days (V2) and 180 days (V3) after vaccination. All sera were tested for hemagglutination-inhibiting (HAI) antibodies; V1 and V2 sera were also tested by serial radial hemolysis (SRH) assay. Safety diaries were completed daily by participants and reviewed with researchers 7 and 21-28 days after vaccination, with blinding maintained.

Results: 922 participants were enrolled and randomized, 911 were immunized, 908 attended V2 and 898 attended V3. Demographic characteristics did not differ significantly among study groups. General symptoms after vaccination were reported at similar frequencies by each group. Injection site redness was most common after IDV (76%) and pain most common after ADV (38%) but all 3 vaccines were well tolerated. Baseline HAI and SRH titers did not differ significantly among groups but B/Brisbane titers were very high, confounding response assessments. At V2, seroprotection rates (HAI titer ≥40, SRH ≥25 mm^2) to H3N2 were significantly higher after ADV. Protective H1N1 titers were equally frequent among groups by SRH but were more frequent after ADV by HAI assay. The seroprotection rate advantage for ADV over IDV and TIV was statistically significant at 11.4-11.8% for H3N2 and 10.2-12.5% for H1N1, using HAI data. After 6 months, seroprotection rates versus H3N2 and H1N1 had declined by ~25% and no longer differed significantly among groups.

Conclusions: ADV elicited modestly higher seroprotection rates against H3N2 and H1N1 vaccine strains initially but not after 6 months. IDV was not more immunogenic than TIV in this population. All 3 vaccines were well tolerated. Responses to B/Brisbane could not be adequately evaluated.

20. Influenza and frailty in older adults: toward a better understanding of burden of disease

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Affiliation: Geriatric Medicine and Infectious Disease

Introduction: The health impact of influenza is traditionally considered in acute terms. Even so, there is increasing evidence that influenza may have lasting health implications, particularly for frail older adults. We aimed to study Vaccine Effectiveness (VE) and outcomes of influenza-related hospital admissions in relation to frailty.

Methods: During the 2010/2011 influenza season, the Serious Outcomes Surveillance Network included 10 acute care hospitals totalling 6000 inpatient beds across Canada. Active surveillance of all patients admitted with broadly-defined influenza-like illness was used to identify cases (influenza nasopharyngeal swab positive) and controls (swab negative). Study nurses collected demographic data including influenza vaccination status, age, sex and, for patients aged 65+, Comprehensive Geriatric Assessment and Frailty Index (comprising 39 deficits from 10 domains: cognition, mood, sensory, mobility, nutrition, function, skin, continence, chronic illness, medications). Frailty was assessed at baseline (pre-illness), at enrolment and at 30 days post-discharge. VE was calculated using a test-negative case-control design; estimates were adjusted for important confounders including frailty.

Results: The SOS Network enrolled 319 cases and 364 controls aged 65 and over. Adjusted VE was higher in the 65+ group (55%, 95% CI:24-74) than in those <65 (46%, 95% CI:5-70). Mean baseline frailty was equivalent for cases and controls (0.24; SD 0.15). At 30 days post-discharge, those with confirmed influenza had higher frailty than controls (increase from baseline 0.06 vs. 0.02; $p<0.05$), representing a mean accumulation of three new persistent deficits.

Conclusions: VE was higher in for older vs. younger adults when adjusted for frailty. Hospital admission for influenza appeared to have greater impact on frailty than admission with other illnesses, suggesting that prevention of frailty is an important indication for influenza vaccination. Comprehensive Geriatric Assessment and focus on frailty were unique features of this study.

21. A Cost effective real-time PCR assay for the detection of adenovirus

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Introduction: Real-time polymerase chain reaction (PCR) is a highly sensitive and accurate method for detection of human adenoviruses. However, cost prohibits its use in many laboratories. To improve costs, an in-house real-time PCR was evaluated and nucleic acid extraction (NAE) was replaced with homogenization and heat treatment (HH).

Methods: The performance of virus culture with direct fluorescence antibody (DFA) testing was compared to the real-time PCR assay following HH or NAE on an automated instrument (MagNAPure). The limit of detection (LoD), dynamic range, inter- and intra-experimental variations were assessed by 10-fold serial dilutions of cultured adenovirus (n=24). Analytical specificity was evaluated against a wide range of organisms including various adenovirus types. For clinical validation, 196 clinical specimens [swabs in universal transport media (UTM)] were tested in parallel using all three methods. A modified gold standard (2 of 3 concordant results) was used to determine sensitivity, specificity, accuracy, and precision. Discordant results were resolved using manual DNA extraction followed by a commercial real-time PCR.

Results: The real-time PCR was highly specific and detected all serogroups of adenovirus. The LoD for the in-house real-time PCR following HH treatment or NAE were equally sensitive at 12 and 18 copies/reaction, respectively, and was ~100-fold more sensitive than cell culture and DFA. Compared to the modified gold standard, the clinical sensitivity of each assay was 100%, 97.5 % and 69.2%, respectively.

Conclusions: The in-house real-time PCR following HH treatment is an effective strategy for the detection of adenovirus, at a cost comparable to virus culture and DFA.

22. Universal Infant Rotavirus Implementation in two delivery models: Maritime Universal Rotavirus Vaccination Project

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Introduction: The National Advisory Committee on Immunization recommended rotavirus vaccine (RVV) for all infants (May 2011). As part of a multiyear project evaluating rotavirus epidemiology and vaccine implementation, we compared implementation strategies for improving uptake of the vaccine and level of engagement of public health nurses (PHN) and physicians as the providers of the vaccine in two of the three sites (Saint John, NB is the control site).

Methods: In PEI, vaccines are administered by PHN and in Halifax (Capital Health), NS by physicians. Process evaluation detailed stakeholder engagement prior to program roll-out and communication strategies to improve RVV uptake. Implementation of the vaccine program at both sites included an education session with immunizing PHN and First Nations nurses, and physicians, distribution of a fact sheet, communication to physicians about the new immunization schedule, and public announcements through various media, including through physician organizations. Additional strategies to engage physicians in NS included an invitation for membership on project working groups, an education needs assessment, an online webinar, and distribution of flyers with all routine childhood vaccine orders.

Results: In PEI, the educational in-service was attended by 43 (97.7%) of 44 immunizing PHN compared to 8 (1.9%) of 405 immunizing physicians in NS. Only 3 (0.7%) physicians participated in the online webinar (of note, 10 NS non-immunizing PHN participated). Program roll-outs for the first year were qualitatively similar to previous new vaccine programs in both jurisdictions. At the end of the first year, vaccine coverage was >90% in PEI and <30% in NS.

Conclusions: Despite strategies used to involve physicians in NS, PHN were more engaged at both sites in learning about the program. There were considerable differences in uptake of the vaccine in year one, likely related to vaccine provider engagement in learning about and implementing the vaccine program.

23. Investigating the role of KSHV microrna in bypass of oncogene-induced senescence

N. Sachrajda, A.M. Leidal & C. McCormick

The author requests that this abstract not be published.

24. Respiratory syncytial virus (RSV) infection of human mast cells causes the production of chemokines and type I interferons

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Introduction: Respiratory syncytial virus (RSV) is the leading cause of infant bronchiolitis and hospitalization worldwide. Mast cells are granulocytes that are essential in the immune response to pathogens and can produce mediators including histamine, leukotrienes, chemokines, and cytokines that influence vasodilation, bronchoconstriction, and immune cell recruitment to sites of infection. Since mast cells are abundant in the airways at the site of RSV infection, we examined the human mast cell response to RSV.

Methods: Cord blood-derived human mast cells (CBMC) were infected with RSV. In some experiments RSV infection was blocked by pre-incubation with palivizumab (Synagis) or the type I interferon (IFN) receptor was blocked with a specific antibody during infection. At various times post-infection the supernatants from CBMC cultures were harvested and assayed by ELISA for cytokines, chemokines, and leukotriene C4. RNA prepared from CBMC was analyzed for the expression of cytokines, chemokines, and IFN-stimulated genes (ISGs).

Results: CBMC infection with RSV resulted in low levels of RSV antigen expression. RSV inoculated mast cells did not degranulate or produce leukotriene C4, but did selectively up-regulate the expression of several chemokines including CXCL10. CXCL10 is important in the anti-viral response since it can mediate the recruitment of activated T cells and natural killer cells. In response to RSV, CBMC also substantially up-regulated the expression of type I IFNs as well as several ISGs, such as ISG56, that have important anti-viral properties. Direct treatment of CBMC with IFN- induced the production of CXCL10 and up-regulated the expression of ISG56. Blockade of the type I IFN receptor during RSV infection of CBMC significantly reduced the induction of CXCL10, indicating a causal link between RSV-mediated type I IFN induction and CXCL10 production.

Conclusions: In summary, our data show that human mast cells respond to RSV by producing pro-inflammatory cytokines such as CXCL10 and type I IFN. Mast cell chemokine production may enhance inflammation and effector cell recruitment during RSV disease.

25. Novel acyl carrier protein synthase (ACPS) inhibitors: effect on bacterial growth and ability to maintain infection in a topical mouse model

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Introduction: Using antibiotics as tools for fighting disease became widespread in 1946. However, it was not long before random mutations and selective pressures contributed to many susceptible bacteria becoming resistant. This has continued to the present, despite several new classes of antibiotics having been discovered/developed. There is a critical need for alternative antibiotic targets to ameliorate this potential healthcare crisis. Acyl carrier protein synthase (AcpS) is a widely conserved, essential bacterial enzyme with no known mammalian homologue. Small molecule inhibitors of AcpS have been developed at the IWK Health Centre's Chemoinformatics and Drug Discovery Laboratory (CDDL), utilizing a combination of computational modeling, rational drug design, synthetic organic chemistry, enzymology, and microbiology. A number of novel chemical entities (NCEs) have been shown to inhibit the growth of a variety of *Staphylococcus sp.,* including Methicillin-Resistant *Staphylococcus Aureus* (MRSA). Discerning the mechanism of action (MOA) of these compounds is challenging, though we have recently confirmed their involvement in lipid and protein metabolism with no effect on nucleic acid metabolism.

Methods: The direct effect of selected NCEs on target enzyme activity alone was first established; briefly, an AcpS in vitro enzyme assay was carried out in the presence of inhibitor compound or vehicle alone (dimethylsulphoxide; DMSO), to provide IC_{50} data. MIC data was also accumulated for compound effect on MRSA and a panel of other relevant bacteria, including some Gram negative strains, and the cidal vs. static effect was also determined by plating for cfu. Lastly, a lead compound (NCE 0631) was chosen to be evaluated in a mouse model of topical infection. Mice were given surface wounds and infected with MRSA, followed by treatment with a standard pharmacy topical cream containing either the drug candidate or vehicle. Animals were weighed daily, and at the completion of the investigation swabs were taken of the wound site and bacteria cfu were determined.

Results: A number of compounds tested were able to inhibit AcpS in a standard in vitro enzyme assay, at low micromolar concentrations. In vivo, compounds were shown to exhibit both cidal and static effects, at various concentrations, confirming the need for additional work to delineate the specific MOA of these NCEs. NCE 0631 was able to reduce, more effectively than vancomycin, the severity of a topical mouse model of MRSA infection.

Conclusions: A family of NCEs has been generated, capable of potent inhibition of growth of Gram positive and Gram negative bacteria. The effect of at least one of these compounds on MRSA *in vivo* is an inhibition of MRSA infection in a mouse model of topical infection. Further experiments are required to more specifically determine the anti-infective MOA, as well as pharmacokinetics in animal models of administration.

26. Dog nectin-4 is an epithelial cell receptor for canine distemper virus that facilitates virus entry and syncytia formation

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Introduction: Morbilliviruses are highly contagious pathogens that are responsible for some of the most devastating diseases that affect mammals worldwide. Members of this genus include measles virus (MeV), canine distemper virus (CDV), peste des petits ruminants virus (PPRV), rinderpest virus (RPV), phocine distemper virus (PDV) and dolphin morbillivirus (DMV). CDV produces a contagious disease that elicits high mortality in a wide range of terrestrial carnivores. Both CDV and MeV enter susceptible cells using surface protein receptors, including the lymphotropic receptor, SLAM, which is expressed on the surfaces of activated T- and B-lymphocytes, macrophages, and dendritic. Recently, human nectin-4 was identified as an epithelial cell receptor for MeV. Here we confirm that CDV uses dog nectin-4 as an entry receptor to infect host epithelial cells and promote cell-to-cell spread, similar to MeV.

Methods: CDV titration assays were performed in both dog and human epithelial cell lines to quantify the susceptibility of these cells to virus infection. Dog nectin-4 was identified as the cellular receptor responsible for virus entry into these cells and was subsequently cloned from both MDCK cells and dog placenta. RNAi and antibody inhibition assays were carried out to confirm the importance of dog nectin-4 in CDV pathogenesis.

Results: Two splice variants of dog nectin-4 were identified. Both dog nectin-4 and human nectin-4 could function as an entry factor for CDV 5804PeH. Inhibition of dog nectin-4 expression by RNAi or nectin-4 antibodies decreased CDV titers and EGFP fluorescence. Finally, dog nectin-4 also promoted syncytia formation, which could be inhibited by siRNA treatment.

Conclusions: This study identifies nectin-4 as an epithelial receptor for CDV. Given the recent evidence in the literature that nectin-4 is a potential tumor associated marker for breast, lung, and ovarian cancers, the possibility of using CDV as an oncolytic agent is very compelling.

27. Dog nectin-4 V domain facilitates canine distemper virus entry and viral cell-to-cell spread

Sebastien Delpeut, Ryan S. Noyce, Christopher Richardson

The author requests that this abstract not be published.

28. Effectiveness of a passive educational strategy aimed at improving disinfection of personal items among healthcare professionals in the emergency department at a tertiary care centre

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Introduction: Previous studies have suggested inanimate objects belonging to healthcare workers may contribute to the transmission of microorganisms from patient-to-patient in the healthcare setting. This study examines the effectiveness of posters in the emergency room as a reminder to disinfect personal items.

Methods: A group of 10 healthcare professionals in the emergency department (ED) had selected personal items (cell phone, stethoscopes, pagers, identification cards, sleeves) swabbed to identify microorganisms. Anonymized results were posted in several locations throughout the department, which included a reminder to disinfect personal items. A week after the results were posted, a separate group of 10 healthcare professionals had the same items tested. The results were analyzed based on type and colony counts of bacteria using a mixed analysis of variance.

Results: A total of 15 participants (7 pre and 8 post) were analyzed based on the cell phone, identification card and sleeve findings. Overall, a statistically significant increase in colony count was observed in the post-education period (p = 0.01). Mean colony count increased from 38.0 CFU (95% CI 26.7, 49.3) pre-education to 58.2 CFU (95% CI 47.6, 68.8) post-education. There was no significant change in the mean number of types of bacteria observed in the pre and post education periods (pre-mean 3.9 /post-mean 3.7, p = 0.7*).* The bacteria isolated were predominantly Gram-negative, however a number of different types of Gram-positive bacteria were present as well.

Conclusion: Despite its predominant use in healthcare the current evidence suggests the use of passive education alone is insufficient to result in significant change in cleaning practice among healthcare workers. While our sample size requires the results to be interpreted cautiously; they are consistent with prior studies regarding passive educational strategies. We suggest that healthcare institutions carefully examine their policies to reduce equipment reservoir sources, and look further at this hypothesis.

29. Formulation in Depovax[tm] enhances the immunogenicity of recombinant protein based anthrax vaccines

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30. Subversion of Autophagy by Kaposi's Sarcoma-Associated Herpesvirus Impairs Oncogene-Induced Senescence

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The author requests that this abstract not be published

31. A genetic analysis of the mouse adaptation of human pandemic H1N1 (A/CALIFORNIA/07/09)

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Introduction: Influenza A is a zoonotic respiratory pathogen. Through antigenic drift, cross-species adaptation can occur and allow for an influenza virus to infect a new host. Currently there is concern that Avian Flu will evolve and adapt to humans, creating a novel and deadly human virus. Mice are not a natural host for influenza, however, through serial passage of the virus in mice, species adaptation can occur and influenza can become highly virulent in the mouse model. Genetic changes identified during adaptation may identify regions targeted during host adaptation. In addition the mouse-adapted virus can be used in vaccine challenge studies.

Methods: Plaque purified A/California/07/09 (pH1N1) human strain of influenza was nasally inoculated into 10 mice. Mice were monitored daily using a standardized scoring method. Three days post infection, the mice were euthanized and their lungs harvested. Lung homogenate was then inoculated into 10 more mice. This process was repeated for a total of 10 passages. In parallel to the mouse monitoring, the virulence of the virus was assayed using TCID50's.

Results: Through progressive passaging of the virus the mice exhibited greater sickness based on both weight loss and clinical scores. The dose that will infect 50% of tissue cultures (TCID50) and the dose that is lethal to 50% of mice (MLD50) increased after mouse adaptation, indicating an increased level of virulence.

Conclusions: We have successfully mouse adapted a human strain of influenza that can be used in vaccine challenge experiments. We are in the process of further characterizing the adapted virus to determine the genetic changes that allowed this adaptation to occur.

32. A retrospective review of the school-based human papillomavirus (HPV) immunization program: evaluating the effects of public health nursing engagement strategies with schools, parents and youth on HPV vaccine uptake in greater Halifax

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Introduction: In Canada, Nova Scotia (NS) has the highest rate of cervical cancer of which, most cases are attributed to the Human Papillomavirus (HPV) specifically, strains 16 and 18. In 2007, the HPV vaccine was approved for adolescent Canadian girls and a successful school-based immunization program was implemented in NS in that same year. Little is known however, about which strategies if any, used by public health nurses (PHNs) help improve the HPV vaccine uptake in particular, the use of nurse-led engagement strategies targeting schools, parents and youth. The purpose of this study is to examine the relationship between HPV vaccine refusal, uptake and adherence of adolescent girls in a school-based HPV vaccination program and strategies used to promote the vaccine by PHNs during the 2010-2011 school year.

Methods: A retrospective exploratory correlation design study was used to examine the relationship between PHN strategies, and uptake of the HPV vaccine. A secondary analysis of public health coverage data for 2010-2011, and information about nursing activities/strategies used in the schools from a questionnaire helped to identify which strategies if any, were successful in improving vaccine uptake.

Results: Sixteen (61.5%) of 26 nurses participated in the study, providing information on nursing engagement strategies used in 48 (69.5%) of 69 schools, with 3291 (76.3%) of 4312 females eligible for publicly funded HPV vaccine. 2441 (74.2%) students completed the HPV three dose series; 297 (9%) initiated the vaccine, and there were 553 (16.8%) refusals. After multinominal logistic regression analysis, the model revealed that the likelihood of initiating the HPV vaccine series was significantly associated with providing reminder calls for consent return ($p = .017$), reminder calls after missed clinic ($p = .004$), HPV health education to teachers ($p = .000$), and a thank-you to teachers and school personnel ($p = .000$). Completion of the three dose series was associated with the consents being returned to the students' teacher ($p = .003$), and a PHN being assigned to a school ($p = .025$).

Conclusions: This study is, to our knowledge, one of the first studies to explore the relationship between nursing engagement strategies used with schools, parents and youth and levels of uptake of the HPV vaccine in a school-based immunization program. These findings will help to guide PHNs best practice to ensure optimal uptake of the HPV vaccine.

33. Responding to public health need: A multicentre Canadian trial to assess the immunogenicity of a 2 dose schedule of human papillomavirus vaccine in young adolescents compared to 3 doses in young women

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Introduction: Global use of Human Papillomavirus (HPV) vaccines to prevent cervical cancer is impeded by cost. As quadrivalent-HPV vaccine is more immunogenic in girls than women, a 2-dose schedule for school-aged girls may be possible and offer improved uptake and reduced cost in the context of Canadian school-based immunization programs. We determined whether mean antibody levels to HPV-16 and 18 one month post last vaccine dose among girls given 2-doses was non-inferior to women given 3-doses.

Methods: A Canadian, phase III, multi-center, age stratified, non-inferiority immunogenicity, study of 830 healthy females was conducted August 2007 to February 2011. 675 (81%) completed all follow up blood samples. Girls (9-13 years) were randomized 1:1 to 3-doses of quadrivalent-HPV vaccine at 0, 2, 6 months (N=261) or 2-doses at 0, 6 months (N=259). Women (16-26 years) received 3doses at 0, 2, 6 months (N=310). Antibody levels were measured at 0, 7, 18, 24 and 36 months. The primary outcome was non-inferiority (95%CI, lower bound >0.5) of Geometric Mean Titre (GMT) ratios for HPV-16 and HPV-18 for girls (2-doses) compared with women (3-doses) one month after the last dose. Secondary outcomes were non-inferiority of GMT ratios of girls versus women to HPV-6 and HPV-11; non-inferiority of GMT ratios of girls receiving 2 versus 3 doses of vaccine to all 4 HPV types; and durability of non-inferiority to 36 months

Results: GMT responses (95% CI) one month after last vaccination for HPV-16, 18, 6 and 11 were: girls (2-doses) 7344 (6310-8547); 1169 (1021-1338); 2117 (1787-2508); and 2339 (2088-2619) and women (3-doses) 3545 (3083-4076); 664 (586-752); 943 (807-1101); and 1268 (1143-1408). GMT ratios (95% CI) were non-inferior for girls (2-doses)/women (3-doses): 2.07 (1.62-2.65); 1.76 (1.41-2.19); 2.25 (1.71-2.96); and 1.84 (1.53-2.22) for HPV-16,18,6 and 11 respectively. GMT ratios remained non-inferior to 36 months for HPV-16, 18, 6 and 11. Antibody responses in girls were non-inferior after 2 versus 3 doses for all 4 vaccine genotypes at month 7, but not for HPV-18 by Month 24 or HPV-6 by Month 36.

Conclusions: Two doses of HPV vaccine in girls was non-inferior to 3 doses in women one month after the last vaccination for HPV-16 and 18 and supports the potential for an alternative pediatric schedule. Evaluation of vaccine effectiveness and duration of protection will be critical if 2-dose programs are implemented.

34. Development of an anti-fungal boosting agent

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The author requests that this abstract not be published.

35. RCAN1 suppresses inflammation during respiratory tract infections

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Introduction: Down syndrome (DS) is the most common chromosomal anomaly and is caused by trisomy of chromosome 21. It is associated with a variety of physical and cognitive impairments, as well as increased risk of respiratory tract infections. However the gene(s) responsible for the increased susceptibility to these infections remain undefined. Here we examine the role of the DS associated gene Regulator of calcineurin 1 (RCAN1) in the regulation of inflammation and host defense during repiratory tract infection.

Methods: A P. aeruginosa lung infection model was used in order to assess the immune response in wild-type and RCAN1 deficient mice. Protein arrays, EMSA, ELISA and Western blot analysis were used to examine the inflammatory response both in vivo and in vitro.

Results: RCAN1-deficient mice did not survive beyond 24 hours following infection with 1 LD50 of P. aeruginosa due to uncontrolled systemic inflammation. However, following infection with a sublethal dose of bacteria, RCAN1 deficient mice displayed greatly enhanced bacterial clearance due to enhanced inflammatory cytokine production leading to increased neutrohpil infiltration at the site of infection. The dysregulation of inflammatory cytokine production was found to be due to aberrant activation of the IκB-NFκB, calcineurin-NFAT and ERK-STAT3 pro-inflammatory transcription factor pathways.

Conclusions: Our results indentify RCAN1 as a central negative regulator of pro-inflammatory transcription factor activation during bacterial respiratory tract infections. The impaired survival observed in RCAN1-deficient mice further suggests that RCAN1 is essential for minimizing systemic inflammation during lung infections. Given the potent negative regulatory effects of Rcan1 on three pro-inflammatory pathways, overexpression of the protein in DS could have profound immunosuppressive effects accounting in part for the increased risk of respiratory tract infections in these patients.

36. Universal Infant Rotavirus vaccine coverage in two delivery models: Maritime Universal Rotavirus Vaccination Project

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Introduction: Universal rotavirus (RV) infant vaccine (V) was recommended by the National Advisory Committee on Immunization (NACI) in 2011. In a pilot project, we are comparing public health- to physician-delivered RVV programs in Prince Edward Island (PEI) and Capital Health, Nova Scotia (CH- NS) to determine disease incidence and hospitalizations (H), adverse event rates, and vaccine coverage (VC). We report here VC and RVH.

Methods: All infants born after 1 Oct 2010 were eligible for RVV, given as 2 dose (age 2 and 4 months) live, oral Rotarix™ vaccine. In PEI, RVV is delivered in public health nursing clinics and electronic records are completed as part of the immunization registry. In CH-NS, RVV is given in family doctor offices and RVV recorded on paper or electronic reciprocal notification forms that are sent to public health, then entered into a database. Retrospective surveillance for RVH was conducted 2008-2010 in PEI, and prospective surveillance 2010-present. In CH-NS, RVH were collected prospectively 2008-present. The birth cohort/month is the denominator

Results: In PEI there were 35 RVH 2008-10, 31 RVH in 2011 and none to date in 2012. More broadly no RV season has been seen in PEI in 2012. In CH-NS there were 61 RVH in 2008-10, 9 in 2011, and 6 to date in 2012. VC in PEI for dose 1 and 2 is ~96% and 93%, respectively and in CH-NS, VC is 27 and 25%.

Conclusions: Vaccine coverage is higher in the public health-delivered RVV program than in individual physician practices. In the setting with public health-delivered RVV and high VC (PEI), no RV admissions have occurred in 2012 and the RV season is absent. In the low VC setting, no change in RV epidemiology has been observed. The change in RV epidemiology in PEI is likely due to direct protection and herd immunity.

37. Project HaliVax: A community based vaccine delivery program for homeless adults

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Introduction: In 2010-2011 49% of homeless adults were immunized to influenza and 12% reported being immunized to pneumococcus as an adult. Both rates are below nation standards despite current guidelines recommending influenza and pneumococcal vaccines for this high-risk group. We hypothesized that a community based vaccine delivery program will increase vaccine uptake among homeless adults.

Methods: Study staff partnered with the Metro Outreach Street Health nurses to organize a community based vaccine delivery program for homeless adults from October 22nd to 28th 2012. During the same time period study staff met with health care providers of homeless adults to educate them on the current immunization guidelines. From January 15th to February 15th 2013 a survey was administered to homeless adults to measure vaccination rates. Information gathered included demographics, medical history, access to health care, vaccination history and vaccination knowledge.

Results: During the vaccination delivery program 340 doses of influenza and 70 doses of pneumococcal vaccine were administered. Following this a total of 104 individuals were surveyed. Thirty six percent reported being immunized to influenza in the 2012-2013 season. Twenty four percent reported being immunized to pneumococcus.

Conclusions: Immunization rates to influenza decreased and pneumococcal rates increased following the implementation of a community based vaccine delivery program.

38. Human mast cell production of Type III interferons and their impact on natural killer cell function during viral infection

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Introduction: Mast cells can be infected by several viruses, resulting in cytokine and chemokine production. Our group has previously shown that supernatants from reovirus-infected human Cord Blood-derived mast cells (CBMC) induced substantial chemotaxis of Natural Killer (NK) cells via a CXCL8 dependent mechanism. In the current study, we investigate mast cell production of the type III IFNs IL-29, IL-28A and IL-28B following virus infection and the impact of these on NK cell function.

Methods: CBMC were infected with reovirus and supernatants harvested 24 h post-infection for ELISA or further assays. mRNA was extracted for qPCR analysis. NK cells obtained from peripheral blood of healthy donors were cultured for 24 h in the presence of CBMC supernatants and both CD69 and IFNγ expression analyzed by FACS. Mx1, Perforin 1 (PRF1) and Granzyme B (GZM B) mRNA levels were analyzed by qPCR.

Results: Expression of IL-29, IL-28A and IL-28B mRNA was induced in CBMC after reovirus infection. However, only IL-29 and IL-28A protein production was observed. Culture of NK cells with supernatants from reovirus-infected CBMC up-regulated CD69 expression and PRF1 mRNA levels without modifying IFNγ production or GZM B mRNA expression. Purified NK cells responded to IL-29 treatment with the induction of Mx1 mRNA, but no changes were observed in other parameters such as CD69 expression.

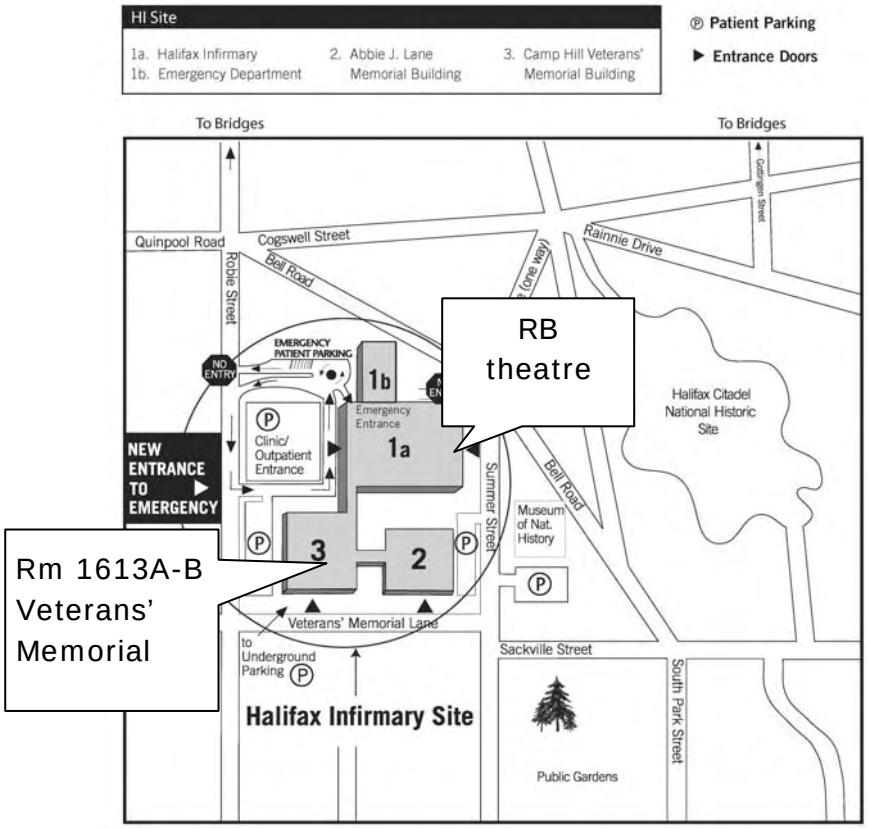
Conclusions: Mast cells can produce type III IFNs, such as IL-29, following viral infection. The products of virally infected mast cells can induce the early activation of NK cells which may be particularly important in the context of mast cell-mediated NK cell recruitment to sites of early viral infection. IL-29 alone does not reproduce the activating effects of mast cell supernatants on NK cells. The role of mast cell derived type III IFNs in responses to viral infections remains to be determined**.**

Photos by Mary Halpine
3rd year medical student
Saint John NB Dalhousie campus

Photos taken in summer 2011 while on a medical elective in a small fishing village in St. Lucia.

The top poster advertises a "Soca Frenzy" dance party, the bottom poster warns against transmission of Leptospirosis through rats.

QEII Halifax Infirmary Site



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