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Keynote Speakers

Autoreactive T Cells and Chronic Fungal Infection Drive Esophageal Carcinogenesis

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Abstract

Humans with autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), a T cell-driven autoimmune disease caused by impaired central tolerance, are susceptible to chronic fungal infection and esophageal squamous cell carcinoma (ESCC). However, the relationship between autoreactive T cells and chronic fungal infection in ESCC development remains unclear. We find that kinase-dead Ikka knockin mice develop APECED-like phenotypes, including impaired central tolerance, autoreactive T cells, chronic fungal infection, and ESCCs expressing specific human ESCC markers. Using this model, we investigated the link between ESCC and fungal infection. Autoreactive CD4 T cells permit fungal infection and incite tissue injury and inflammation. Antifungal treatment or autoreactive CD4 T cell depletion rescues, whereas oral fungal administration promotes, ESCC development. Inhibition of inflammation or EGFR activity decreases fungal burden. Fungal infection is highly associated with ESCCs in non-autoimmune human patients. Therefore, autoreactive T cells and chronic fungal infection, fostered by inflammation and epithelial injury, promote ESCC development.

Microbial Genomics: A Case Study in Evolutionary Biology

Shiladitya DasSarma

Institute of Marine and Environmental Technology and Department of Microbiology and Immunology, University of Maryland School of Medicine, Baltimore, MD, USA

Abstract

Complete genome sequencing of microorganisms became possible in the 1990s beginning with a handful of diverse bacterial and archaeal species and expanding exponentially into the many thousands of microbial genomes available today. The astronomical numbers of genes and genomes represent both an opportunity and challenge to understanding the evolution of life on Earth. We have focused on how genome sequences in a coherent archaeal clade can be used to study protein adaptation and evolution to extreme conditions, including high salinity and low water activity and sub-zero temperatures. We used both comparative genomics at the whole genome level to determine broad protein properties and a combination of experimental and modeling studies of an extremophilic enzyme for exploring its detailed molecular structure and function. These studies illustrate the enormous power of microbial genomics, in combination with molecular biology, biochemistry, structural biology, and genetics, to address fundamental problems in biology. Such an approach has significant implications from biotechnology to astrobiology.

Biography

Dr. DasSarma earned his PhD from MIT with Nobel laureate HG Khorana, and received his postdoctoral training at Massachusetts General Hospital, Harvard Medical School. He served as a faculty member at the University of Massachusetts-Amherst and Director of the Molecular Biology and Biotechnology Computer Facility before moving to the University of Maryland where he is currently a Professor at the Institute of Marine and Environmental Technology. His lab led the first complete genome sequencing project of an extremely halophilic Archaeon published as a cover article in the Proceedings of the National Academy of Science USA and featured in American Scientist.

Metabolism in microbial communities exploited for chemical production, balancing our health and in ecosystem engineering

E. Elias Hakalehto

University of Helsinki, University of Eastern Finland and Finnoflag Oy, Finland Finland

Abstract

Traditional industrial biotechnology is usually applying aseptic conditions for its processes. However, in natural ecosystems aseptics is seldom prevailing. Therefore, our understanding on the metabolic networks and interactions between various members of the microbial communities show way for novel solutions both in the utilization of industrial side streams and in regaining balance of our gut microbiome, for instance. In the city of Tampere, Finland, an experiment is going on for demonstrating the economically feasible conversion of zero fiber deposits of the lake bottom into industrial chemicals. In a corresponding fashion, it is possible to solve individual human health problems by the aid of microbial communities, as we return the balance to the lake ecosystem. Seeing the parallelisms in various microbial processes increases exchange of ideas between different fields of applied microbiology. The universal approach of understanding functions in various microbial ecosystems could make useful tools both for achieving goals of health-promoting human microbiome and profitable industrial processes. In the Tampere case, 1.5 M tons of deposited waste of paper and pulp industries could be converted into chemicals worth of hundreds of millions of Euros. Worldwide, corresponding zero fiber deposits could be found in several thousands of factory sites and in their surroundings. Also other sectors of our industries could benefit from microbes and their interactions in finding profitable solutions for cleaning the environment in a climate-friendly way.

Biography

E. Elias Hakalehto, PhD, is an Adjunct Professor in the Universities of Helsinki and Eastern Finland, in agroecological microbiology and biotechnical microbial analytics, respectively. In his R&D company Finnoflag Oy, he has carried out numerous hands on projects on ecosystem engineering, modern biorefinery R&D projects and microbiome studies. His company has been active for 25 years.

Dr. Hakalehto has conducted more than 100 investigations in the fields of microbiology and biotechnology for various clients in industries, research industries, clinical sector and authorities. He is the vice president in the International Society on Environmental Indicators. Dr. Hakalehto chaired the 22nd international conference of the society in Helsinki, Finland, August 2017. He is the author of more than 50 research papers, more than 70 patent applications, and more than 100 book chapters for international publishers, such as Springer, Wiley, CRC Press, Elsevier and others. Between 2015-18 he edited the four part Microbiological Hygiene series for Nova Scientific Publishers Inc., N.Y. USA. He has been the principal technology provider in the EU six nation Baltic Sea research project ABOWE for biorefineries, as well as in the “Zero waste from zero fiber” project in Tampere, Finland, funded by the Finnish Ministry of Agriculture and Forestry in years 2018-19. Elias Hakalehto is also the inventor of PMEU (Portable Microbe Enrichment Unit), which has been developed for the enhanced analysis of patient samples, environmental and process specimens. He has carried out eight industrial biorefinery pilot projects during his career.

His main interests are the microbiological communities, and the activities of strains as members of these communities. Globally, the use of microbiology in solving the big issues of our time, such as environmental changes.

Lantibiotics: a large untapped pipeline of attractive scaffolds for the development of novel antibiotics

Martin Handfield, MS, PhD*

Oragenics Inc., USA

Abstract

Lantibiotics are polycyclic lanthipeptides that represent a large untapped pipeline of novel antibiotics. There is considerable evidence that indicates that lantibiotics may be well tolerated as therapeutic agents in humans. Mutacin 1140 (MU1140) is a naturally produced lantibiotic by the Gram-positive bacterium *Streptococcus mutans*. One of the most exciting characteristics of MU1140 is that it acts via a novel mechanism of action termed Lipid-II abduction. This unusual mechanism of action is thought to improve antibiotic durability due to the inherent difficulty in development of antibiotic resistance via modification of the pyrophosphate moiety of its target, Lipid-II. We have recently proposed a set of blueprints that may enable and foster future therapeutic development of lantibiotics, considering the classic pitfalls related to their production, purification and formulation. The use of these blueprints led to the design and preclinical testing of a second-generation homologs of MU1140, one of which was prioritize for clinical testing for the treatment of *C. difficile* infections. The lead compound was selected from a library of over 700 single and multiple substitution variants of MU1140. Top performers were triaged based on testing for potency, solubility, manufacturability, and physicochemical and/or metabolic stability in biologically-relevant systems. The best performers in vitro were further evaluated orally in the Golden Syrian hamster model of CDAD. In vivo testing ultimately identified OG716 as the lead compound, which conferred 100% survival and no relapse at 3 weeks post infection. MU1140-derived variants are particularly attractive for further clinical development considering their novel mechanism of action.

Biography

Dr. Handfield is Oragenics' Senior Vice President of R&D. Prior to joining Oragenics (NYSE: OGEN), he was a Tenured Associate Professor at the Center for Molecular Microbiology and the Department of Oral Biology at the University of Florida College of Dentistry. During that time, he also co-founded *iviGene Corp.* and *Epicure Corp.* to commercialize several technologies. Dr. Handfield holds degrees in Biochemistry, Microbiology and Immunology from the Université Laval College of Medicine (Canada). He did his postdoctoral training under the mentorship of Dr. Jeffrey D. Hillman, the Founder (ret.) of Oragenics.

Ion and Nutrient Trafficking in Malaria Parasites

Sanjay A. Desai

Division of Intramural Research, NIAID, National Institutes of Health, MD

Abstract

Dr. Sanjay A. Desai is a Senior Investigator in the NIAID/DIR. His laboratory uses molecular and cellular methods to study how malaria parasites acquire nutrients and other essential solutes from human plasma. The presentation will describe several ion channel unique to malaria parasites, identified through pioneering patch-clamp studies of infected human erythrocytes in the Desai lab. These channels are distinct from mammalian transporters, are essential for intracellular parasite development, and are being pursued as important, unexploited antimalarial drug targets.

Biography

Dr. Desai received his M.D.-Ph.D. from Washington University in St. Louis. Following an internal medicine residency and infectious diseases fellowship at Duke University Medical Center, he joined the Division of Intramural Research at the NIH and is now a Senior Investigator.

The Desai laboratory uses a multidisciplinary approach to study transmembrane transport of nutrients and other solutes in bloodstream malaria parasites. Malaria remains an important global health problem; with increasing drug resistance and the lack of an effective vaccine, new therapies are needed and should be based on a rigorous understanding of parasite biology. To identify and characterize targets for antimalarial therapies, the lab utilizes molecular biology including CRISPR and heterologous expression, structural biology including cryoEM, biochemical methods including electrophysiology, drug discovery, genetics, and epigenetics.

The Role of Gut Microbiome in the Increase of Autoimmune Diabetes in Finland

Jouni Pesola^{1,2*} and E. Elias Hakalehto²⁻⁴

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²University of Eastern Finland, Kuopio, Finland; ³Finnoflag Oy, Kuopio and Siilinjärvi, Finland; ⁴University of Helsinki, Finland

Abstract

During last decades the autoimmune or type 1 diabetes (T1D) has increased around the world, incidence being highest in Finland. In addition to predisposing genes, the environmental factors related to gut microbiome are very important in the pathogenesis of the disease. In the intestines, which is the largest immunological organ, host-microbe interactions have an important role in the development and maturation of the immune system. Unique individual alimentary microbiome is a combination of microbes originating from the close environment during early life with the strains obtained during birth being mostly of maternal origin. Delivery method and early feeding have the most significant impact on the development of it. PMEU (Portable Microbe Enrichment Unit; Finnoflag Oy, Finland) has been successfully used for the investigation of the characteristics and changes of the constitution of the microbiome. It

has revealed the Bacteriological Intestinal Balance (BIB) referring to balanced existence between different enterobacterial as well as other main groups that is characteristic for the healthy microbiome.

We have applied the PMEU method for studying the enterobacterial microbiota of the infants with genetic predisposition to the T1D. The PMEU method has been useful in the investigation of the microbiome between different feeding groups and after medications, such as antibiotics. The PMEU method has opened a new window for understanding the interactions between host and the microbiome. This approach can be used to discover the relationships between the gut microbiome and the pathophysiology of the T1D, as well as other autoimmune diseases. Both the role of BIB and the factors influencing the development of the microbiome are discussed.

To die or not to die, ROS has the final say

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¹Public Health Research Institute, New Jersey Medical School, Rutgers University, USA.

²State Key Laboratory of Molecular Vaccinology and Molecular Diagnostics, School of Public Health, Xiamen University, China

Abstract

Although death is one of the most important events for all organisms, it is still poorly understood. Death is commonly thought to derive from a variety of lethal assaults in a stress-specific manner. Finding that a surge in reactive oxygen species (ROS) correlates with killing by three different antimicrobial classes suggested that a general mechanism may account for most, if not all, death elicited by severe stress. Challenges to ROS-based killing led to finding examples beyond antimicrobial stress, but the absence of a causal relationship left the idea vulnerable to criticism. We describe a novel assay for cell death that establishes ROS as the cause rather than a consequence of death triggered by both antimicrobial and environmental stressors. The assay also reveals a misconception associated with the traditional killing assay. The key idea is that when bacterial cells fail to form colonies on drug-free agar after lethal stress, they are not necessarily dead at the time of stressor removal and plating: they can die on the agar plate after stressor removal during colony growth. A post-stress surge in ROS was readily observed, and blocking that surge allowed cells, thought by traditional assays to have been killed, to survive. Cellular repair renders most stressor-specific primary damage only potentially lethal; nevertheless, primary damage can lead to a surge of intracellular ROS that causes massive secondary damage, overwhelms the repair capacity of a cell, and generates even more ROS-mediated damage. Eventually, ROS accumulation becomes self-stimulating, which executes the final stage of the death process.

Biography

Xilin Zhao, Ph.D., Principal Investigator, Public Health Research Institute; Associate Professor, Department of Microbiology,

Biochemistry & Molecular Genetics, New Jersey Medical School, Rutgers University; Professor, School of Public Health, Xiamen University, China. Research interests currently address stress-mediated bacterial suicide, with a focus on redox imbalance, reversing antimicrobial resistance using CRISPR, development of novel antimicrobials and antimicrobial enhancers, and non-invasive imaging of gut microbiota and infection. He has published >90 publications, with >7,000 citations. He has been awarded numerous research grants, including the NIH Director's New Innovator Award and Bill and Melinda Gates Foundation Global Health Grand Challenge Award.

Factors influencing the evolution of carbapenem resistance in *Klebsiella pneumoniae*

Peijun Ma^{1,2,3*}, Alejandro Pironti¹, Hannah H. Laibinis¹, Lorrie He¹, Abigail Manson¹, Ashlee M. Earl¹, Roby P. Bhattacharyya^{1,2,3}, Deborah T. Hung^{1,2,3}

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²Department of Molecular Biology and Center for Computational and Integrative Biology, Massachusetts General Hospital, Boston, United States

³Department of Genetics, Harvard Medical School, Boston, United States

Abstract

In this era of rising antibiotic resistance, many studies have been focused on understanding resistance mechanisms. However, our understanding of mechanisms influencing the evolution of antibiotic resistance is limited. Here, we investigated the roles of two factors in the evolution of antibiotic resistance: the choice of a specific antibiotic and the genetic backgrounds of bacterial isolates. First, by measuring resistance frequencies of *Klebsiella pneumoniae* isolates to antibiotics used to treat multi-drug infections, including 4 carbapenems and faropenem, we showed that the evolution of resistance is influenced differently by mechanistically and structurally similar antibiotics. Specifically, we observed higher resistance frequencies to ertapenem and faropenem. More importantly, prior exposure to ertapenem or faropenem endangers the use of other carbapenems by increasing the resistance frequencies to these other carbapenems. Secondly, we found that *K. pneumoniae* isolates of the ST258 sequence type, the lineage most strongly associated with carbapenem resistance in the United States and Europe, in general, have high-level activities of mobile genetic elements (MGEs), causing higher mutation rates, and thus higher resistance frequencies compared to non-ST258 strains. ST258 strains lack the CRISPR-Cas system, and they have a greater propensity to take up resistance genes. This work provides a molecular basis for the predominance of carbapenem resistance appearing in ST258 strains. Together, we demonstrated that choice of antibiotics and regulation of MGEs are two important factors affecting the evolution of carbapenem resistance. Our findings imply that evolution of antibiotic resistance may be reduced by considering these factors during drug development and antibiotic prescription.

Biography

Dr. Peijun Ma received her undergraduate degree in Biological Engineering from Harbin Institute of Technology in China and received her Ph.D. in Biological Sciences from Vanderbilt University in the United States. During her Ph.D., Dr. Ma studied the function and mechanisms of circadian clocks in cyanobacteria. Currently she is a postdoctoral associate in Deborah Hung's laboratory at the Broad Institute of MIT and Harvard. Her major project is to understand mechanisms that influence or regulate the evolution of antibiotic resistance.

Targeting Malaria Parasite and Host Liver Cell Interactions with a Phage Display Library

Sung Jae Cha, Marcelo Jacobs-Lorena*

Johns Hopkins Bloomberg School of Public Health, Department of Molecular Microbiology and Immunology and Malaria Research Institute, 615 N. Wolfe St., Baltimore, USA

Abstract

Previously, using a phage peptide display library, our group has identified Plasmodium parasite ligands and corresponding host cell receptors important for ookinete-mosquito midgut interaction, sporozoite-mosquito salivary gland interaction and sporozoite-Kupffer cell interaction in the mammalian liver. Here we report on a phage display library screen for peptides that bind

to hepatocytes, the sporozoite target for infection of the liver. We hypothesize that such peptides may be mimotopes (structural mimics) of Plasmodium sporozoite ligands for hepatocyte interaction. A prime candidate peptide from this screen - HP1 - binds to a ~25 kDa hepatocyte membrane protein and an anti-HP1 antibody recognizes a ~45 kDa sporozoite surface protein (a candidate ligand). Immunization with HP1 protected 50 % mice from *P. berghei* challenge. Significantly, anti-HP1 antibody inhibited *P. falciparum*-human hepatoma cell (HepG2) interaction by 87 % compared to control antisera. This sporozoite ligand is a potential vaccine antigen targeting malaria liver invasion.

Migration of Multidrug Resistant (MDR) zoonotic Salmonella Spp.and Campylobacter Spp.from poultry meat/ farm environment to human and forecasting their MDR pattern on public health in Bangladesh perspective.

Suvamoy Datta^{*}, Maruf Abony

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Abstract

Zoonotic Bacteria typically cycle in domestic animals without causing disease in their typical hosts. When they get transmitted into human, the disease that is produced can be severe. Poultry meat and farm environmental samples were analyzed for detection of similar drug resistant biotypes in clinical setting. Poultry meat and environmental samples were analyzed for detection of zoonotic Salmonella spp. and Campylobacter spp. and a total of 244 Salmonella spp. and 156 Campylobacter spp. were obtained and identified using API identification kit. A number of 1200 clinical Salmonella spp. and 920 clinical Campylobacter spp. were identified and observed by cross checking biotype and drug resistant pattern of poultry based isolates. Based on forecasting data, by the year 2019 Campylobacter spp. isolated from clinical origin will be more than 90% resistant against Sulfomethoxazole/Cotrimoxazole, Nalidixic Acid and Ciprofloxacin. Also the overall drug resistant pattern of Nalidixic acid in both clinical and poultry samples are 83% and 75% respectively. In case of Salmonella spp. isolates similarity in drug resistant between poultry and clinical isolates can be seen in Cotrimoxazole, Nalidixic acid and Netilmycin. This study also revealed that drug resistance pattern increased in the last 4 years 43.61% isolates were MDR in 2015, 48.26% in 2016 , 50.43% in 2017 and 57.83% in 2018, which will increase to 61.74%, 66.52% and 71.3% for the years 2019, 2020 and 2021 respectively based on forecasting of obtained data. Overall 49.78 % of the strains became Multidrug resistant (resistant to 5 or more then 5 antibiotics tested). Presence of these drug resistant zoonoses indicates unregulated use of antibiotics in poultry farming and no adherence to Good Farming Practice and HACCP. Undercooked or raw poultry samples, or food products contaminated by poultry environmental factors may cause catastrophic health issues among general population of Bangladesh.

Biography

Suvamoy Datta was born in 1974 in the village of Senerkhil of Feni district. Suvamoy Datta have completed my B.Sc (Hons) and M.Sc degree from the Department of Microbiology, University of Dhaka and Ph.D degree from the University of Tokyo, Japan with MONBUKAGAKUSHO (Japan Government) scholarship. Suvamoy Datta was awarded Young Scientist Award for my Ph.D research from International Scientific Congress - CHRO-2009, Japan. Dr. Suvamoy Datta also have completed my Postdoctoral research work on Cancer drug development with prestigious Hormel Postdoctoral fellowship at University of Minnesota, USA. Now Dr. Suvamoy Datta is working as Professor & Chairman of the Department of Microbiology, Primeasia University, Dhaka, Bangladesh. Dr. Datta have a total of 35 (Thirty five) publications where 30 (Thirty) are in International Journals most are based on research at Primeasia University in context to Bangladesh and most of my publications are well recognized in terms of accession or citation.

Dr. Datta was invited as Plenary Speaker at MESMAC International Conference, 2019, Kerala, India to talk on "Forecasting of Multi-drug resistance in UTI patients". Dr. Datta was awarded travel grant as Invited Presenter at Regional Conference on Safe Science, 2018 which was held in Kualalumpur, Malayasia for my research on "Multi-drug resistance pattern in UTI patients". Dr. Datta am invited as Speaker at Climate 2020 conference which will be held in Amsterdam, Netherlands. Dr. Datta have supervised more than 40 students for their graduate research works. Dr. Datta basically works on Molecular pathogenesis, Multidrug resistant & Urinary tract infection, Food safety & Environmental Hygiene, and Climate change & Diseases etc. Now Dr. Datta is working as Executive Editor of the Journal of Primeasia University (JPAU).

Poster Presentations

Regulatory roles of the transcription factor cyclic AMP-responsive element-binding protein H in lipoprotein homeostasis

Jung Hoon Lee, Min Jae Lee

College of Medicine, Seoul National University, Korea

Abstract

Chylomicrons and very low-density lipoproteins (VLDLs) are types of lipoproteins arose from the small intestine and the liver, respectively, carrying dietary fat and triglyceride throughout the body. Apolipoproteins are the protein components of lipoproteins, controlling the synthesis, trafficking, and catabolism of lipoproteins. Therefore, they are of considerable physiological importance and are associated with various disorders, including dyslipidemia, cardiovascular and neurodegenerative diseases. Among them, ApoA-IV is thought to act primarily reverse cholesterol transport and intestinal lipid absorption via chylomicron assembly and secretion. ApoC-II plays crucial roles in triglyceride metabolism in plasma, as it is a cofactor of lipoprotein lipase which hydrolyzes triglyceride-rich lipoproteins and releases free fatty acids that are directed to and utilized by peripheral tissues, such as heart, adipose and muscle tissues. In contrast, ApoC-III inhibits the activity of lipoprotein lipase, thus delays catabolism of triglyceride-rich lipoproteins.

Cyclic AMP-responsive element binding protein H is an endoplasmic reticulum-bound transcription factor that is exclusively expressed in liver and small intestine. Here, we show that cyclic AMP-responsive element binding protein H plays a key role in maintaining normal distribution of chylomicron and VLDLs in circulation by controlling the hepatic and intestinal expression of apolipoprotein genes. Given the crucial roles of apolipoproteins in lipoprotein homeostasis, we propose that cyclic AMP-responsive element binding protein H control metabolism of chylomicrons and VLDLs by regulating the proper ratio of apolipoprotein levels.

Biography

Dr. Jung Hoon Lee is currently a Research Assistant Professor at the Seoul National University College of Medicine. Dr. Lee received her Ph.D. in Pharmaceutical Sciences from the University of Pittsburgh in 2009. After completion of her degree, she started her post-doctoral research at the Harvard School of Public Health. She was appointed as a research assistant professor at the Kyunghee University in 2011 and moved to the Seoul National University in 2015.

Intracellular Polysaccharide Storage is Essential for the Colonization of Commensal Bifidobacterium Breve UCC2003 in the Murine Gut

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²Biochemistry of Dairy Products, Instituto de Productos Lácteos de Asturias-Consejo Superior de Investigaciones Científicas (IPLA-CSIC), Spain

Abstract

Bifidobacteria are predominant commensal bacteria of the human gastrointestinal tract (GIT) widely used as probiotics. The mechanism through which these strains reside within their host and exert health benefits is not fully understood. Some gut commensals synthesize and store an intracellular polysaccharide (IP), which acts as an energy and carbon reserve and is implicated in host colonization and persistence. *In silico* genome analysis of Bifidobacterium breve UCC2003 (and various other bifidobacterial species) revealed the presence of genes predicted to be involved in IP metabolism. Furthermore, analysis of human gut metagenomes revealed the ubiquitous presence of homologs of such IP metabolism genes, indicating that this is a key function in the GIT.

The aim of this study was to investigate the role of IP production in bifidobacterial colonization of the human GIT. For this purpose, genes encoding a glycogen phosphorylase (Bbr_0060) and a phosphoglucomutase (Bbr_1595), involved in glycogen breakdown and synthesis, respectively, were inactivated in B. breve UCC2003 by insertional mutagenesis. Phenotypic analysis revealed that both genes are essential for growth on several carbohydrates (e.g. maltose, maltodextrin and starch), probably due to the irreversible accumulation of IP. We furthermore investigated IP production/storage in B. breve UCC2003 and its role in the GIT colonization of mice. *In vivo* analysis demonstrated that both genes are essential for efficient *in vivo* murine gut colonization. Such findings shed light on genes involved in bifidobacterial colonization and persistence.

CCR5 Targeting Drugs Enhance Suppression of HIV Infection in CD34+ Hematopoietic Humanized Mice Treated with Standard cART Therapy

Matthew Weichseldorfer¹, Yvonne Affram¹, Lauren M. Neal¹, Alonso Heredia¹, Yutaka Tagaya¹, Sandra Medina- Moreno, Juan Zapata, Francesca Benedetti¹, Davide Zella¹, Frank Denaro², Marvin Reitz¹, Joseph Bryant¹, Fabio Romerio¹ and Olga S. Latinovic^{1*}

¹Institute of Human Virology, University of Maryland School of Medicine, USA

²Morgan State University, USA

Abstract

The effectiveness of combined antiretroviral therapy (cART) is evidenced by control of peripheral blood viral load. However, there is HIV reservoir persistence upon termination of cART. We anticipate that viral evolution detected despite the establishment of smaller reservoirs and a concomitant reduction in residual viral replication by cART could be further reduced by entry inhibitors. This idea is based on indications that entry inhibitors intensification correlates with a reduction in infected cells containing 2-LTR+ unintegrated circular DNA. As determined by p* values for plasma viral RNA and proviral DNA, we show improved suppression of HIV infection in human CD34+ hematopoietic stem cell-engrafted NSG mice by combined treatment with cART and CCR5 targeting drugs over cART alone. We observed better preservation of human CD4+T-cells and CD4+/CD8+ cell ratios in infected mice treated with cART plus CCR5 targeting drugs compared to controls, as judged by flow cytometry and quantified confocal microscopy. Proviral DNA became undetectable in cART treated mice and plasma viral RNA persisted, indicating the existence of non-peripheral blood reservoirs of infected cells. To verify this, we utilized confocal microscopy and looked in mouse tissues for human T- cells expressing the HIV p24. Those cells were readily detectable, but showing spleen, brain and intestine tissues as reservoirs for residual infected cells. We established correlations with greater depletion of HIV reservoirs and reduced establishment of visualized HIV infection sites in various solid tissues when entry inhibitors were included with cART. This study may serve as a model for future HIV latency studies.

Biography

Dr. Olga S. Latinovic is an assistant professor working at the Institute of Human Virology led by Robert C. Gallo, M.D. at the University of Maryland, School of Medicine in Baltimore, MD, USA. Her research focus is on developing novel antiviral therapy strategies using various HIV entry inhibitors, with a particular focus in understanding antiviral synergistic activity and its mechanism between CCR5 antagonists and CCR5 antibodies. Most recent work includes HIV suppression in humanized mice. Dr. Latinovic wrote the book *Micromechanics and Structure of Soft and Biological Materials* and published by Verlag Dr. Muller in 2010.

Computational approaches to the gut microbiome and its association with diet, disease, and antibiotics

Kyle Bittinger, PhD

Division of Gastroenterology, Hepatology, and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA, USA

Abstract

Shotgun metagenomic sequencing is now routinely used to investigate the human gut microbiome. How do we take full advantage of metagenomic sequence data to study the microbiome, how do we connect with other 'omics technologies, and how do we ensure that our results are reliable and reproducible? Here, we address these questions in the context of gut microbiome associations with diet, disease, and antibiotic use.

Involvement of OprF and Cell Wall Detachment in Outer Membrane Vesicle Biogenesis

Shrestha Mathur*, Susan Erickson and Jeffery Schertzer

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Abstract

Many gram-negative bacteria, including the opportunistic pathogen *Pseudomonas aeruginosa*, produce Outer Membrane Vesicles (OMVs). These vesicles are known to carry different types of cargo and have many functional roles, including virulence, threat avoidance, biofilm development, etc. Although there are many studies focusing on initial step of OMV biogenesis, very little is known about the later steps such as release of connections between the outer membrane and the peptidoglycan (PG) cell wall. We hypothesize that transmembrane anchoring proteins of the OmpA family, including OprF in *P. aeruginosa*, may be important players in the release of OMVs. OprF mutants exhibit a hypervesiculation phenotype compared to wild type strain. OprF has also been consistently identified as one of the most abundant proteins in vesicles, while other PG associated proteins are typically excluded. Interestingly, OprF is known to adopt two stable conformations. In the closed conformation it acts as an anchor between OM and PG. In the open conformation it is completely detached from PG and acts as a porin. We predict that the specific attachment of OprF via its C-terminal region to the PG is vital in OMV formation. We created an OprF mutant that lacks twelve conserved amino acids involved in the PG attachment process. Our results indicate that deletion of the attachment site on OprF does indeed lead to increased OMV biogenesis, while showing no negative effects on membrane stress or cell lysis. Overall, these analyses will help us elucidate the biomechanical role of OprF in OMV formation by *P. aeruginosa*.

Biography

Shrestha Mathur is a PhD candidate at Binghamton University. She received a bachelor's degree in Genetics, Microbiology and Chemistry and a master's degree in Microbiology from Bangalore University, India. Her recent publications include "Effect of essential oils on biofilm formation by *Proteus mirabilis*" (Int. J. Pharm. Bio. Sci., 2013) and "Anti-biofilm activity and bioactive component analysis of eucalyptus oil against urinary tract pathogens" (Int. J. Curr. Microbiol. App. Sci, 2014). Her research interests include biofilm formation, quorum sensing, host-microbe interactions and mechanisms and models of various infectious diseases.

Session III: Virology Bacteriology and Parasitology

Plant Virus Nanoparticles: New Applications for Developing Countries

Kathleen Hefferon*

Department of Food Sciences, Cornell University, Ithaca, NY

Abstract

For over two decades now, plants have been explored for their potential to act as production platforms for biopharmaceuticals, such as vaccines and monoclonal antibodies. Without a doubt, the development of plant viruses as expression vectors for pharmaceutical production have played an integral role in the emergence of plants as inexpensive and facile systems for the generation of therapeutic proteins. More recently, plant viruses have been designed as non-toxic nanoparticles which can target a variety of cancers and thus empower the immune system to slow or even reverse tumor progression. The following presentation describes the employment of plant virus expression vectors for the treatment of some of the most challenging diseases known today. The presentation concludes with a projection of the multiple avenues by which virus nanoparticles could impact developing countries.

Biography

Kathleen Hefferon received her PhD from the Department of Medical Biophysics, University of Toronto and completed her postdoctoral fellowship at Cornell University. Kathleen has published multiple research papers, chapters and reviews, and has written three books. Kathleen is the Fulbright Canada Research Chair of Global Food Security and has been a visiting professor at the University of Toronto over the past year. Her research interests include virus expression vectors, food security agricultural biotechnology and global health. Kathleen lives in New York with her husband and two children.

Limiting *Campylobacter Jejuni* Pathogenesis with Linoleic Acids Over-Producing *Lactobacillus Casei*

Zajeba Tabashsum, Mengfei Peng and Debabrata Biswas*

Animal and Avian Sciences, University of Maryland, College Park, MD

Abstract:

Problem Statement: Campylobacter is one of the most common causes of foodborne illness in the US and Europe. More than 90% of cases of campylobacteriosis are caused by *Campylobacter jejuni* (CJ). Poultry and poultry products are major sources of campylobacteriosis. Appropriate measure to reduce the colonization of CJ in chicken gut is required to control campylobacteriosis.

Approach: Recently, we found that in the presence of prebiotic-like components (peanut flour), production of metabolites specifically linoleic acid (LA) by *Lactobacillus casei* (LC) increased 100 folds and that higher concentration of LA could outcompete several enteric pathogens, including CJ. Therefore, we developed a genetically engineered LC strain by overexpressing linoleate isomerase (*mcra*, myosin cross-reactive antigen) gene and named as LC+*mcra*. We also verified the ability of LC+*mcra* to inhibit CJ growth, adhesion, and invasion of chicken cells with or without natural poultry growth promoter, such as berry pomace extracts (BPE).

Results: Both LC+*mcra* itself and its byproducts inhibited the growth of CJ more than 6 logs within 48 h. We also found that LC+*mcra* and its byproducts reduced both adherence and invasion ability of CJ to the chicken macrophage (HD-11) and fibroblast (DF-1) cells, altered the expression of virulence genes (*ciaB*, *cdtB*, *cadF*, *flaA* and *flab*) and physiological properties (motility and hydrophobicity) of CJ. In mixed culture condition, LC+*mcra* with CJ in the presence of BPE amplified these effects including CJ growth inhibition (>3 log CFU/mL) and disrupting host cells/CJ interactions. Cell-free cultural supernatant (CFCS) of LC+*mcra* in the presence of BPE also showed reduction of CJ growth, interaction of CJ with DF-1 and HD-11 cells, and expression of multiple CJ virulence genes.

Conclusion: This finding indicates that BPE and LC+*mcra* in combination might be able to prevent colonization of CJ in poultry and reduce cross-contamination in poultry products that cause campylobacteriosis in human.

Biography

Associate Professor, Foodborne Bacterial Infections and Prevention, University of Maryland, College Park, MD. As a bacteriologist, Dr. Biswas has committed to develop crosscutting research programs for targeting mechanism of colonization of various zoonotic bacterial pathogens in animal reservoirs and preventive measure of those bacterial infections in human gut. He investigates the role of natural products in control of colonization of zoonotic/foodborne bacterial pathogens in animal guts and mechanisms of their antimicrobial activity/survival ability in the presence of synthetic antibiotics and/or natural antimicrobial components. Dr. Biswas's team has also investigated the effective alternative and natural organic products such as a function bioactive plant extracts, pre-biotics, probiotics, its combination (synbitics) for alternative source of therapeutic and sub-therapeutic (growth promoter) components for organic and conventional farm animal production and stimulate the growth probiotic and the production of its bioactive byproducts by genetically engineered beneficial bacteria.

EuPathDB & ClinEpiDB – Integrated resources for eukaryotic pathogen omics and epidemiological studies of infectious diseases

Jessica C Kissinger^{1,2,3*} on behalf of the EuPathDB and ClinEpiDB team

¹Center for Tropical and Emerging Global Diseases

²Institute of Bioinformatics and

³Department of Genetics, University of Georgia, USA

Abstract

We live in exciting times. The prospects for gaining knowledge from data are immense yet the challenge of collecting and integrating the data in order to gain knowledge is equally immense. The infectious disease challenge involves both the host and pathogen. I will present a family of resources, which provide online open access to genome sequences, omics data and in some cases, associated microbiome, clinical and epidemiological data for >400 eukaryotic pathogens of humans and animals including

protists and fungi. The Eukaryotic Pathogen Database (EuPathDB.org) Bioinformatics Resource Center (BRC) (soon to be VEuPathDB following our merger with the VectorBase BRC) integrates structured sample and clinical data from >500 datasets encompassing transcript and protein expression, sequence and structural variation, epigenomics, clinical and field isolates, metabolites and metabolic pathways and host-pathogen interactions. MicrobiomeDB which provides a unique perspective on microbiome data mining and ClinEpiDB, an epidemiological data mining resource funded by the Bill & Melinda Gates Foundation to explore several of their groundbreaking studies like GEMS and MAL-ED. These resources are the result of a collaboration between researchers at the University of Pennsylvania, the University of Liverpool and the University of Georgia.

Biography

Dr. Jessica Kissinger is an evolutionary genomicist who joined the Center for Tropical and Emerging Global Diseases at the University of Georgia in 2002. She is a Distinguished Research Professor of Genetics and Director of UGA's Institute of Bioinformatics. Her research focuses on the evolution and genomics of apicomplexan pathogens (*Toxoplasma* and *Cryptosporidium* in particular) and the challenges of data integration in support of systems biology approaches. She is a joint-PI of the NIAID Bioinformatics Resource Center (BRC) – EuPathDB.org which supports parasitic and fungal pathogens and an investigator on the BMGF funded epidemiological resource ClinEpiDB.

Session IV: Food and Environmental Microbiology and Microbial Genetics, Cell Biology and Bacteriology

Species-Level Identification from 16S Via Simultaneous Weighted Analysis of All 16S Hypervariable Regions

Seth Crosby

Washington University Genetics, MO, USA

Abstract

MVRSION is a bench and informatic system which employs simultaneous weighted analysis eight of nine 16S hyper variable regions. We use Fluidigm Juno to amplify and index the regions in up to 192 samples per run. These are sequenced and analyzed in parallel, using the MVRSION computational protocol. Both accuracy and economy exceed other 16S methods, such as QIIME.

Application of Multiple Methods For The Detection And Enumeration Of Pathogenic Vibrios in The Mid-Atlantic Region of the United States

Salina Parveen*

Department of Agriculture, Food and Resource Sciences, University of Maryland Eastern Shore MD, USA

Abstract

Vibrio parahaemolyticus (Vp) and *V. vulnificus* (Vv) infect humans through shellfish and seawater. Detection methods are tedious, expensive and time consuming. In this study, we applied the colony overlay procedure for peptidases (COPP) assay, direct plating (DP) on CHROMagar Vibrio and MPN-real-time PCR (MPN-PCR) for the identification of total *Vibrionaceae* (TV), Vp and Vv in seawater and oysters to determine whether the simple and rapid COPP assay can be used as an indicator of pathogenic vibrios. A total of 330 oyster and 330 seawater samples were collected from five sites in the Chesapeake Bay, MD and three sites in the Delaware Bays, DE, USA from May to October 2016 and 2017 and analyzed using these methods. All oyster and seawater samples were positive for TV by the COPP assay. Positive Vp for seawater and oysters by MPN-PCR were 89% and 92%, respectively in MD; 100% for both in DE; and by DP were 32% and 76% in MD; 71% and 87% in DE. Positive Vv for seawater and oysters by MPN-PCR were 99% and 100% in MD; 100% for both in DE; and by DP were 47% and 86% in MD and 58% and 77% in DE. TV positively

correlated ($r = 0.5-0.69$; $p < 0.05$) with MPN-PCR or DP for *Vv* in oysters and seawater. TV was significantly correlated ($r = 0.63-0.65$; $p < 0.05$) with MPN-PCR or DP for *Vp* in seawater but not in oysters. The COPP assay is a viable alternative to DP or MPN-PCR as an indicator of total *Vp* and *Vv* levels in seawater and *Vv* in oysters, but is not an indicator of levels of pathogenic strains.

Biography

Dr. Salina Parveen is a Professor in Food Science and Technology Program, Department of Agriculture, Food and Resource Sciences at the University of Maryland Eastern Shore, MD, USA. Dr. Parveen holds a B.S. in Botany and an M.S. in Microbiology from the University of Dhaka, Bangladesh and a Ph.D. in Food Science and Human Nutrition, specializing in Microbiology and Molecular Biology from the University of Florida, FL, USA. Dr. Parveen teaches graduate level courses in Microbiology and Toxicology. She is a certified trainer for Seafood HACCP and SCP, and has over 25 years' experience in teaching, research and outreach service associated with food safety, water quality, food and environmental microbiology. Dr. Parveen has an excellent record of grantmanship and received several awards for outstanding academic performance. Dr. Parveen published more than 150 peer-reviewed journal articles, book chapters and abstracts, and made over 55 invited presentations. She also serve on several national and international scientific committees and the Editorial Board member of many peer-reviewed journals.

Nit1C: A Unique Gene Cluster Essential for Bacterial Cyanotrophy

Daniel A. Kunz

Division of Biochemistry & Molecular Biology, Department of Biological Sciences, University of North Texas, Denton Texas, USA

Abstract

Cyanotrophic bacteria exhibit the unique ability of utilizing toxic cyanide as a sole nitrogen source for growth. Recent studies have shown this ability to parallel the existence on bacterial genomes of a conserved gene cluster designated Nit1C. Nit1C consists of a seven-gene operon (*nitB-nitH*) encoding respectively, for a hypothetical protein, nitrilase, radical SAM enzyme, GNAT acetyl transferase, AIR synthetase, hypothetical, and flavin oxidoreductase. A σ -54-type transcriptional regulator (*nitA*) predicted to respond to nitrogen limitation typically resides nearby. While relatively rare (0.2% of 130,000 genomes), Nit1C is widely distributed across Gram negative (*Proteobacteria*), and Gram positive (*Firmicutes*, *Actinobacteria*) bacteria, and *Cyanobacteria*, but distinctly absent in Archae. Its presence in only 1% of representative *Pseudomonas fluorescens* and *P. putida* strains lends support to the idea that the cluster was probably acquired by horizontal gene transfer. The molecular basis of its essentiality to cyanotrophy is currently not understood. Computer modeling of the hypothetical NitB protein suggests a possible role in sulfur transfer possibly the thiolation of uridine in tRNA. Interestingly, conserved iron-sulfur binding motifs in the radical SAM NitD protein have counterparts found in only one other protein that being Elp3, a protein implicated in various diseases including cancer. Besides a role in transcription, Elp3 has also been shown to modify wobble uridines in tRNA. We speculate that Nit1C arose in response to plants having evolved the capacity for cyanide production (cyanogenesis) placing a demand on associated bacteria for the synthesis of a modified base due to cyanide-induced stress.

Biography

Dr. Kunz received his graduate training in Microbiology at the University of Minnesota. There he worked with Peter Chapman and Stanley Dagley being one of the first to describe TOL plasmids encoding aromatic hydrocarbon degradation. He received post-doctoral training in Biochemistry at the University of Miami before being employed by the DuPont Company where his activities focused on microbial biotransformations. He moved to the University of North Texas some thirty years where he serves as Full Professor in the Department of Biological Sciences. His career and interests are in microbial diversity, metabolism and genetics, with special focus on cyanotrophic bacteria.

A Diverse Range of Human Gut Bacteria Have the Potential to Metabolize the Dietary Component Gallic Acid

María Esteban-Torres^{1,2*}, Laura Santamaría¹, Raúl Cabrera-Rubio^{2,3}, Laura Plaza-Vinuesa¹, Fiona Crispie^{2,3}, Blanca de las Rivas¹, Paul Cotter^{2,3}, Rosario Muñoz¹

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²APC Microbiome Ireland, Ireland

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Abstract

The human gut microbiota contains a broad variety of bacteria that possess functional genes, with resultant metabolites that affect human physiology and therefore health. Dietary gallates are phenolic components present in many foods and beverages and are regarded as having health-promoting attributes. However, the potential for metabolism of these phenolic compounds by the human microbiota remains largely unknown. The emergence of high-throughput sequencing (HTS) technologies allows this issue to be addressed. In this study, HTS was used to assess the incidence of gallate-decarboxylating bacteria within the gut microbiota of healthy individuals for whom bacterial diversity was previously determined to be high. This process was facilitated by the design and application of degenerate PCR primers to amplify a region encoding the catalytic C subunit of gallate decarboxylase (LpdC) from total metagenomic DNA extracted from human fecal samples. HTS revealed that the primary gallate-decarboxylating microbial phyla in the intestinal microbiota were *Firmicutes* (74.6%), *Proteobacteria* (17.6%), and *Actinobacteria* (7.8%). Gallate-decarboxylating bacteria corresponded to 53 genera, i.e., 47% of the bacterial genera detected previously in the same human fecal samples. Among these, *Anaerostipes* and *Klebsiella* accounted for the majority of reads (40%). The usefulness of the HTS-LpdC method was demonstrated by the production of pyrogallol from gallic acid, as expected for functional gallate decarboxylases, among representative strains belonging to species identified in the human gut microbiota by this method. This could be of considerable relevance for the *in vivo* production of pyrogallol, a physiologically important bioactive compound.

Biography

María Esteban-Torres obtained her PhD in Biology and Food Science in 2014 at the Autonomía University of Madrid, Spain. In 2015 she started her Postdoctoral research at APC Microbiome Ireland in Cork, Ireland. Her research fields are microbiology, molecular biology, functional genomics and food science. Her scientific interest is focused on elucidating molecular players involved in microbe-host interactions pertaining to *Bifidobacterium* and *Lactobacillus* species, representing common human gut commensals with probiotic benefits. In particular, she investigates the metabolism of phenolic compounds and carbohydrates from the diet in these bacteria, and its role in colonization and survival in the gastrointestinal tract.



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