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

MARCH 1, 2017

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DETAILS OF ARTICLES

1. **Droplet digital PCR quantifies host inflammatory transcripts in feces reliably and reproducibly.**
   Jennifer Stauber, Nurmohammad Shaikh, M Isabel Ordiz, Phillip I. Tarr, Mark J Manary

**ABSTRACT**

The gut is the most extensive, interactive, and complex interface between the human host and the environment and therefore a critical site of immunological activity. Non-invasive methods to assess the host response in this organ are currently lacking. Feces are the available analyte which have been in proximity to the gut tissue.

We applied a method of concentrating host transcripts from fecal specimens using a existing bead-based affinity separation method for nucleic acids and quantified transcripts using droplet digital PCR (ddPCR) to determine the copy numbers of a variety of key transcripts in the gut immune system. ddPCR compartmentalizes the reaction in a small aqueous droplet suspended in oil, and counts droplets as either fluorescent or non-fluorescent. Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was used to normalize transcript concentration.

This method was applied to 799 fecal samples from rural Malawian children, and over 20,000 transcript concentrations were quantified. Host mRNA was detected in >99% samples, a threshold for target detection was established at an average expression of 0.02 copies target/GAPDH, above which correlation coefficient between duplicate measurements is >0.95. Quantities of transcript detected using ddPCR were greater than standard qPCR. Fecal sample preservation at the time of collection did not require immediate freezing or the addition of buffers or enzymes. Measurements of transcripts encoding immunoactive proteins correlated with a measure of gut inflammation in the study children, thereby substantiating their relevance. This method allows investigators to interrogate gene expression in the gut.

WEB: [10.1016/j.cellimm.2016.03.007](10.1016/j.cellimm.2016.03.007)

IMPACT FACTOR: 2.4

CITED HALF-LIFE: 8.9

**UW EDITORIAL COMMENT:**

The authors propose a novel method for the direct measurement of gut epithelial immunology using conservative transcript isolation and droplet digital PCR (ddPCR). Figure 4 shows that a comparison of assays by ddPCR and qPCR performed similarly in measuring relative abundances of GAPDH and IL-1β. Additional research is needed to test ddPCR method for detection of fecal host transcripts across other disorders and populations to establish the method’s generalizability.

2. **Feedback control of AHR signalling regulates intestinal immunity**
   Chris Schiering, Emma Wincent, Amina Metidji, Andrea Iseppon, Ying Li, Alexandre J. Potocnik, Sara Omenetti, Colin J. Henderson, C. Roland Wolf, Daniel W. Nebert & Brigitta Stockinger

**ABSTRACT**

The aryl hydrocarbon receptor (AHR) recognizes xenobiotics as well as natural compounds such as tryptophan metabolites, dietary components, and microbiota-derived factors, and it is important for
maintenance of homeostasis at mucosal surfaces. AHR activation induces cytochrome P4501 (CYP1) enzymes, which oxygenate AHR ligands, leading to their metabolic clearance and detoxification. Thus, CYP1 enzymes have an important feedback role that curtails the duration of AHR signalling, but it remains unclear whether they also regulate AHR ligand availability in vivo. Here we show that dysregulated expression of Cyp1a1 in mice depletes the reservoir of natural AHR ligands, generating a quasi AHR-deficient state. Constitutive expression of Cyp1a1 throughout the body or restricted specifically to intestinal epithelial cells resulted in loss of AHR-dependent type 3 innate lymphoid cells and T helper 17 cells and increased susceptibility to enteric infection. The deleterious effects of excessive AHR ligand degradation on intestinal immune functions could be counter-balanced by increasing the intake of AHR ligands in the diet. Thus, our data indicate that intestinal epithelial cells serve as gatekeepers for the supply of AHR ligands to the host and emphasize the importance of feedback control in modulating AHR pathway activation.

WEB: 10.1038/nature21080
IMPACT FACTOR: 38.1
CITED HALF-LIFE: >10.0

UW EDITORIAL COMMENT: The authors report that experimentally inducing cytochrome P4501 enzymes in a mouse model decreases AHR-dependent intestinal immune responses. Using a mouse strain that reports AHR activity with a fluorescent protein, Cyp1-knockout mice were observed to have increased AHR activity primarily in intestinal epithelial cells. In knockouts with transplanted wild-type bone marrow, mice maintained their high AHR activity, providing evidence of the role of AHR ligand metabolism in regulating intestinal immune system via non-hematopoietic cells. The authors also demonstrate that dietary supplementation with AHR ligands counter-balanced the introduction of cytochrome P4501 enzymes, which could inform therapeutic avenues for dysregulation.

Naama Geva-Zatorsky, Esen Sefik, Lindsay Kua, Lesley Pasman, Tze Guan Tan, Adriana Ortiz-Lopez, Tsering Bakto Yanortsang, Liang Yang, Ray Jupp, Diane Mathis, Christophe Benoist, Dennis L. Kasper.

ABSTRACT
Within the human gut reside diverse microbes coexisting with the host in a mutually advantageous relationship. Evidence has revealed the pivotal role of the gut microbiota in shaping the immune system. To date, only a few of these microbes have been shown to modulate specific immune parameters. Herein, we broadly identify the immunomodulatory effects of phylogenetically diverse human gut microbes. We monocolonized mice with each of 53 individual bacterial species and systematically analyzed host immunologic adaptation to colonization. Most microbes exerted several specialized, complementary, and redundant transcriptional and immunomodulatory effects. Surprisingly, these were independent of microbial phylogeny. Microbial diversity in the gut ensures robustness of the microbiota’s ability to generate a consistent immunomodulatory impact, serving as a highly important epigenetic system. This study provides a foundation for investigation of gut microbiota-host mutualism, highlighting key players that could identify important therapeutics.

WEB: 10.1016/j.cell.2017.01.022
IMPACT FACTOR: 12.552
CITED HALF-LIFE: 4.0
UW EDITORIAL COMMENT:
Researchers established an explanatory model of human-derived immunomodulatory microbes and molecules in monocolonized gnotobiotic mice. Transcriptome analysis of colonic and small intestine tissues showed major inter-individual variability and this background variation made it difficult for the authors to determine microbe-specific effects. Figure 2 provides the average frequencies of each immunocyte population per microbe type.

4. The anti-inflammatory drug mesalamine targets bacterial polyphosphate accumulation.
Jan-Ulrik Dahl, Michael J. Gray, Daphne Bazopoulou, Francois Beaufay, Justine Lempart, Mark J. Koenigsknecht, Ying Wang, Jason R. Baker, William L. Hasler, Vincent B. Young, Duxin Sun & Ursula Jakob

ABSTRACT
Mesalamine serves as the gold standard in treating ulcerative colitis. However, its precise mechanism(s) of action remains unclear. Here, we show that mesalamine treatment rapidly decreases polyphosphate levels in diverse bacteria, including members of the human gut microbiome. This decrease sensitizes bacteria towards oxidative stress, reduces colonization and attenuates persister cell and biofilm formation, suggesting that mesalamine aids in diminishing the capacity of bacteria to persist within chronically inflamed environments.

WEB: [10.1038/nmicrobiol.2016.267](10.1038/nmicrobiol.2016.267)
IMPACT FACTOR: 24.7
CITED HALF-LIFE: N/A

UW EDITORIAL COMMENT:
The researchers used multiple testing methods to confirm that mesalamine affects polyphosphate levels in a wide variety of bacteria. Healthy human subjects were treated with clinically-relevant doses of mesalamine-based drugs and gastrointestinal luminal samples were then observed for polyphosphate kinase levels (PPK – a bacterial enzyme that enables the synthesis of polymers). As soon as mesalamine was detectable in luminal samples, polyphosphate levels dramatically decreased. *Ex vivo* treatment of bacteria cultivated from human fecal content with mesalamine caused a dramatic reduction in polyphosphate content. Kinetic studies using purified E. Coli PPK also confirmed mesalamine’s role in inhibiting PPK. These finding suggest mesalamine is an effective ulcerative colitis therapeutic due to a direct alteration of the bacteria’s ability to colonize in a chronically inflamed environment, and therefore it may have wider therapeutic applications.

5. A prominent glycy radical enzyme in human gut microbiomes metabolizes trans-4-hydroxy-L-proline.

ABSTRACT
The human microbiome encodes vast numbers of uncharacterized enzymes, limiting our functional understanding of this community and its effects on host health and disease. By incorporating
information about enzymatic chemistry into quantitative metagenomics, we determined the abundance and distribution of individual members of the glycyl radical enzyme superfamily among the microbiomes of healthy humans. We identified many uncharacterized family members, including a universally distributed enzyme that enables commensal gut microbes and human pathogens to dehydrate trans-4-hydroxy-l-proline, the product of the most abundant human posttranslational modification. This "chemically guided functional profiling" workflow can therefore use ecological context to facilitate the discovery of enzymes in microbial communities.

WEB: 10.1126/science.aai8386
IMPACT FACTOR: 34.6
CITED HALF-LIFE: >10

UW EDITORIAL COMMENT: The authors sought to develop a workflow for metagenomic and metatranscriptomic analyses to discover and characterize microbial enzymes. They used a combination of bioinformatic tools to generate a network that clusters sequences of enzymes sharing similar chemical and biological functions. Experiments verified homology and structuralchemical inferences provided by the model. Their analysis focused on glycyl radical enzymes (GREs) in the human gut microbiome, which have previously been difficult to accurately subtype due to high amino acid similarities and many superfamilies with unknown functions. This analysis identified GRE enzymes involved in anaerobic short-chain fatty acid production and L-proline biosynthesis, both of which are key mediators of healthy microbiota-host symbioses.

6. Microbial Respiration and Formate Oxidation as Metabolic Signatures of Inflammation-Associated Dysbiosis.
   Elizabeth R. Hughes, Maria G. Winter, Breck A. Duerkop, Luisella Spiga, Tatiane Furtado de Carvalho, Wenhan Zhu, Caroline C. Gillis, Lisa Büttner, Madeline P. Smoot, Cassie L. Behrendt, Sara Cherry, Renato L. Santos, Lora V. Hooper, Sebastian E. Winter.
   Cell Host & Microbe. Volume 21, Issue 2, 8 February 2017, Pages 208–219

ABSTRACT
Intestinal inflammation is frequently associated with an alteration of the gut microbiota, termed dysbiosis, which is characterized by a reduced abundance of obligate anaerobic bacteria and an expansion of facultative Proteobacteria such as commensal E. coli. The mechanisms enabling the outgrowth of Proteobacteria during inflammation are incompletely understood. Metagenomic sequencing revealed bacterial formate oxidation and aerobic respiration to be overrepresented metabolic pathways in a chemically induced murine model of colitis. Dysbiosis was accompanied by increased formate levels in the gut lumen. Formate was of microbial origin since no formate was detected in germ-free mice. Complementary studies using commensal E. coli strains as model organisms indicated that formate dehydrogenase and terminal oxidase genes provided a fitness advantage in murine models of colitis. In vivo, formate served as electron donor in conjunction with oxygen as the terminal electron acceptor. This work identifies bacterial formate oxidation and oxygen respiration as metabolic signatures for inflammation-associated dysbiosis.

WEB: 10.1016/j.chom.2017.01.005
IMPACT FACTOR: 12.552
CITED HALF-LIFE: 4.0
UW EDITORIAL COMMENT:
Researchers used metagenomic shotgun sequencing of a murine model of gut inflammation to identify microbial genes enriched during inflammation during the ecological shift in species that leads to dysbiosis. Subsequent studies with bacterial model organisms demonstrated that molybdopterin cofactor-dependent enzymes are required for blooms of Enterobacteriaceae species during periods of gut inflammation.

Tsuyoshi Miki, Ryosuke Goto, Mayuka Fujimoto, Nobuhiko Okada, Wolf-Dietrich Hardt
*Cell Host & Microbe*, Volume 21, Issue 2, 8 February 2017, Pages 130-131

ABSTRACT
The bactericidal lectin RegIIIβ is inducibly produced by intestinal epithelial cells as a defense against infection by enteropathogens. In the gut lumen, RegIIIβ kills not only certain enteropathogens, but also some commensal bacteria; thus, RegIIIβ is also thought to be an innate immune effector shaping microbiota composition and establishing intestinal homeostasis. Using the streptomycin mouse model for *Salmonella* colitis, we show that RegIIIβ can promote sustained gut colonization of *Salmonella* Typhimurium and prolong enteropathy. RegIIIβ expression was associated with suppression of *Bacteroides* spp. in the gut lumen, prolonged disease-associated alterations in colonic metabolism, and reduced luminal vitamin B6 levels. Supplementation with *Bacteroides* spp. or vitamin B6 accelerated pathogen clearance from the gut and remission of enteropathy. Our findings indicate that interventions at the level of RegIIIβ and supplementation with *Bacteroides* spp. or vitamin B6 might open new avenues for therapeutic intervention in the context of *Salmonella* colitis.

IMPACT FACTOR: 12.552
CITED HALF-LIFE: 4.0

UW EDITORIAL COMMENT:
Controlling the RegIIIb-dependent effects might be a promising avenue for treating Salmonella-induced diarrhea. Researchers found that RegIIIβ is either uninvolved or redundant for enteropathy in the day 3 streptomycin mouse model (Salmonella diarrhea treated with streptomycin) but at later stages of infection, RegIIIβ seems to promote sustained gut luminal colonization by non-typhoidal Salmonella Typhimurium (*S. Tym*). Deficiency of RegIIIβ accelerates *S. Tym* clearance. Based on the patterns of colonization over infection, the authors propose that reduced colonization levels observed ten days after infection are linked to reduced mucosal inflammation, which they verified by gene expression analysis. Researchers also drew a link between reduced levels of gut luminal vitamin B6, which is provided by food or retrieved from commensal gut bacteria, in *S. Tym*-infected mice to RegIIIβ inflicted changes of microbiota. Therapeutic administration of B6 to wild-type mice infected with *S. Tym* significantly reduced the pathogen load, indicating B6’s role in regulating gut infection by fostering clearance and recovery from *S. Tym* infection.
Determinant Variables, Enteric Pathogen Burden, Gut Function, and Immune-Related Inflammatory Biomarkers Associated with Childhood Malnutrition: A Prospective Case-Control Study in Northeastern Brazil.
*Pediatric Infectious Disease. Epub ahead of print. 2017 Feb 22.*

**ABSTRACT**
Malnutrition results in serious consequences for growth and cognitive development in children. We studied select child and maternal biological factors, socio-economic factors, enteric pathogenic burden, and gut function biomarkers in 402 children 6-24 months of age in North-eastern Brazil. In this prospective case-control study, not being fed colostrum (odds ratio [OR] = 3.29, 95% confidence interval [CI] 1.73-6.26), maternal age ≥18 years (OR = 1.88, 95% CI 1.10-3.22), and no electrical fan (OR = 2.46, 95% CI 1.22-4.96) or bicycle (OR = 1.80, 95% CI 1.10-2.95) in the household were positively associated, and higher birth weight (OR = 0.27, 95% CI 0.19-0.38), larger head circumference (OR = 0.74, 95% CI 0.66-0.82), and shortness of breath in the last two weeks (OR = 0.49, 95% CI 0.27-0.90) were negatively associated with malnutrition. Subclinical enteric pathogen infections were common, and enteroaggregative Escherichia coli infections were more prevalent in malnourished children (p = 0.045). Biomarkers such as the lactulose:mannitol test, myeloperoxidase, neopterin, and calprotectin were highly elevated in both malnourished and nourished children. Nourished children had a better systemic immune response than the malnourished children, as detected by elevated serum amyloid A-1 (SAA-1) and soluble cluster of differentiation protein 14 (sCD14) biomarkers (P < 0.001). SAA-1 and sCD14 were also associated with better nutritional z-scores. Neonatal, maternal, and socio-economic factors were associated with malnutrition in children. There was a substantial subclinical enteric pathogen burden, particularly with EAEC, in malnourished children.

**WEB:** 10.1097/INF.0000000000001569
**IMPACT FACTOR:** 2.6
**CITED HALF-LIFE:** 7.7

**UW EDITORIAL COMMENT:**
This Brazil-based study is another publication from the MAL-ED multicenter longitudinal case-control study. The most common enteric pathogens in fecal samples included enteropathic, enteroinvasive, and enteroaggregative *E. coli, Giardia spp.*, and *C. jejuni/coli* for both nourished and malnourished children (Figure 2). Biomarkers for intestinal and systemic inflammation, including myeloperoxidase, neopterin, and calprotectin, were present in high concentrations in both groups, which indicates chronic, endemic environmental enteropathy. Limitations of this study included lack of daily morbidity data and data about the quality and quantity of complementary food intake, which may have influenced recorded nutrition status.
9. **Akkermansia muciniphila improves metabolic profiles by reducing inflammation in chow diet-fed mice**

**ABSTRACT**
Abnormal shifts in the composition of gut microbiota contribute to the pathogenesis of metabolic diseases, including obesity and type 2 diabetes (T2DM). The crosstalk between gut microbes and the host affects the inflammatory status and glucose tolerance of the individuals, but the underlying mechanisms have not been elucidated completely. In this study, we treated the lean chow diet-fed mice with *Akkermansia muciniphila*, which is thought to be inversely correlated with inflammation status and body weight in rodents and humans, and we found that *A. muciniphila* supplementation by daily gavage for five weeks significantly alleviated body weight gain and reduced fat mass. Glucose tolerance and insulin sensitivity were also improved by *A. muciniphila* supplementation compared with the vehicle. Furthermore, *A. muciniphila* supplementation reduced gene expression related to fatty acid synthesis and transport in liver and muscle; meanwhile, endoplasmic reticulum (ER) stress in liver and muscle was also alleviated by *A. muciniphila*. More importantly, *A. muciniphila* supplementation reduced chronic low-grade inflammation, as reflected by decreased plasma levels of lipopolysaccharide (LPS)-binding protein (LBP) and leptin, as well as inactivated LPS/LBP downstream signaling (e.g. decreased phospho-JNK and increased IKBA expression) in liver and muscle. Moreover, metabolomics profiling in plasma also revealed an increase in anti-inflammatory factors such as α-tocopherol, β-sitosterol and a decrease of representative amino acids. In summary, our study demonstrated that *A. muciniphila* supplementation relieved metabolic inflammation, providing underlying mechanisms for the interaction of *A. muciniphila* and host health, pointing to possibilities for metabolic benefits using specific probiotics supplementation in metabolic healthy individuals.

**WEB:** 10.1530/JME-16-0054
**IMPACT FACTOR:** 2.9
**CITED HALF-LIFE:** 8.5

**UW EDITORIAL COMMENT:**
This mouse-model study explains *A. muciniphila*’s role in decreasing metabolic endotoxemia and inflammation signaling. Figure 5 provides a straightforward diagram of functional interaction between *A. muciniphila* and host metabolism. The authors report different findings from a previous study on chow diet-fed mice ([Everard et al 2013](#)) but explain the differences as a result of different diet methods (more protein and less carbohydrates in the diet of the current study). A second observed difference was the lack of change in gene expression relative to lipid synthesis or transport in fat tissues of chow-fed mice, which the authors also attribute to the difference in chow-diets. This is something that should be replicated to confirm the effects of different diet treatments.

10. **Host cell attachment elicits posttranscriptional regulation in infecting enteropathogenic bacteria.**
Naama Katsowich, Netanel Elbaz, Ritesh Ranjan Pal, Erez Mills, Simi Kobi, Tamar Kahan, Ilan Rosenshine
ABSTRACT
The mechanisms by which pathogens sense the host and respond by remodeling gene expression are poorly understood. Enteropathogenic Escherichia coli (EPEC), the cause of severe intestinal infection, employs a type III secretion system (T3SS) to inject effector proteins into intestinal epithelial cells. These effectors subvert host cell processes to promote bacterial colonization. We show that the T3SS also functions to sense the host cell and to trigger in response posttranscriptional remodeling of gene expression in the bacteria. We further show that upon effector injection, the effector-bound chaperone (CesT), which remains in the EPEC cytoplasm, antagonizes the posttranscriptional regulator CsrA. The CesT-CsrA interaction provokes reprogramming of expression of virulence and metabolic genes. This regulation is likely required for the pathogen’s adaptation to life on the epithelium surface.

WEB: 10.1126/science.aah4886
IMPACT FACTOR: 34.7
CITED HALF-LIFE: >10.0

UW EDITORIAL COMMENT:
Researchers report how pathogenicity islands virulence genes in enteropathogenic E. coli (EPEC) respond upon attachment to a host gut cell. HeLa cells were infected with an EPEC strain containing a green fluorescent tag attached to the NIeA effector protein, which influences host secretory and inflammasome pathways. Only the EPEC cells attached to HeLa cells fluoresced, suggesting that NIeA is expressed exclusively by bacteria attached to host cells. An EPEC surface component, type III secretion system (T3SS), senses the host cell and triggers a signaling pathway which induces host inflammation. Additional work reported in this study elucidates the role of T3SS in host sensing.

ADDITIONAL ARTICLES OF INTEREST (FEBRUARY PUBLICATIONS)

Gut-Brain Cross-Talk in Metabolic Control

Intestinal commensal bacteria mediate lunch mucosal immunity and promote resistance of newborn mice to infection.

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

Dynamics of the human microbiome in inflammatory bowel disease

Statoviruses, A novel taxon of RNA viruses present in the gastrointestinal tracts of diverse mammals.

Campylobacter jejuni and associated immune mechanisms: short-term effects and long-term implications for infants in low-income countries.

Reinforcement of intestinal epithelial barrier by arabinoxylans in overweight and obese subjects: A randomized controlled trial: Arabinoxylans in gut barrier.

The human gut microbiome as source of innovation for health: Which physiological and therapeutic outcomes could we expect?

Toward a Personalized Approach in Prebiotics Research
Changes in Intestinal Motility and Gut Microbiota Composition in a Rat Stress Model

Dietary Fiber and Prebiotics and the Gastrointestinal Microbiota.

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

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

Tryptophan: A gut microbiota-derived metabolites regulating inflammation

Enteric Pathogens and Their Toxin-Induced Disruption of the Intestinal Barrier through Alteration of Tight Junctions in Chickens.

EED Biology & Review Articles

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 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**

*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
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

Overcoming the limited availability of human milk oligosaccharides: challenges and opportunities for research and application

Efficacy of Probiotics Versus Placebo in the Prevention of Necrotizing Enterocolitis in Preterm Very Low Birth Weight Infants: A Double-Blind Randomized Controlled Trial

Eosinophils, probiotics, and the microbiome.

A Combined Intervention of Zinc, Multiple Micronutrients, and Albendazole Does Not Ameliorate Environmental Enteric Dysfunction or Stunting in Rural Malawian Children in a Double-Blind Randomized Controlled Trial

Gut Health Diagnostics & Research

Dynamics and Trends in Fecal Biomarkers of Gut Function in Children from 1-24 Months in the MAL-ED Study.

Fecal Markers of Environmental Enteropathy and Subsequent Growth in Bangladeshi Children.

Etiology of Diarrhea, Nutritional Outcomes and Novel Intestinal Biomarkers in Tanzanian Infants: A Preliminary Study.

Co-culture of Living Microbiome with Microengineered Human Intestinal Villi in a Gut-on-a-Chip Microfluidic Device.

MiniBioReactor Arrays (MBRAs) as a Tool for Studying C. difficile Physiology in the Presence of a Complex Community.
Reverse Engineering Human Pathophysiology with Organs-on-Chips.

Human Microbiota-Associated Mice: A Model with Challenges

Contributions of microbiome and mechanical deformation to intestinal bacterial overgrowth and inflammation in a human gut-on-a-chip.

Optimization of Quantitative PCR Methods for Enteropathogen Detection

Use of quantitative molecular diagnostic methods to identify causes of diarrhoea in children: a reanalysis of the GEMS case-control study

Diagnostics: Filling in the missing pieces

Natural history of the infant gut microbiome and impact of antibiotic treatment on bacterial strain diversity and stability

Gut check

Population-level analysis of gut microbiome variation

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

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

Environmental Enteric Dysfunction is Associated with Poor Linear Growth and Can be Identified by Host Fecal mRNAs

Commendation for Exposing Key Advantage of Organ Chip Approach

Biomarkers of Environmental Enteropathy are Positively Associated with Immune Responses to an Oral Cholera Vaccine in Bangladeshi Children

Shifts in Lachnospira and Clostridium sp. in the 3-month stool microbiome are associated with preschool age asthma

Other Gut Infections/Health

The Role of Fibronectin in the Adherence and Inflammatory Response Induced by Enteroaggregative Escherichia coli on Epithelial Cells.

Early-life enteric infections: relation between chronic systemic inflammation and poor cognition in children.

GEMS extend understanding of childhood diarrhoea
Infectious disease: something in the water

Genomic diversity of EPEC associated with clinical presentations of differing severity. Gene-microbiota interactions contribute to the pathogenesis of inflammatory bowel disease

Taking it Personally: Personalized Utilization of the Human Microbiome in Health and Disease

Enrichment of the lung microbiome with gut bacteria in sepsis and the acute respiratory distress syndrome

Giardia: a pathogen or commensal for children in high-prevalence settings?

Tuft Cells: New Players in Colitis.

PGE2 is a direct and robust mediator of anion/fluid secretion by human intestinal epithelial cells

Dysbiosis is not an answer

Epidemiology and Impact of Campylobacter Infection in Children in 8 Low-Resource Settings: Results From the MAL-ED Study

The microbiota and immune response during Clostridium difficile infection

Enterocyte Purge and Rapid Recovery Is a Resilience Reaction of the Gut Epithelium to Pore-Forming Toxin Attack

Microbiome & Infection

Discovery of Reactive Microbiota-Derived Metabolites that Inhibit Host Proteases

A purified membrane protein from Akkermansia muciniphila or the pasteurized bacterium improves metabolism in obese and diabetic mice

Microbiome-Modulated metabolites at the Interface of Host Immunity

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

Formation of propionate and butyrate by the human colonic microbiota.

Xenobiotic Receptor-Mediated Regulation of Intestinal Barrier Function and Innate Immunity.

Identifying species of symbiont bacteria from the human gut that, alone, can induce intestinal Th17 cells in mice

Microbiota Diurnal Rhythmicity Programs Host Transcriptome Oscillations
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

Impact of the gut microbiota on enhancer accessibility in gut intraepithelial lymphocytes.

Universality of human microbial dynamics

Reparative inflammation takes charge of tissue regeneration

Intrinsic Defense Mechanisms of the Intestinal Epithelium

Lipocalin 2 Protects from Inflammation and Tumorigenesis Associated with Gut Microbiota Alterations

Gut Microbial Metabolites Fuel Host Antibody Responses

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

Microbiome-wide association studies link dynamic microbial consortia to disease

Host-microbe interaction: Rules of the game for microbiota

The Host Shapes the Gut Microbiota via Fecal MicroRNA

Another Reason to Thank Mom: Gestational Effects of Microbiota Metabolites

Preterm infant gut microbiota affects intestinal epithelial development in a humanized microbiome gnotobiotic mouse model.

Development of the gut microbiota and mucosal IgA responses in twins and gnotobiotic mice
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

Integrated multi-omics of the human gut microbiome in a case study of familial type 1 diabetes

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

Adaptive immune response in symptomatic and asymptomatic enteric protozoal infection: evidence for a determining role of parasite genetic heterogeneity in host immunity to human giardiasis

The Liver at the Nexus of Host-Microbial Interactions

Modeling human enteric dysbiosis and rotavirus immunity in gnotobiotic pigs.

Linking the Human Gut Microbiome to Inflammatory Cytokine Production Capacity

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