START CENTER
STRATEGIC ANALYSIS, RESEARCH & TRAINING CENTER

GUT HEALTH DIGEST

UNIVERSITY OF WASHINGTON STRATEGIC ANALYSIS, RESEARCH & TRAINING (START) CENTER
REPORT TO THE BILL & MELINDA GATES FOUNDATION

MAY 1, 2017

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2. **Causal Pathways from Enteropathogens to Environmental Enteropathy: Findings from the MAL-ED Birth Cohort Study.** {abstract & UW comment} {full article}
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4. **Engineering bacterial thiosulfate and tetrathionate sensors for detecting gut inflammation.** {abstract & UW comment} {full article}
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    - Basic biology underlying the mechanism by which T-regulatory cells promote peripheral immune tolerance.

7. **Bap180/Baf180 is required to maintain homeostasis of intestinal innate immune response in Drosophila and mice.** {abstract & UW comment} {full article}
    - Basic biology of the transcription factor Bap180 and its role in mediating antimicrobial immune response and inflammation in Drosphila and mice.

8. **Age-Associated Microbial Dysbiosis Promotes Intestinal Permeability, Systemic Inflammation, and Macrophage Dysfunction.** {abstract & UW comment} {full article}
    - Mouse-model study of aging-related changes in intestinal microbiota composition and their effects on gut health.

9. **Engineered Regulatory Systems Modulate Gene Expression of Human Commensals in the Gut.** {abstract & UW comment} {full article}
    - Development of a novel tool for the visualization of bacterial strains in the gut using fluorescence microscopy.

10. **Next-generation probiotics: the spectrum from probiotics to live biotherapeutics** {abstract & UW comment} {full article}
    - A review of next-generation probiotics and the emerging concept of live biotherapeutic products.

DETAILS OF ARTICLES

1. Association between Enteropathogens and Malnutrition in Children Aged 6-23 mo in Bangladesh: a Case-Control Study.
   Platts-Mills JA, Taniuchi M, Uddin MJ, Sobuz SU, Mahfuz M, Gaffar SA, Mondal D, Hossain MI, Islam MM, Ahmed AS, Petri WA, Haque R, Houpt ER, Ahmed T.
   Am J Clin Nutr. 2017 Apr 5. pii: ajcn138800. doi: 10.3945/ajcn.116.138800. [Epub ahead of print]

ABSTRACT
Background: Early exposure to enteropathogens has been associated with malnutrition in children in low-resource settings. However, the contribution of individual enteropathogens remains poorly defined. Molecular diagnostics offer an increase in sensitivity for detecting enteropathogens but have not been comprehensively applied to studies of malnutrition.
Objective: We sought to identify enteropathogens associated with malnutrition in Bangladesh.
Design: Malnourished children [weight-for-age z score (WAZ) <-2] aged 6-23 mo in Dhaka, Bangladesh, and identified by active community surveillance were enrolled as cases, and normal-weight children (WAZ >-1) of the same age and from the same community were enrolled as controls. Stools were collected at enrollment and, for cases, after a 5-mo nutritional intervention. Enrollment and follow-up stools were tested by quantitative polymerase chain reaction for 32 enteropathogens with the use of a custom-developed TaqMan Array Card.
Results: Enteropathogen testing was performed on 486 cases and 442 controls upon enrollment and 365 cases at follow-up. At enrollment, the detection of enteroaggregative Escherichia coli (OR: 1.39; 95% CI: 1.05, 1.83), Campylobacter spp. (OR: 1.46; 95% CI: 1.11, 1.91), heat-labile enterotoxin-producing E. coli (OR: 1.55; 95% CI: 1.04, 2.33), Shigella/enteroinvasive E. coli (OR: 1.65; 95% CI: 1.10, 2.46), norovirus genogroup I (OR: 1.66; 95% CI: 1.23, 2.25), and Giardia (OR: 1.73; 95% CI: 1.20, 2.49) were associated with malnourished cases, and the total burden of these pathogens remained associated with malnutrition after adjusting for sociodemographic factors. The number of these pathogens at follow-up was negatively associated with the change in WAZ during the intervention (-0.10 change in WAZ per pathogen detected; 95% CI: -0.14, -0.06), whereas the number at enrollment was positively associated with the change in WAZ (0.05 change in WAZ per pathogen detected; 95% CI: 0.00, 0.10).
Conclusions: A subset of enteropathogens was associated with malnutrition in this setting. Broad interventions designed to reduce the burden of infection with these pathogens are needed.

WEB: 10.3945/ajcn.116.138800
IMPACT FACTOR: 7.409
CITED HALF-LIFE: >10.0

UW EDITORIAL COMMENT: The primary strength of this study is its exploratory analysis of a broad range of pathogens (Figure 2) and depth of data collection, which enables a detailed graphical comparison of the prevalence of various bacteria between cases and controls. No association was found between the quantity of pathogens (all species) and nutrition status, although this may have been affected by the exclusion of cases with severe diarrhea since the detection of high quantities of enteropathogens in the absence of diarrhea is difficult.

2. Causal Pathways from Enteropathogens to Environmental Enteropathy: Findings from the MAL-ED Birth Cohort Study.
   Kosek MN; MAL-ED Network Investigators.
   EBioMedicine. 2017 Mar 8. pii: S2352-3964(17)30083-X. [Epub ahead of print]

ABSTRACT

Background: Environmental enteropathy (EE), the adverse impact of frequent and numerous enteric infections on the gut resulting in a state of persistent immune activation and altered permeability, has been proposed as a key determinant of growth failure in children in low- and middle-income populations. A theory-driven systems model to critically evaluate pathways through which enteropathogens, gut permeability, and intestinal and systemic inflammation affect child growth was conducted within the framework of the Etiology, Risk Factors and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development (MAL-ED) birth cohort study that included children from eight countries.

Methods: Non-diarrheal stool samples (N=22,846) from 1253 children from multiple sites were evaluated for a panel of 40 enteropathogens and fecal concentrations of myeloperoxidase, alpha-1-antitrypsin, and neopterin. Among these same children, urinary lactulose:mannitol (L:M) (N=6363) and plasma alpha-1-acid glycoprotein (AGP) (N=2797) were also measured. The temporal sampling design was used to create a directed acyclic graph of proposed mechanistic pathways between enteropathogen detection in non-diarrheal stools, biomarkers of intestinal permeability and inflammation, systemic inflammation and change in length- and weight- for age in children 0-2years of age.

Findings: Children in these populations had frequent enteric infections and high levels of both intestinal and systemic inflammation. Higher burdens of enteropathogens, especially those categorized as being enteroinvasive or causing mucosal disruption, were associated with elevated biomarker concentrations of gut and systemic inflammation and, via these associations, indirectly associated with both reduced linear and ponderal growth. Evidence for the association with reduced linear growth was stronger for systemic inflammation than for gut inflammation; the opposite was true of reduced ponderal growth. Although Giardia was associated with reduced growth, the association was not mediated by any of the biomarkers evaluated.

Interpretation: The large quantity of empirical evidence contributing to this analysis supports the conceptual model of EE. The effects of EE on growth faltering in young children were small, but multiple mechanistic pathways underlying the attribution of growth failure to asymptomatic enteric infections had statistical support in the analysis. The strongest evidence for EE was the association between enteropathogens and linear growth mediated through systemic inflammation.

WEB: 10.1016/j.ebiom.2017.02.024
IMPACT FACTOR: 1.37
CITED HALF-LIFE: n/a

UW EDITORIAL COMMENT: A well-evidenced causal diagram is presented in Figure 4, providing a detailed network of functional pathogen groupings (virus, invasive bacteria, non-invasive bacteria, *Cryptosporidium*, and *Giardia*) and their causal associations with fecal biomarkers of gut inflammation and permeability, systemic inflammation, and anthropometry (z-scores: ΔLAZ and ΔWAZ). At age 1, only invasive bacteria are positively associated with an increase in neutrophil activity linked to mucosal inflammation. By age 2, both invasive and non-invasive bacteria pathogen groups are linked to mucosal inflammation and systemic inflammation. *Cryptosporidium* is also associated with systemic inflammation and *Giardia* is significantly associated with mean growth z-scores.

3. The Gut Microbiome: Connecting Spatial Organization to Function
   Carolina Tropini, Kristen A. Earle, Kerwyn Casey Huang. Justin L. Sonnenburg
   Cell Host & Microbe. Volume 21, Issue 4, p433–442, 12 April 2017.

ABSTRACT
The first rudimentary evidence that the human body harbors a microbiota hinted at the complexity of host-associated microbial ecosystems. Now, almost 400 years later, a renaissance in the study of microbiota spatial organization, driven by coincident revolutions in imaging and sequencing technologies, is revealing functional relationships between biogeography and health, particularly in the vertebrate gut. In this Review, we present our current understanding of principles governing the localization of intestinal bacteria, and spatial relationships between bacteria and their hosts. We further discuss important emerging directions that will enable progressing from the inherently descriptive nature of localization and -omics technologies to provide functional, quantitative, and mechanistic insight into this complex ecosystem.
WEB: 10.1016/j.chom.2017.03.010
IMPACT FACTOR: 12.944
CITED HALF-LIFE: 4.0

UW EDITORIAL COMMENT: This review article provides a comprehensive synthesis of what is known about the organization of the gut microbiome. It recaps the biogeography and spatial distribution of microbes in the human gut, including known mechanisms by which the gut organizes itself to regulate inflammation. It also discusses several methods for improved imaging of gut microbes and mucosal surfaces. Importantly, the authors conclude with an assertion that while the gnotobiotic mouse have played an essential role as a model organism for microbiome research, there are critical physiological, anatomical, and microbiological differences that make further research using human tissues essential for the advancement of microbiome therapies.

4. Engineering bacterial thiosulfate and tetrathionate sensors for detecting gut inflammation.
   Kristina N-M Daeffler, Jeffrey D Galley, Ravi U Sheth, Laura C Ortiz-Velez, Christopher O Bibb, Noah F Shroyer, Robert A Britton, Jeffrey J Tabor.
   Molecular Systems Biology (2017) 13, 923.

ABSTRACT
There is a groundswell of interest in using genetically engineered sensor bacteria to study gut microbiota pathways, and diagnose or treat associated diseases. Here, we computationally identify the first biological thiosulfate sensor and an improved tetrathionate sensor, both two-component systems from marine *Shewanella* species, and validate them in laboratory *Escherichia coli.* Then, we port these sensors into a gut-adapted probiotic *E. coli* strain, and develop a method based upon oral gavage and flow cytometry of colon and fecal samples to demonstrate that colon inflammation (colitis) activates the thiosulfate sensor in mice harboring native gut microbiota. Our thiosulfate sensor may have applications in bacterial diagnostics or therapeutics. Finally, our approach can be replicated for a wide range of bacterial sensors and should thus enable a new class of minimally invasive studies of gut microbiota pathways.

WEB: 10.15252/msb.20167416
IMPACT FACTOR: 10.581
CITED HALF-LIFE: 5.0

UW EDITORIAL COMMENT: Researchers demonstrated sensitivity and specificity of the bacterial biosensors by testing the dose-response activity of ThSR in response to thiosulfate and alternative terminal electron acceptors that are expected in anerobic respiration. Importantly, these biosensors function in both aerobic and anaerobic conditions of the gut ecosystem. The flow cytometry methods used in this experiment provide higher resolution measurements of bacterial populations than microscopy or luciferase determinations from fecal samples, though the technology may limit broader use as a diagnostic. Additionally, these biosensors are unlikely to be able to colonize the epithelial mucosal boundary due to the short incubation time and competition from native bacteria, so the scope of inflammation detectable by this methodology is limited. Finally, while this thiosulfate sensor system is sensitive to mouse gut inflammation, it is unknown whether thiosulfate is a marker of human inflammation.

5. Regulation of intestinal permeability: the role of proteases.
   Van Spaendonk H, Ceuleers H, Witters L, Patteet E, Joossens J, Augustyns K, Lambeir AM, De Meester I, De Man JG, De Winter BY.
   World J Gastroenterol. 2017 Mar 28;23(12):2106-2123.

ABSTRACT
The gastrointestinal barrier is - with approximately 400 m^2 - the human body's largest surface separating the external environment from the internal milieu. This barrier serves a dual function: permitting the absorption of nutrients, water and electrolytes on the one hand, while limiting host contact with noxious luminal antigens on the other hand. To maintain this selective barrier, junction protein complexes seal the intercellular space between adjacent epithelial cells and regulate the paracellular transport. Increased intestinal permeability is associated with and suggested as a player in the pathophysiology of various gastrointestinal and extra-intestinal diseases such as inflammatory bowel disease, celiac disease and type 1 diabetes. The gastrointestinal tract is exposed to high levels of endogenous and exogenous proteases, both in the lumen and in the mucosa. There is increasing evidence to suggest that a dysregulation of the protease/antiprotease balance in the gut contributes to epithelial damage and increased permeability. Excessive proteolysis leads to direct cleavage of intercellular junction proteins, or to opening of the junction proteins *via* activation of protease activated receptors. In addition, proteases regulate the activity and availability of cytokines and growth factors, which are also known modulators of intestinal permeability. This review aims at outlining the mechanisms by which proteases alter the intestinal permeability. More knowledge on the role of proteases in mucosal homeostasis and gastrointestinal barrier function will definitely contribute to the identification of new therapeutic targets for permeability-related diseases.

WEB: 10.3748/wjg.v23.i12.2106
IMPACT FACTOR: 2.787
CITED HALF-LIFE: 5.1

UW EDITORIAL COMMENT: Table 1 provides a list of serine, cysteine, and metallo-proteases and their effect on intestinal permeability. The authors discuss the mechanistic role of proteases in mediating barrier function and multiple regulatory mechanisms that control protease activity.

6. Foxp3 Reprograms T Cell Metabolism to Function in Low-Glucose, High-Lactate Environments
   Alessia Angelin, Luis Gil-de-Gómez, Satinder Dahiya, Jing Jiao, Lili Guo, Matthew H. Levine, Zhonglin Wang, William J. Quinn III, Piotr K. Kopinski, Liqing Wang, Tatiana Akimova, Yujie Liu, Tricia R. Bhatti, Rongxiang Han, Benjamin L. Laskin, Joseph A. Baur, Ian A. Blair, Douglas C. Wallace, Wayne W. Hancock, Ulf H. Beier.
   Cell Metab. 2017 Apr 11. pii: S1550-4131(16)30651-9. doi: 10.1016/j.cmet.2016.12.018. [Epub ahead of print].

ABSTRACT
Immune cells function in diverse metabolic environments. Tissues with low glucose and high lactate concentrations, such as the intestinal tract or ischemic tissues, frequently require immune responses to be more pro-tolerant, avoiding unwanted reactions against self-antigens or commensal bacteria. T-regulatory cells (Tregs) maintain peripheral tolerance, but how Tregs function in low-glucose, lactate-rich environments is unknown. We report that the Treg transcription factor Foxp3 reprograms T cell metabolism by suppressing Myc and glycolysis, enhancing oxidative phosphorylation, and increasing nicotinamide adenine dinucleotide oxidation. These adaptations allow Tregs a metabolic advantage in low-glucose, lactate-rich environments; they resist lactate-mediated suppression of T cell function and proliferation. This metabolic phenotype may explain how Tregs promote peripheral immune tolerance during tissue injury but also how cancer cells evade immune destruction in the tumor microenvironment. Understanding Treg metabolism may therefore lead to novel approaches for selective immune modulation in cancer and autoimmune diseases.

WEB: 10.1016/j.cmet.2016.12.018
IMPACT FACTOR: 17.303
CITED HALF-LIFE: 4.6

UW EDITORIAL COMMENT: Previous research (Poutahidis et al. 2013) suggested a role for L-lactate metabolism in promoting tolerance to commensal bacteria by regulating inflammation in gut tissues. This study provides evidence that Foxp3 can enable T-regulatory cells to develop resistance to the suppressive effects of L-lactate by increasing nicotinamide adenine dinucleotide oxidation. The authors suggest that metabolic adaptations of T-regulatory cells enable ischemic tissues to be protected from by an environment that favors the presence of T-regulatory cells. Dysfunction in T-regulatory cells metabolism may be associated with autoimmune disorders and excess inflammation.

7. Bap180/Baf180 is required to maintain homeostasis of intestinal innate immune response in Drosophila and mice
   He X, Yu J, Wang M, Cheng Y, Han Y, Yang S, Shi G, Sun L, Fang Y, Gong ST, Wang Z, Fu YX, Pan L, Tang H. *Nature Microbiology* **2**, Article number: 17056 (2017)

ABSTRACT
Immune homeostasis is a prerequisite to protective immunity against gastrointestinal infections. In Drosophila, immune deficiency (IMD) signaling (tumour necrosis factor receptor/interleukin-1 receptor, TNFR/IL-1R in mammals) is indispensable for intestinal immunity against invading bacteria. However, how this local antimicrobial immune response contributes to inflammatory regulation remains poorly defined. Here, we show that flies lacking intestinal Bap180 (a subunit of the chromatin-remodeling switch/sucrose non-fermentable (SWI/SNF) complex) are susceptible to infection as a result of hyper-inflammation rather than bacterial overload. Detailed analysis shows that Bap180 is induced by the IMD–Relish response to both enteropathogenic and commensal bacteria. Upregulated Bap180 can feed

back to restrain overreactive IMD signaling, as well as to repress the expression of the pro-inflammatory gene eiger (TNF), a critical step to prevent excessive tissue damage and elongate the lifespan of flies, under pathological and physiological conditions, respectively. Furthermore, intestinal targeting of Baf180 renders mice susceptible to a more aggressive infectious colitis caused by Citrobacter rodentium. Together, Bap180 and Baf180 serve as a conserved transcriptional repressor that is critical for the maintenance of innate immune homeostasis in the intestines.

WEB: 10.1038/nmicrobiol.2017.56
IMPACT FACTOR: n/a
CITED HALF-LIFE: n/a

UW EDITORIAL COMMENT: These authors explored the basic biology of the transcription factor Bap180 and its role in mediating antimicrobial immune response and inflammation in Drosphila and mice models. However, the authors note that there is a functional disparity in how Bap180/Baf180 modulates the expression of AMPs and inflammatory cytokines in different species. Unlike flies where bacterial overburden is tolerated to avoid serious intestinal damage due to hyperinflammation, mammals have evolved Baf180 signaling to tightly control both bacterial burden and inflammatory response. Gut flora can induce bap180 expression and may influence the intestinal epithelia by causing intestinal inflammation to lengthen the bacterial lifespan.

8. Age-Associated Microbial Dysbiosis Promotes Intestinal Permeability, Systemic Inflammation, and Macrophage Dysfunction
   Netusha Thevaranjan, Alicja Puchta, Christian Schulz, Avee Naidoo, J.C. Szamosi, Chris P. Verschoor, Dessi Loukov, Louis P. Schenck, Jennifer Jury, Kevin P. Foley, Jonathan D. Schertzer, Maggie J. Larché, Donald J. Davidson, Elena F. Verdú, Michael G. Surette, Dawn M.E. Bowdish. *Cell Host & Microbe*. Volume 21, Issue 4, p455–466.e4, 12 April 2017.

ABSTRACT
Levels of inflammatory mediators in circulation are known to increase with age, but the underlying cause of this age-associated inflammation is debated. We find that, when maintained under germ-free conditions, mice do not display an age-related increase in circulating pro-inflammatory cytokine levels. A higher proportion of germ-free mice live to 600 days than their conventional counterparts, and macrophages derived from aged germ-free mice maintain anti-microbial activity. Co-housing germ-free mice with old, but not young, conventionally raised mice increases pro-inflammatory cytokines in the blood. In tumor necrosis factor (TNF)-deficient mice, which are protected from age-associated inflammation, age-related microbiota changes are not observed. Furthermore, age-associated microbiota changes can be reversed by reducing TNF using anti-TNF therapy. These data suggest that aging-associated microbiota promote inflammation and that reversing these age-related microbiota changes represents a potential strategy for reducing age-associated inflammation and the accompanying morbidity.

WEB: 10.1016/j.chom.2017.03.002
IMPACT FACTOR: 12.944
CITED HALF-LIFE: 4.0

UW EDITORIAL COMMENT: The authors findings suggest that age-related changes in the microbiome lead to a weakening of the intestinal barrier, which causes the release of bacterial products and causes inflammation and reduced immune function. Previous research has validated microbial translocation as a cause of systemic inflammation and reduced intestinal permeability, but this study is one of the first to link aging-related changes in the microbiome to this cause of inflammation. Figure 4 depicts age-associated compositional differences of the intestinal microbiota of old versus young mice.

9. Engineered Regulatory Systems Modulate Gene Expression of Human Commensals in the Gut
   Bentley Lim, Michael Zimmermann, Natasha A. Barry, Andrew L. Goodman.
   Cell. Volume 169, Issue 3, 20 April 2017, Pages 547–558.e15

ABSTRACT
The gut microbiota is implicated in numerous aspects of health and disease, but dissecting these connections is challenging because genetic tools for gut anaerobes are limited. Inducible promoters are particularly valuable tools because these platforms allow real-time analysis of the contribution of microbiome gene products to community assembly, host physiology, and disease. We developed a panel of tunable expression platforms for the prominent genus *Bacteroides* in which gene expression is controlled by a synthetic inducer. In the absence of inducer, promoter activity is fully repressed; addition of inducer rapidly increases gene expression by four to five orders of magnitude. Because the inducer is absent in mice and their diets, *Bacteroides* gene expression inside the gut can be modulated by providing the inducer in drinking water. We use this system to measure the dynamic relationship between commensal sialidase activity and liberation of mucosal sialic acid, a receptor and nutrient for pathogens.

WEB: 10.1016/j.cell.2017.03.045
IMPACT FACTOR: 1.28.710
CITED HALF-LIFE: 9.0

UW EDITORIAL COMMENT: This is one of two studies published in the April issue of *Cell* that provides a tool for visualizing bacterial strains in the gut with fluorescent proteins. In this study, the authors designed a panel of synthetic tetracycline-regulated promoters to control gene activity in *Bacteroides* species. In this mouse model study, researchers initiated gene activity in the mouse's gut through the addition of anhydrotetracycline to the drinking water. Theoretically, this regulated gene expression system could be used to deliver therapeutic compounds in appropriate dosages and with precise timing. The second *Cell*-published study also synthetically modified *Bacteroides* promoters, using red and green fluorescent protein genes to demonstrate the colonization of bacteria in specific locations in the gut (Whitaker et al.: Tunable Expression Tools Enable Single-Cell Strain Distinction in the Gut Microbiome).

10. Next-generation probiotics: the spectrum from probiotics to live biotherapeutics
    O'Toole, P.W., Marchesi, J.R., and Hill, C.
    Nature Microbiology. 2, Article number: 17057 (2017).

ABSTRACT
The leading probiotics currently available to consumers are generally drawn from a narrow range of organisms. Knowledge of the gut microbiota and its constituent actors is changing this paradigm, particularly given the phylogenetic range and relatively unknown characteristics of the organisms under investigation as novel therapeutics. For this reason, and because their development is likely to be more

amenable to a pharmaceutical than a food delivery route, these organisms are often operationally referred to as next-generation probiotics, a concept that overlaps with the emerging concept of live biotherapeutic products. The latter is a class of organisms developed exclusively for pharmaceutical application. In this Perspective, we discuss what lessons have been learned from working with traditional probiotics, explore the kinds of organisms that are likely to be used as novel microbial therapeutics, discuss the regulatory framework required, and propose how scientists may meet this challenge.

WEB: 10.1038/nmicrobiol.2017.57
IMPACT FACTOR: n/a
CITED HALF-LIFE: n/a

UW EDITORIAL COMMENT: Table 1 lists selected example of next-generation probiotics, including two strains of *bacteroides ovatus* V975 (expressing KGF-2 and TGF-β1) that target intestinal inflammation, among other microbes aimed at clearing infectious agents and targeting other diseases. This review also explains the distinctions drawn by American and European regulatory agencies in regards to the review of probiotics as drugs (per the FDA, "live biotheraputic product (LBP)") rather than food/supplements and the difference in regulatory pathways required based on this distinction.

ADDITIONAL ARTICLES OF INTEREST (APRIL PUBLICATIONS)

Tunable Expression Tools Enable Single-Cell Strain Distinction in the Gut Microbiome (referenced in #9)

MicrobiomeAnalyst: a web-based tool for comprehensive statistical, visual and meta-analysis of microbiome data.

Biomarkers of Environmental Enteric Dysfunction: The good, the bad and the ugly.

Severity of pancreatitis-associated intestinal mucosal barrier injury is reduced following treatment with the NADPH oxidase inhibitor apocynin.

Mice with infectious colitis exhibit linear growth failure and subsequent catch-up growth related to systemic inflammation and IGF-1.

Targeting the gut microbiota with inulin-type fructans: preclinical demonstration of a novel approach in the management of endothelial dysfunction.

Molecular insight into Evolution of Symbiosis between Breast-Fed Infants and a Member of the Human Gut Microbiome Bifidobacterium longum

Honeybee gut microbiota promotes host weight gain via bacterial metabolism and hormonal signaling.

Interleukin-23 Increases Intestinal Epithelial Cell Permeability In Vitro

An insider's perspective: Bacteroides as a window into the microbiome

Antibiotics, Pediatric Dysbiosis, and Disease

Which dietary components modulate longitudinal growth?

Influence of diet on the gut microbiome and implications for human health.

Intestinal, extra-intestinal and systemic sequelae of Toxoplasma gondii induced acute ileitis in mice harboring a human gut microbiota.

ARTICLE ARCHIVE (JAN 2016-MARCH 2017)

EED Biology & Review Articles

Application of penalized linear regression methods to the selection of environmental enteropathy biomarkers.

Environmental enteropathy is associated with cardiometabolic risk factors in Peruvian children.

Biomarkers of Environmental Enteric Dysfunction Among Children in Rural Bangladesh.

Environmental Enteric Dysfunction is Associated with Carnitine Deficiency and Altered Fatty Acid Oxidation.

Determinant Variables, Enteric Pathogen Burden, Gut Function, and Immune-Related Inflammatory Biomarkers Associated with Childhood Malnutrition: A Prospective Case-Control Study in Northeastern Brazil.

The Association Between Fecal Biomarkers of Environmental Enteropathy and Rotavirus Vaccine Response in Nicaraguan Infants.

Systemic inflammation, growth factors, and linear growth in the setting of infection and malnutrition

Environmental Enteric Dysfunction and the Fecal Microbiota in Malawian Children

Environmental Enteric Dysfunction and Growth Failure/Stunting in Global Child Health

Biomarkers of Environmental Enteropathy, Inflammation, Stunting, and Impaired Growth in Children in Northeast Brazil.

Environmental enteropathy.

Environmental Enteropathy: Elusive but Significant Subclinical Abnormalities in Developing Countries.

Endomicroscopic and Transcriptomic Analysis of Impaired Barrier Function and Malabsorption in Environmental

Environmental Enteric Dysfunction in Children.

Environmental Enteric Dysfunction Includes a Broad Spectrum of Inflammatory Responses and Epithelial Repair Processes.

The Impact of Environmental Enteropathy and Systemic Inflammation on Infant Growth Failure

Small Intestine Bacterial Overgrowth and Environmental Enteropathy in Bangladeshi Children.

Decoding Hidden Messages: Can Fecal Host Transcriptomics Open Pathways to Understanding Environmental Enteropathy?

Plasma Tryptophan and the Kynurenine–Tryptophan Ratio are Associated with the Acquisition of Statural Growth Deficits and Oral Vaccine Underperformance in Populations with Environmental Enteropathy

Malnutrition Is Associated with Protection from Rotavirus Diarrhea: Evidence from a Longitudinal Birth Cohort Study in Bangladesh

Nutrition/metabolism

Nopal feeding reduces adiposity, intestinal inflammation and shifts the cecal microbiota and metabolism in high-fat fed rats

Western diets, gut dysbiosis, and metabolic diseases: Are they linked?

Nutrition, infection and stunting: the roles of deficiencies of individual nutrients and foods, and of inflammation, as determinants of reduced linear growth of children

Microbiome, Growth Retardation, and Metabolism: Are they related?

Linking Dietary Patterns with Gut Microbial Composition and Function.

Impacts of resistant starch and wheat bran consumption on enteric inflammation in relation to colonic bacterial community structures and short-chain fatty acid concentrations in mice.

Diet-Microbiota Interactions Mediate Global Epigenetic Programming in Multiple Host Tissues

Systemic inflammation, growth factors, and linear growth in the setting of infection and malnutrition.

Environmental Enteric Dysfunction is Associated with Altered Bile Acid Metabolism

Metabolic alterations in children with environmental enteric dysfunction.

Genetic and Metabolic Signals during Acute Enteric Bacterial Infection Alter the Microbiota and Drive Progression to Chronic Inflammatory Disease

Interactions between intestinal pathogens, enteropathy and malnutrition in developing countries.

Child Stunting is Associated with Low Circulating Essential Amino Acids.

Diet–microbiota interactions as moderators of human metabolism

Protein malnutrition impairs intestinal epithelial turnover: a potential mechanism of increased cryptosporidiosis in a murine model

A Comparison of Diarrheal Severity Scores in the MAL-ED Multisite Community-Based Cohort Study.

Metabolomic Changes in Serum of Children with Different Clinical Diagnoses of Malnutrition.

Mortality in children with complicated severe acute malnutrition is related to intestinal and systemic inflammation: an observational cohort study.

Steroid Administration and Growth Impairment in Children with Crohn's Disease.

Effects of a gut pathobiont in a gnotobiotic mouse model of childhood undernutrition

A Dietary Fiber-Deprived Gut Microbiota Degrades the Colonic Mucus Barrier and Enhances Pathogen Susceptibility

Microbiome Therapies

Pili-like proteins of Akkermansia muciniphila modulate host immune responses and gut barrier function.

The anti-inflammatory drug mesalamine targets bacterial polyphosphate accumulation

*Akkermansia muciniphila i*mproves metabolic profiles by reducing inflammation in chow diet-fed mice

Longitudinal change of selected human milk oligosaccharides and association to infants' growth, an observatory, single center, longitudinal cohort study

Abrupt suspension of probiotics administration may increase host pathogen susceptibility by inducing gut dysbiosis

Toward a Personalized Approach in Prebiotics Research

Dietary Fiber and Prebiotics and the Gastrointestinal Microbiota.

A microbial protein that alleviates metabolic syndrome

Can probiotics modulate human disease by impacting intestinal barrier function?

Human Milk Oligosaccharides Influence Neonatal Mucosal and Systemic Immunity.

Oral Microbiota in Infants Fed a Formula Supplemented with Bovine Milk Fat Globule Membranes - A Randomized Controlled Trial.

Dietary Prebiotics and Bioactive Milk Fractions Improve NREM Sleep, Enhance REM Sleep Rebound and Attenuate the Stress-Induced Decrease in Diurnal Temperature and Gut Microbial Alpha Diversity.

Impact of prebiotics on metabolic and behavioral alterations in a mouse model of metabolic syndrome.

Starter formula enriched in prebiotics and probiotics ensures normal growth of infants and promotes gut health: a randomized clinical trial.

Diet-induced extinctions in the gut microbiota compound over generations

Microbiome: Eating for trillions

An important chapter in the infection-malnutrition story.

Lactobacillus plantarum strain maintains growth of infant mice during chronic undernutrition

Gut bacteria that prevent growth impairments transmitted by microbiota from malnourished children

Sialylated Milk Oligosaccharides Promote Microbiota-Dependent Growth in Models of Infant Undernutrition

Effects of bovine colostrum on recurrent respiratory tract infections and diarrhea in children.

Sialylated galacto-oligosaccharides and 2'-fucosyllactose reduce necrotising enterocolitis in neonatal rats

Rebooting the microbiome.

Fecal microbiota transplantation: in perspective.

Fecal Microbiota-based Therapeutics for Recurrent Clostridium difficile Infection, Ulcerative Colitis and Obesity

Microbial therapeutic interventions.

High-affinity monoclonal IgA regulates gut microbiota and prevents colitis in mice

Stable Engraftment of Bifidobacterium longum AH1206 in the Human Gut Depends on Individualized Features of the Resident Microbiome

Protein- and zinc-deficient diets modulate the murine microbiome and metabolic phenotype

Fecal Microbiota-based Therapeutics for Recurrent Clostridium difficile Infection, Ulcerative Colitis and Obesity

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Gut check

Population-level analysis of gut microbiome variation

Childhood undernutrition, the gut microbiota, and microbiota-directed therapeutics

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Commendation for Exposing Key Advantage of Organ Chip Approach

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Other Gut Infections/Health

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GEMS extend understanding of childhood diarrhoea

Infectious disease: something in the water

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Dysbiosis is not an answer

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The microbiota and immune response during *Clostridium difficile* infection

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Microbiome & Infection

The shape of the microbiome in early life

Dysbiosis and the immune system.

Dysbiosis in intestinal inflammation: Cause or consequence

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Gastrointestinal Inflammation and Repair: Role of Microbiome, Infection, and Nutrition

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Persistent microbiome alterations modulate the rate of post-dieting weight regain

Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson's Disease

Influence of early life exposure, host genetics and diet on the mouse gut microbiome and metabolome

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Universality of human microbial dynamics

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Intrinsic Defense Mechanisms of the Intestinal Epithelium

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IFN-γ Hinders Recovery from Mucosal Inflammation during Antibiotic Therapy for Salmonella Gut Infection

Limited diversity sparks inflammation at the mucosal border

Rhythm and bugs: circadian clocks, gut microbiota, and enteric infections.

I'll have a turkey and cheese sandwich

A microbial perspective of human developmental biology

The microbiome and innate immunity

The microbiota in adaptive immune homeostasis and disease

Interactions between the microbiota and pathogenic bacteria in the gut

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Host-microbe interaction: Rules of the game for microbiota

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Host Selection of Microbiota via Differential Adhesion

Tummy Time: The Infant Microbiota–IgA Connection

Antibiotics, birth mode, and diet shape microbiome maturation during early life

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Host-Protozoan Interactions Protect from Mucosal Infections through Activation of the Inflammasome

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Culture of previously uncultured members of the human gut microbiota by culturomics