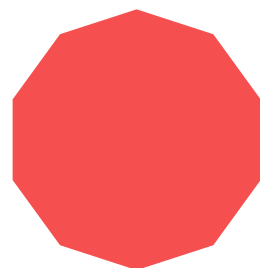
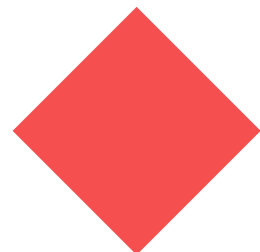


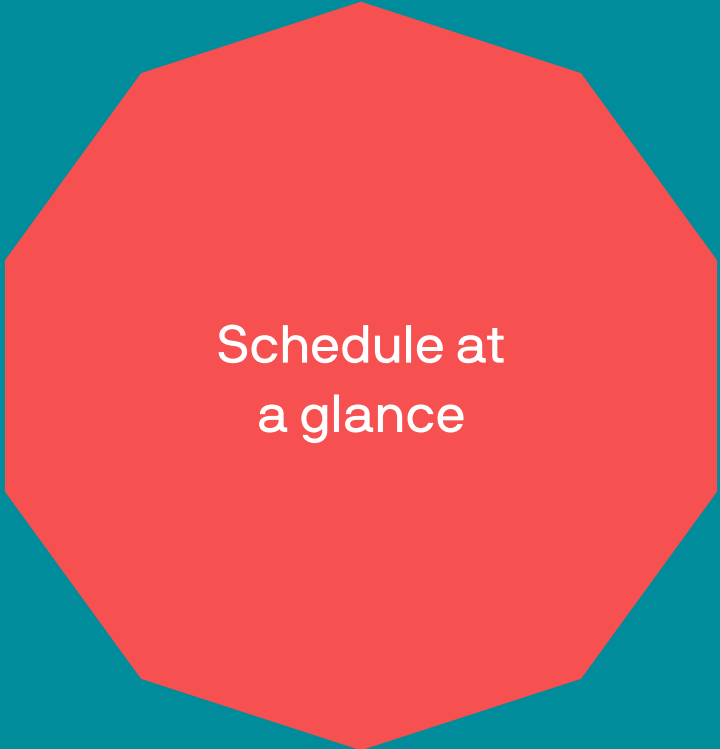
Welcome to the 2021 Symposium on Innovative Therapeutics for *Cryptosporidium*.

Cryptosporidiosis has been recognized as one of the leading causes of morbidity and mortality from diarrhea in children under 5 years of age in low-resource settings. Despite the magnitude and significance of the problem, only a single drug is approved to treat *Cryptosporidium* infection, and new therapies are urgently needed.

PATH, a global team of innovators working to accelerate health equity, is pleased to convene the third Symposium to put the spotlight on Crypto. Similar to the first two meetings, in San Francisco, California (2016) and Seattle, Washington (2018), we have assembled leading researchers to present and discuss the current state of work on Crypto—from early discovery to clinical development and commercialization, veterinary medicine, diagnostics, and vaccines. Our goal is to share research, highlight opportunities for collaboration, and spark innovation toward making new and improved therapies a reality.

Thank you for joining us!



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Schedule at
a glance

Day 1 - Monday, January 11		Start	End
Opening		8:00	8:35
Robert Choy	Welcome	8:00	
Paul Kelly	Keynote address: Cryptosporidiosis: a perspective from a low-income country	8:05	
Q&A		8:25	
Enabling tools and diagnostics		8:35	9:40
Lisa Funkhouser-Jones	Testing drug and metabolite efficacy and reversibility in an air-liquid interface culture system for <i>Cryptosporidium parvum</i>	8:35	
Chelsea Marie	<i>Cryptosporidium</i> diagnostics: Landscape, priorities, and prospects in 2020	8:50	
Jennifer Zambriski	Crypto, calves, piglets, and Quik Chek: Virginia to Zambia and back!	9:05	
Q&A		9:20	
Break		9:40	9:50
Therapeutics, part I		9:50	10:55
Beatriz Baragaña	Developing inhibitors of lysyl tRNA synthetase (KRS) for the treatment of cryptosporidiosis	9:50	
Wesley Van Voorhis	Bumped-Kinase Inhibitors for the treatment of cryptosporidiosis	10:05	
Ujjini Manjunatha	The role of gastrointestinal exposure for treating <i>Cryptosporidium</i> infection and its implications for clinical development	10:20	
Q&A		10:35	
Closing - Day 1		10:55	11:00

Day 2 - Wednesday, January 13		Start	End
Opening		8:00	8:05
Robert Choy	Welcome	8:00	
Endemic setting studies		8:05	8:45
Pui-Ying Iroh Tam	Cryptosporidiosis in adults and children: Results from a phase 2a trial for <i>Cryptosporidium</i> diarrhoea in Malawi, and preliminary results on evaluation of respiratory cryptosporidiosis in paediatric diarrhoeal disease	8:05	
Carol Gilchrist	Genomic analysis of the Bangladesh <i>Cryptosporidium</i> parasites	8:20	
Q&A		8:35	
Therapeutics, part II		8:45	9:45
Marvin Meyers	Progress towards the optimization of Triazolopyridazine MMV665917 as a novel drug to treat cryptosporidiosis	8:45	
Melissa Love	Cryptosporidiosis drug discovery at Calibr at Scripps Research: An overview	9:00	
Frederick Buckner	Induction of drug resistance in <i>Cryptosporidium parvum</i> to methionyl-tRNA synthetase inhibitors	9:15	
Q&A		9:30	
Break		9:45	9:55
Vaccine development and host immune response		9:55	10:55
Wilbur Chen	The potential use of human challenge models for accelerating the development of therapeutics for <i>Cryptosporidium</i>	9:55	
Boris Striepen	The biology of <i>Cryptosporidium</i> host-parasite interaction	10:10	

Christopher Hunter	Regulation of innate and adaptive immunity to <i>Cryptosporidium</i>	10:25	
Q&A		10:40	
Concluding remarks		10:55	11:00
Virtual reception		16:00	17:30

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Program

Day 1 - Monday, January 11

Opening

Day 1

8:00-8:05

Welcome

Robert Choy

Associate Director, Research and Preclinical Development, PATH

Day 1

8:05-8:35

**Keynote address:
Cryptosporidiosis: a
perspective from a
low-income country**

Paul Kelly

Professor of Tropical Gastroenterology, Blizard Institute, Barts and The London School of Medicine, Queen Mary University of London; Tropical Gastroenterology and Nutrition Group, University of Zambia School of Medicine

Enabling tools and diagnostics

Day 1

8:35-8:50

**Testing drug and
metabolite efficacy
and reversibility in an
air-liquid interface
culture system for
*Cryptosporidium
parvum***

Lisa Funkhouser-Jones

Postdoctoral Research Associate, Department of Molecular Microbiology, Washington University School of Medicine

Summary: The development of effective therapeutics for cryptosporidiosis has been hindered by a paucity of robust culture systems for *Cryptosporidium*. We recently described an in vitro platform for complete life cycle development and long-term growth of *C. parvum* using “air-liquid interface” (ALI) cultures derived from intestinal epithelial stem cells. ALI cultures supported parasite expansion >100-fold and led to the production of infectious oocysts that were transmissible between cultures and to mice. This unique, long-term culture platform was used to test “cidal” versus “static” effects of anti-*Cryptosporidium* compounds and is currently being used to profile microbiota-related metabolites that influence parasite invasion and growth.

Day 1

8:50-9:05

***Cryptosporidium*
diagnostics:
landscape, priorities,
and prospects in 2020**

Chelsea Marie

Assistant Professor of Medicine, University of Virginia

Summary: *Cryptosporidium* was recently revealed to be a top-five cause of childhood diarrheal illness globally. Beyond acute infection, *Cryptosporidium* has been associated with negative impacts on growth and cognitive development. As novel therapeutics are advanced into clinical use, high-performance diagnostics will be a critical component of the anti-cryptosporidiosis armamentarium. At the individual level, rapid, point-of-care diagnostic tests can accelerate treatment of infected patients, thus shortening the duration of disease, and limiting transmission. Diagnostics are also essential for recruiting patients and evaluating efficacy of the new

Day 1

9:05-9:20

**Crypto, calves,
piglets, and Quik
Chek: Virginia to
Zambia and back!**

Jennifer Zambriski

Assistant Professor of Epidemiology, Virginia-Maryland College of Veterinary Medicine

Summary: An update from the Zambriski Lab including validation of the Quik Chek diagnostic in the calf model of cryptosporidiosis and plans for propagation of Zambian field isolates of *C. parvum* and *C. hominis* in calves and gnotobiotic piglets at Virginia Tech. and repurposed therapeutics in clinical trials. As therapeutics options expand, diagnostics will be key for developing evidence-based treatment guidelines and monitoring the impact of interventions on transmission and burden of *Cryptosporidium* at the population level. Diagnostics are also vital to answering fundamental research questions, including the development of protective immunity to cryptosporidiosis in humans.

Day 1

9:20-9:40

Questions and answers

Day 1

9:40-9:50

Break

Day 1

9:50-10:05

Developing inhibitors of lysyl tRNA synthetase (KRS) for the treatment of cryptosporidiosis

Beatriz Baragaña

Medicinal Chemist, University of Dundee

Summary: The lack of effective treatment for malnourished or immunocompromised children infected with *Cryptosporidium* is estimated to lead to more than 200,000 deaths a year. New drugs for cryptosporidiosis are of high priority; however, there are few chemically validated targets for this apicomplexan parasite. We successfully identified an opportunity for pathogen hopping based on the structural homology between *Plasmodium falciparum* KRS1 and *C. parvum* KRS. Following biochemical and fragment screens, several small-molecule hits have been identified and then optimized by using a structure-based approach, supported by structures of *C. parvum* KRS (CpKRS). These series of compounds inhibit CpKRS and *C. parvum* and *C. hominis* in culture. We have identified drug-like selective inhibitors of CpKRS capable of clearing parasites from mouse models of cryptosporidiosis infection. Our work validates *C. parvum* KRS as a promising target for the development of drugs for cryptosporidiosis.

Day 1

10:05-10:20

Bumped-Kinase Inhibitors for the treatment of cryptosporidiosis

Wesley C. Van Voorhis

Professor of Medicine, Division of Allergy and Infectious Diseases; Adjunct Professor of Global Health and Microbiology; and Director, Center for Emerging and Re-emerging Infectious Diseases, University of Washington

Summary: Bumped-Kinase Inhibitors (BKIs), designed to inhibit calcium-dependent protein kinase 1 (CDPK1), have shown efficacy in several animal models of cryptosporidiosis. Finding potency has been easy but finding BKIs with the correct safety profile for the target population—children younger than 2 years—has been far more challenging. Safety issues have included inhibition of off-target protein kinases, gastrointestinal toxicity, developmental issues, cardiovascular issues, and bone toxicity issues. None of these safety issues appear to be intrinsic

to BKIs' structure-activity relationship for efficacy. We discuss our proposed solutions for safety issues and the way forward to a preclinical lead that can advance to Investigational New Drug status for human cryptosporidiosis therapy.

Day 1

10:20-10:35

**The role of
gastrointestinal
exposure for treating
Cryptosporidium
infection and its
implications for
clinical development**

Ujjini Manjunatha

Group Leader, Cryptosporidiosis, Novartis Institute for Tropical Diseases

Summary: Diarrheal infections kill ~500,000 children under the age of 5 every year, primarily in the developing world. Cryptosporidiosis is one of the major infectious diarrheal diseases caused by the apicomplexan parasite *Cryptosporidium*, an obligate intracellular parasite. Recently, we validated *Cryptosporidium* PI(4) kinase as a promising molecular target with the pyrazolopyridine compound KDU731. The inhibition of CpPI(4)K affects inner membrane complex formation and parasite replication in all stages of the *Cryptosporidium* life cycle. Oral treatment with KDU731 resulted in significant improvements in both immunocompromised mouse model as well as neonatal calf model. However, KDU731 intravenous treatment was not efficacious in mouse cryptosporidiosis model despite similar plasma exposure, suggesting systemic exposure alone may not be sufficient for in vivo efficacy of CpPI(4)K inhibitors. Considering that *Cryptosporidium* primarily infects intestinal epithelial cells facing the lumen, gastrointestinal exposure alone can drive pharmacodynamic effect in vivo for anti-parasitic agents. Soft drugs are therapeutic agents that undergo predictable metabolism to inactive metabolites and rapidly clear from systemic circulation after exerting their therapeutic effect. Using a soft drug strategy, we demonstrated that direct gastrointestinal exposure is necessary and sufficient for anti-*Cryptosporidium* activity mediated by CpPI4K inhibition. Thus, considering the most vulnerable pediatric patient population, such as malnourished children under 2 years of age, drugs with minimal systemic exposure could potentially lower the risk of off-target toxicity and drug-drug

interactions, thereby enhancing the therapeutic index. In addition, efforts are also in progress to establish a *Cryptosporidium* controlled human healthy adult infection model to demonstrate scientifically robust proof of concept and prospect of benefit of an anti-parasitic agent to treat cryptosporidiosis.

Day 1

10:35-10:55

Questions and answers

Day 1

10:55-11:00

Closing

Day 2

8:00-8:05

Welcome

Robert Choy

*Associate Director, Research and
Preclinical Development, PATH*

Endemic setting studies

Day 2

8:05-8:20

Cryptosporidiosis in adults and children: Results from a phase 2a trial for *Cryptosporidium* diarrhoea in Malawi, and preliminary results on evaluation of respiratory cryptosporidiosis in paediatric diarrhoeal disease

Pui-Ying Iroh Tam

Head, Paediatrics and Child Health Research Group, Malawi-Liverpool-Wellcome Trust Clinical Research Programme

Summary: In persons with HIV and also in young children in the developing world, the sole agent currently licensed for treatment—nitazoxanide—has little-to-no efficacy compared with placebo in HIV-positive and immunocompromised persons with cryptosporidiosis. One potential therapeutic, clofazimine (CFZ), was recently evaluated in a phase 2A randomised, double-blind, placebo-controlled trial. Twenty-two Part A participants were randomised (12 to CFZ, 10 to placebo) and 11 participants entered into Part B. Twenty Part A and 10 Part B subjects completed the study according to protocol. At study entry, the Part A CFZ group had higher *Cryptosporidium* shedding, total stool weight, and more diarrhoeal episodes compared to the placebo group. Compared to those who received placebo, the CFZ group change over the inpatient period in total daily *Cryptosporidium* shedding increased by 1.02 log₂ *Cryptosporidium* per gram stool (95% upper confidence limit: 2.50), total stool weight decreased by 45.3 g (p=0.37), and number of diarrhoeal episodes increased by 2.32 (p=0.87). The most frequent solicited adverse effects were diarrhoea (9/12, 75%), abdominal pain (8/12, 67%), and malaise (6/12, 50%). Three CFZ and one placebo subject died during the study. Plasma levels of CFZ in participants with cryptosporidiosis were 2-fold lower than Part B controls. Although our findings do not support the efficacy of CFZ for the treatment of cryptosporidiosis in a severely immunocompromised

HIV population, lessons learned in this trial can be used to assess the therapeutic potential of drugs for cryptosporidiosis treatment. Preliminary results on evaluation of respiratory cryptosporidiosis in paediatric diarrhoeal disease will also be presented.

Day 2

8:20-8:35

Genomic analysis of the Bangladesh *Cryptosporidium* parasites

Carol Gilchrist

Associate Professor, University of Virginia Department of Medicine

Summary: Cryptosporidiosis in disadvantaged Bangladeshi infants is associated with diarrheal disease, growth failure, and developmental delay. We have sequenced 67 *C. hominis* isolates from children at our urban study location in Bangladesh. Rapid recombination (occurring at intervals of >300 bp) and nucleotide changes contributed to genetic diversity. We identified several regions of genomic instability where the nucleotide diversity was high. The genes within this polymorphic DNA encoded several membrane proteins, one of which was the highly polymorphic *gp60* gene. Parasite infections increase during the Bangladesh rainy season and contract during the next dry season. We have been able to show that some *gp60* genotypes were detected only in the first year of the study and others only in the next year. Yet to be determined is whether this genetic diversity could contribute to either the development or spread of resistance to new anti-cryptosporidiosis drugs.

Day 2

8:35-8:45

Questions and answers

Day 2

8:45-9:00

Progress towards the optimization of triazolopyridazine MMV665917 as a novel drug to treat cryptosporidiosis

Marvin J. Meyers

Associate Professor of Chemistry and Director of the Chemical Biology Program, Saint Louis University

Summary: Triazolopyridazine-based compound MMV665917 is a promising lead compound for *Cryptosporidium* drug development that possesses many characteristics of the ideal target product profile. It is curative in an immunocompromised mouse model of chronic *Cryptosporidium* infection, efficacious in dairy calf and piglet clinical models, and active against both *C. parvum* and *C. hominis*. Furthermore, MMV665917 undergoes biliary excretion, attaining both high sustained intestinal and systemic levels. These qualities make MMV665917 a particularly exciting *Cryptosporidium* drug lead. However, it has some liabilities, including only modest in vitro potency and marginal in vitro inhibition of the human Ether-a-go-go-Related Gene (hERG) potassium ion channel, resulting in a suboptimal therapeutic index. We have recently initiated a medicinal chemistry strategy to develop structure-activity relationships and identify related compounds with improved potency and reduced inhibition of the hERG channel. Progress towards these ends will be discussed.

Day 2

9:00-9:15

Cryptosporidiosis drug discovery at Calibr at Scripps Research: An overview

Melissa Love

Principal Investigator, Infectious Disease, Calibr at Scripps Research

Summary: In an effort to find novel therapeutics to treat cryptosporidiosis in young children, Calibr carried out a high-throughput screening campaign of more than 1.2 million compounds, resulting in >350 potent and selective hits that inhibit proliferation of *Cryptosporidium parvum* in HCT-8 host cells. Formal hit assessment included counter-screens against *C. hominis* and mammalian cell lines, and subsequent hit-to-lead candidates were advanced into lead optimization following validation of efficacy in an $\text{INF}\gamma^{-/-}$ mouse model of acute cryptosporidiosis. Currently, two chemical series represent novel lead compounds undergoing

medicinal chemistry optimization to improve efficacy and address liabilities to achieve the criteria set forth by the target product profile. Additional lead compounds have also been identified within ReFRAME, a unique collection of small molecules comprised of annotated, clinical-stage, and approved compounds to accelerate drug discovery in neglected tropical diseases. Next steps include profiling lead compounds in additional animal models of cryptosporidiosis, advanced safety profiling, and exploring additional uncharacterized hits to account for potential attrition.

Day 2

9:15-9:30

**Induction of drug
resistance in
*Cryptosporidium
parvum* to methionyl-
tRNA synthetase
inhibitors**

Frederick S. Buckner

*Professor, University of Washington Department of Medicine,
Division of Allergy and Infectious Diseases; Attending Physician,
University of Washington Medical Center*

Summary: That resistance will develop to new antimicrobial drugs is as certain as death and taxes. However, little is known about antimicrobial resistance in *Cryptosporidium* because of the paucity of drugs for treating this infectious organism. As new antiparasitic treatments are developed for cryptosporidiosis, investigators need to watch for the evolution of resistance. In efficacy experiments with novel methionyl-tRNA synthetase (MetRS) inhibitors in newborn calves, we observed that infection rapidly rebounded in two of three treated animals. Oocysts were isolated from feces of these calves and were determined to have new mutations in the MetRS gene that map to the inhibitor binding pocket. Recombinant MetRS protein containing these mutations had >100-fold increase in IC50 values compared to wild type enzyme. This is the first research to describe the occurrence of and mechanism of antimicrobial resistance in *Cryptosporidium parvum*.

Day 2

9:30-9:45

Questions and answers

Day 2

9:45-9:55

Break

Day 2

9:55-10:10

The potential use of human challenge models for accelerating the development of therapeutics for *Cryptosporidium*

Wilbur H. Chen

Associate Professor of Medicine; Chief, Adult Clinical Studies section, Center for Vaccine Development and Global Health, University of Maryland School of Medicine; Director, University of Maryland Travel Medicine Practice

Summary: There are daunting obstacles to developing drugs and vaccines against *Cryptosporidium*. Among the many problems are the limitations of animal models of infection. For example, the only mammalian model other than humans that results in infection and diarrhea following oral challenge with *C. hominis* is gnotobiotic piglets. This presentation will describe the history of human volunteer challenge models and the re-development of the challenge model for *Cryptosporidium*. Within the context of this presentation will be discussed the unique challenges with the sourcing of oocysts, the ethical and regulatory framework of developing the model, and some of the pragmatic hurdles that must be overcome to implement the *Cryptosporidium* challenge model.

Day 2

10:10-10:25

The biology of *Cryptosporidium* host-parasite interaction

Boris Striepen

Professor of Microbiology and Immunology, Department of Pathobiology, University of Pennsylvania

Summary: The protozoan parasite *Cryptosporidium* is a leading cause of severe diarrhea in young children and an important contributor to early childhood mortality. Children appear to acquire resistance over time, suggesting developing immunity, but currently there are no vaccines to protect children from cryptosporidiosis. We established parasite molecular genetics as well as a natural mouse model of infection to address this. We found *Cryptosporidium* invasion and intracellular establishment to be accompanied by injection of parasite proteins into the host cell, and we distinguish two independent delivery systems. We document that the presence of the parasite and parasite molecules are detected by the infected cell. Infection triggers a potent interferon lambda response in vitro and in vivo and this response requires living parasites and intracellular development. We also find that the parasite triggers

inflammasome-mediated IL-18 secretion and we comprehensively define the components of this system using a battery of mouse mutants. Importantly, we demonstrate that the enterocyte, and likely the infected enterocyte, is crucial to the detection of this pathogen.

Day 2

10:25-10:40

**Regulation of
innate and adaptive
immunity to
*Cryptosporidium***

Christopher Hunter

*Mindy Halikman Heyer Distinguished Professor of Pathobiology,
University of Pennsylvania School of Veterinary Medicine*

Summary: The availability of molecular genetics for *Cryptosporidium* as well as a natural mouse model of infection were utilized to address the role of different innate and adaptive components of the immune response required for long-term resistance to this enteric pathogen. The comparison of different mutant mouse strains affirmed the importance of T cells for clearance of this infection but that there was a robust innate pathway that led to the production of the cytokine IFN- γ , which was a major mediator of parasite control. Transcriptional profiling of enterocytes from infected mice identified the presence of an IFN- γ signature, while the absence of IFN- γ signals in enterocytes resulted in increased susceptibility to this infection. Finally, the use of parasite transgenesis allowed the development of parasite strains that expressed different forms of the model antigen SIINFEKL, and these strains were used to characterize parasite-specific CD8⁺ T cell responses. These studies demonstrate how the ability to genetically engineer *Cryptosporidium* provides new tools to dissect the basis for protective immunity and will provide information that will guide the development of a vaccine for *Cryptosporidium* sp.

Day 2

10:40-10:55

Questions and answers

Day 2

10:55 -11:00

Closing

Virtual reception - 16:00-17:30



Speakers



Beatriz Baragaña, PhD

Beatriz Baragaña, PhD, graduated in organic chemistry and then completed her studies with a PhD under the supervision of Professor Barluenga at Universidad de Oviedo (Spain). After receiving her PhD, she worked as a research fellow at Trinity College Dublin in Professor A. P. Davis' laboratory and then as a postdoctoral medicinal chemist in the Medicinal Chemistry department at Bayer AG in Wuppertal, Germany. She moved to Scotland in 2001, where she gained further industrial experience working for five years at NPIL Pharmaceuticals/Avecia as a research and development chemist and then as a team leader focused on antibody drug conjugates for oncology. In 2007, she joined the University of Dundee, where she leads the Drug Discovery Unit apicomplexan portfolio. In the last 12 years, she has been involved in drug discovery projects for cryptosporidiosis and malaria, including the discovery of DDD498 (M5717), a multistage antimalarial currently in phase 1 clinical trials.

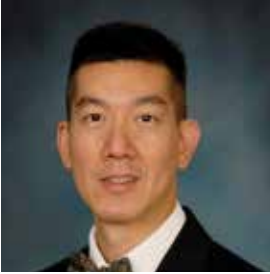
 @baragana_b



Frederick S. Buckner, MD

The research of Fred Buckner, MD, is concentrated on drug discovery for diseases caused by pathogenic protozoa and antibiotic-resistant bacteria. The protozoa include *Trypanosoma cruzi* (Chagas disease), *Trypanosoma brucei* (African sleeping sickness), and *Cryptosporidium* species (diarrheal disease). The laboratory focuses on several biochemical targets for developing antiparasitic drugs, including protein synthesis pathways, proteasome degradation, and protein prenylation. The research is done in collaboration with chemists (mainly in the Fan and Gelb laboratories at the University of Washington) who synthesize small chemical compounds designed to target protozoan or bacterial targets. New compounds are put through a screening cascade to identify the molecules with (1) potent activity on the targets, (2) suitable pharmacokinetic properties, and (3) excellent safety properties. Compounds that meet

the strict screening criteria are then tested in animal efficacy models. A variety of compounds acting by different mechanisms are in advanced stages of preclinical development for Chagas disease, cryptosporidiosis, and Staphylococcal infections.



Wilbur H. Chen, MD, MS, FACP, FIDSA

Wilbur Chen, MD, is an infectious disease-trained physician-scientist, faculty member of the Center for Vaccine Development and Global Health, and director of the University of Maryland Travel Medicine Practice. Dr. Chen has focused his research on the development of vaccines against diarrheal pathogens. He is an active investigator within the US National Institute of Allergy and Infectious Diseases (NIAID)-supported Vaccine and Treatment Evaluation Unit, co-director of the NIAID-funded Collaborative Influenza Vaccine Innovation Centers Clinical Core, and was the principal investigator of the NIAID-funded Food and Waterborne Diseases Integrated Research Network Clinical Research Unit contracts. One of the more unique tools in his clinical research is the use of controlled human infection models, involving pathogens such as *Vibrio cholerae*, *Shigella flexneri*, enterotoxigenic *Escherichia coli*, and influenza to allow for studies on pathogenesis, the exploration of potential mechanisms of protective immunity, and the evaluation of candidate therapeutics and vaccines.



Lisa Funkhouser-Jones, PhD

Lisa Funkhouser-Jones, PhD, received a BS in biology summa cum laude from Baylor University (Waco, Texas) and a PhD in biological sciences from Vanderbilt University (Nashville, Tennessee), studying host-bacterial interactions between insects and their *Wolbachia* symbionts in the laboratory of Seth Bordenstein, PhD. She is a postdoctoral research associate in the laboratory of L. David Sibley, PhD, at Washington University School of Medicine in St. Louis, Missouri, where she contributed

to the development of an in vitro culture system for the protozoan parasite *Cryptosporidium parvum*. She is currently using the system to study meiotic recombination in the parasite as well as characterize drug compounds and microbial metabolites that inhibit *C. parvum* growth and development.

 @DNAdiva87



Carol Gilchrist, PhD

Carol Gilchrist, PhD, is an associate professor in the Department of Medicine at the University of Virginia. A British citizen, she obtained her PhD at the University of Western Ontario, Canada. Dr. Gilchrist's work is focused on using molecular methods to understand the biology and pathogenic phenotype of enteric parasites. She is highly interested in the factors that influence the symptomatic diarrheal disease caused by the protozoan parasites *Entamoeba histolytica* and *Cryptosporidium* spp. Her goal is to understand the factors that promote parasite virulence and consequent host diarrhea. While some information is available on host genetics, little is known about the impact of parasite genetic diversity or the microbe environment on parasite virulence. Dr. Gilchrist is fascinated by the role these may play in the outcome of an infection and her hypothesis is that these play a key role in controlling disease severity.

 @carolgilchris10



Christopher Hunter, PhD

Professor Chris Hunter obtained his PhD in biochemistry (1989) from the University of Glasgow, Britain, and as a postdoctoral fellow at Glasgow developed his interest in the role of cytokines in infectious disease of the central nervous system. This was followed by a postdoctoral fellowship at Stanford University (1992-1996) with Jack Remington, MD, before joining the faculty at the University of Pennsylvania

(1996–present). There his research group continues to study the cytokines that influence innate and adaptive immunity to *Toxoplasma* and *Cryptosporidium*. He has provided extensive service as a journal editor and member of editorial boards as well as extensive peer review for the US National Institutes of Health. He served as chair of the Department of Pathobiology (2007–2018) and director of the Center for Host–Microbial Interactions (2012–2018). He has been the Mindy Halikman Heyer President’s Distinguished Chair since 2015.

 @KingOfPathogens



Pui-Ying Iroh Tam, MD

Pui-Ying Iroh Tam, MD, heads the Paediatrics and Child Health Research Group at the Malawi–Liverpool–Wellcome Trust Clinical Research Programme, where she has been based full-time since 2016. She is a Hong Kong native who received her undergraduate degree from Harvard University, medical degree from the Royal College of Surgeons in Ireland, and residency and fellowship training from Tufts and Boston Universities, respectively. She is a clinician–researcher who works as a consultant pediatrician in Queen Elizabeth Central Hospital, the tertiary-level government referral hospital for the southern region of Malawi. Her research deals with respiratory tract infections and the intersection with diarrheal disease, common infectious conditions in the Malawi setting, antimicrobial resistance, sepsis, and antimicrobial stewardship.



Paul Kelly, MD, FRCP

Paul Kelly, MD, is a professor of tropical gastroenterology at Barts and The London School of Medicine in the United Kingdom. He is also an honorary lecturer at the University of Zambia School of Medicine in Lusaka and an honorary senior lecturer at the London School of Hygiene and Tropical Medicine. Professor Kelly was educated in Oxford and at The

London Hospital; he is both clinically qualified and clinically active in the United Kingdom and Zambia. Professor Kelly has published many research articles related to various aspects of infectious diseases, including four trials of treatment for cryptosporidiosis. His research interests also encompass environmental enteropathy, malnutrition enteropathy, and, more recently, gastric malignancies, hepatitis B, and portal hypertension related to schistosomiasis.



Melissa Love, PhD

Melissa Love completed her PhD in pharmacology in 2014 at the University of Pennsylvania. She joined Case McNamara's group at Calibr as a postdoctoral fellow in December 2014 to begin a drug discovery project for *Cryptosporidium*. Currently, Dr. Love is a principal investigator, leading the Calibr Cryptosporidiosis drug discovery program, and is a key biologist for Calibr's Tuberculosis drug discovery program. Her research interests include global health, especially neglected tropical diseases, and drug discovery.



Ujjini Manjunatha, PhD

Ujjini Manjunatha, PhD, is a group leader for cryptosporidiosis and lead discovery at the Novartis Institute for Tropical Diseases (NITD) in Emeryville, California. NITD is a small-molecule drug discovery research institute within the Novartis Institutes for BioMedical Research. NITD works in collaboration with a number of academic and nonprofit partners focusing on parasitic diseases. In his current role, Manjunatha works closely with the scientific leadership and the management team of the institute to ensure its overall function and success. And he is also leading a team of research investigators and research associates working with drug discovery against malaria, cryptosporidiosis and trypanosomiasis. Dr. Manjunatha received his PhD from the Indian Institute of Science, Bangalore, in 2001 and. He was

then awarded John E. Fogarty International visiting post-doctoral research fellowship to work at the US National Institutes of Health on the mechanism of action of protomanid, a novel anti-tuberculosis drug. He joined NITD Singapore in 2007, and since then has been working on drug discovery and development against various neglected tropical diseases. He has identified a couple of novel class of anti-tuberculosis candidates and are currently being pursued by TB Alliance. Recently, Manjunatha led a multi-disciplinary team of scientists in identifying a novel anti-*Cryptosporidium* candidate, a novel lipid kinase CpPI(4)K (phosphatidylinositol-4-OH kinase) inhibitor with promising in vitro and in vivo activities. NITD team is now focusing on understanding PK-PD relationship in cryptosporidiosis, identifying novel *Cryptosporidium* inhibitors and establishing cryptosporidiosis controlled human infection model for testing a NCEs prior to pediatric clinical studies. He has published over 50 research articles in highly reputed international journals and has a number of patents to his credit.



Chelsea Marie, PhD

Dr. Chelsea Marie is an Assistant Professor of Medicine at the University of Virginia in the Division of Infectious Disease and International Health. She leads a laboratory research program focused on identifying unique immune mechanisms that determine human susceptibility to enteric pathogens. Her recent work identified potassium channels in the membrane of human cells that mediate inflammation and cell death during amebiasis. She has recently co-authored a paper on the role of human protein kinase C in susceptibility to cryptosporidiosis in children, which remains an ongoing area of investigation in her laboratory. Other areas of her research include the cellular and immune mechanisms of environmental enteropathy in children in Bangladesh and the interaction of microbial therapies and the immune

response during treatment for recurrent *Clostridium difficile* infection.

Dr. Marie earned her BS in Microbiology, with minors in Chemistry and Spanish from the University of Oregon and her PhD in Pathobiology from the University of Washington. She is a past CDC Emerging Infectious Disease fellow.



Marvin J. Meyers, PhD

Marvin Meyers completed his PhD in organic chemistry at the University of Illinois, developing subtype-selective ligands for the estrogen receptors alpha and beta, including two tool compounds that are currently sold commercially. From 2000 to 2010, he worked as a medicinal chemist in drug discovery at Pharmacia/Pfizer on new drugs for autoimmune diseases, cardiovascular diseases, and pain, resulting in the discovery of two compounds selected for human clinical trials. In 2010, he was a founding member and eventual director of chemistry for the Center for World Health and Medicine at Saint Louis University (SLU), focusing on the discovery of new drugs for rare and neglected diseases such as malaria, infectious diarrhea, tuberculosis, hepatitis B virus, and muscular dystrophy. In 2018, Dr. Meyers joined the Department of Chemistry at SLU as an associate professor and led the effort to design and launch a new academic program in chemical biology.

 @MeyersChemLab



Boris Striepen, PhD

Boris Striepen, PhD, studied biology at the Universities of Bonn and Marburg and came to the United States as a postdoc in 1995. He was on the faculty of the Center for Tropical and Emerging Global Diseases at the University of Georgia for 18 years and recently moved to the University of Pennsylvania. His laboratory studies the cell and molecular biology of parasites and is currently

focused on *Cryptosporidium*, a leading global cause of mortality in young children due to diarrheal disease. His laboratory pioneered molecular genetics and a natural mouse model for this previously intractable organism and leverages those to understand fundamental parasite biology and to advance urgently needed translation. Dr. Striepen taught undergraduate and graduate classes, directed a US National Institutes of Health training grant program, and served as faculty and director of the Biology of Parasitism summer research course at the Marine Biological Laboratory in Woods Hole, Massachusetts.



Wesley C. Van Voorhis, MD, PhD

Wes Van Voorhis, MD, trained at the Massachusetts Institute of Technology (undergraduate), Cornell Medical College, Rockefeller University (MD/PhD), the University of California, San Francisco for internal medicine, and the University of Washington (UW) as a fellow in infectious diseases. As a UW faculty member, Dr. Van Voorhis researches, practices medicine, teaches, and until 2017, led the university's Division of Allergy and Infectious Diseases. He is the director of the Center for Emerging and Re-emerging Infectious Diseases, which takes a multidisciplinary approach to identifying and developing diagnostic, therapeutic, and vaccine solutions to emerging infectious diseases. For the past 27 years, he has worked in preclinical drug development for malaria, trypanosomes, *Leishmania*, and *Cryptosporidium*. Dr. Van Voorhis works extensively in target-based drug development and, as possible, uses iterative structure-based drug development. His laboratory is currently characterizing a new preclinical drug candidate for the treatment of cryptosporidiosis. Dr. Van Voorhis was the principal investigator of a recently completed clinical trial to test the efficacy of clofazimine for cryptosporidiosis in Malawi.



Jennifer Zambriski, DVM, PhD

Dr. Zambriski is an Assistant Professor of Epidemiology in the Department of Population Health Sciences at the Virginia-Maryland College of Veterinary Medicine. She holds a DVM from Tufts University and a PhD in Epidemiology from Cornell. Her research centers on the human-animal health continuum. She has studied elephant TB in Nepal, Nipah virus in Malaysian bats, and livestock brucellosis in Nicaragua. Her research at Virginia Tech focuses on the epidemiology of cryptosporidiosis in children and cattle, including chemotherapeutic development in the calf model. Prior to joining VT, Dr. Zambriski lived and worked in Indonesia on the UN-FAO Highly Pathogenic Avian Influenza Control Program, designing disease surveillance systems. Dr. Zambriski is an NSF IGERT recipient, spending 2 years in Ethiopia studying Food Systems and Poverty Reduction. She also has the distinction of being one of the first veterinarians to receive an NIH Fogarty International Clinical Research Scholarship, which supported her zoonosis research in Peru.

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Cover photo: A mother and health care worker discuss the use of oral rehydration solution for her infant at a health center in Kampong Thom province in Cambodia.
Photo: PATH/Heng Chivoan