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STRATEGIC ANALYSIS, RESEARCH & TRAINING CENTER

GUT HEALTH DIGEST

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

JUNE 27, 2017

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    - Review of the history, terminology, and etiology of tropical enteropathy, also known as environmental enteropathy.

2. **Detrimental Impact of Microbiota-Accessible Carbohydrate-Deprived Diet on Gut and Immune Homeostasis: An Overview** {Abstract & UW comment} {Full article}
    - Review of the deleterious impact of diets lacking microbiota-accessible carbohydrates on gut microbiota, gut epithelium, and immune cells.

3. **The path towards microbiome-based metabolite treatment.** {Abstract & UW comment} {Full article}
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4. **A methodologic framework for modeling and assessing biomarkers of environmental enteropathy as predictors of growth in infants: an example from a Peruvian birth cohort.** {Abstract & UW comment} {Full article}
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6. **New insights into environmental enteric dysfunction.** {Abstract & UW comment} {Full article}
    - Brief review of EED morphology, biological pathways, and proposed interventions.

7. **Gastrointestinal inflammation by gut microbiota disturbance induces memory impairment in mice.** {Abstract & UW comment} {Full article}
    - Mouse-model experiment linking overexpression of lipopolysaccharides to inflammation and memory impairment.

8. **Improving the detection of environmental enteric dysfunction: a lactulose, rhamnose assay of intestinal permeability in children aged under 5 years exposed to poor sanitation and hygiene.** {Abstract & UW comment} {Full article}
    - Cohort study of intestinal permeability using a two-saccharide assay in three small cohorts from Zambia, Peru, and the United States.

9. **Parasitic protozoa and interactions with the host intestinal microbiota.** {Abstract & UW comment} {Full article}
    - Review of recent research related to the intestinal microbiota and infectious protozoa.

10. **Early Antibiotic Exposure in Low-Resource Settings is Associated with Increased Weight in The First Two Years of Life.** {Abstract & UW comment} {Full article}
    - A MAL-ED birth cohort study of the effects of antibiotic exposure on child health in early life.

DETAILS OF ARTICLES

1. Tropical Enteropathies.
   Louis-Auguste J, Kelly P.
   Current Gastroenterology Reports. 24 May 2017: Vol. 19, Issue 29. [Epub ahead of print].

ABSTRACT
Purpose of Review: The term 'tropical enteropathy' originated in observations in the 1960s that small intestinal morphology and function differed in the tropics from the norms found in temperate climates. It was subsequently shown that this enteropathy is more closely related to environmental conditions than latitude, and it was re-labelled 'environmental enteropathy'. It is now recognised that environmental enteropathy (also now called environmental enteric dysfunction) has implications for the health and linear growth of children in low- and middle-income countries, and it may underlie poor responses to oral vaccination in these countries. The purpose of this review is to define and clarify this enteropathy despite the confusing terminology it has attracted and to contrast it with other enteropathic states.
Recent Findings: Recent work has begun to demonstrate the nature of the mucosal lesion and the relationship with microbial translocation which is currently thought to link a failure of mucosal barrier function and the cascade of systemic inflammation which inhibits growth. The evidence is still correlative rather than definitive, but derives some additional support from animal models. There are some common features between environmental enteropathy and other enteropathies, but there are important differences also. The mechanism of the link between enteropathy and vaccine failure is not understood, and neither is it clear how the more severe form of enteropathy, which we refer to as malnutrition enteropathy, is driven by nutrient depletion and intestinal infection. Tropical enteropathies form a group of disorders which include environmental and nutritional enteropathies. The long-term health implications of these disorders for health in low-income countries are just being explored, but the scale of their effects is very large, with millions of people affected.

WEB: https://link.springer.com/article/10.1007%2Fs11894-017-0570-0
IMPACT FACTOR: 1.0
CITED HALF-LIFE: n/a

UW EDITORIAL COMMENT: Table 1 gives a clear cross-comparison of eight small bowel enteropathies by identifying whether each disorder is associated with 11 different characteristics, such as systematic inflammation, malabsorption, diarrhea, and weight loss. This article summarizes the current literature published on environmental enteropathy, highlights key distinctions between various forms of enteropathy, and provides a history of the development of the terminology and knowledge of this group of disorders.

2. Detrimental Impact of Microbiota-Accessible Carbohydrate-Deprived Diet on Gut and Immune Homeostasis: An Overview
   Daïen CI, Pinget GV, Tan JK, Macia L.
   Frontiers in Immunology. 12 May 2017: Vol. 8, Issue 548.

ABSTRACT
Dietary fibers are non-digestible polysaccharides functionally known as microbiota-accessible carbohydrates (MACs), present in inadequate amounts in the Western diet. MACs are a main source of energy for gut bacteria so the abundance and variety of MACs can modulate gut microbial composition and function. This, in turn, impacts host immunity and health. In preclinical studies, MAC-deprived diet

and disruption of gut homeostasis aggravate the development of inflammatory diseases, such as allergies, infections, and autoimmune diseases. The present review provides a synopsis on the impact of a low-MAC diet on gut homeostasis or, more specifically, on gut microbiota, gut epithelium, and immune cells.

WEB: http://journal.frontiersin.org/article/10.3389/fimmu.2017.00548/full
IMPACT FACTOR: 3.35
CITED HALF-LIFE: n/a

UW EDITORIAL COMMENT: The authors focus their discussion on the impact of a diet lacking microbiota-accessible carbohydrates (MACs), rather than focusing on the benefits of supplementation of MACs, as much of the research has done in this area. By concentrating their review on the negative impacts of low quantities of MACs on gut microbiota, gut epithelium, immune cells, and disease development, the authors are able to highlight the deleterious effect of a MAC-deprive diet which may aid in engendering a shift in the standard Western diet that typically lacks MACs.

3. The path towards microbiome-based metabolite treatment.
   Suez J, Elinav E.
   *Nature Microbiol*ogy. 2017 May 25;2:17075.

ABSTRACT
The increasing evidence pointing towards the involvement of the gut microbiome in multiple diseases, as well as its plasticity, renders it a desirable potential therapeutic target. Nevertheless, classical therapies based on the consumption of live probiotic bacteria, or their enrichment by prebiotics, exhibit limited efficacy. Recently, a novel therapeutic approach has been suggested based on metabolites secreted, modulated or degraded by the microbiome. As many of the host-microorganism interactions pertaining to human health are mediated by metabolites, this approach may be able to provide therapeutic efficacy while overcoming caveats of current microbiome-targeting therapies, such as colonization resistance and inter-individual variation in microbial composition. In this Perspective, we will discuss the evidence that supports pursuing the metabolite-based therapeutic approach as well as issues critical for its implementation. In a broader context, we will discuss how recent advances in microbiome research may improve and refine current treatment modalities, and the potential of combining them with metabolite-based interventions as a means of achieving a person-specific, integrated and efficient therapy.

WEB: 10.1038/nmicrobiol.2017.75
IMPACT FACTOR: 26.8
CITED HALF-LIFE: n/a

UW EDITORIAL COMMENT: Authors discuss the potential benefits of microbiome-based metabolite therapies and ways in which this approach can overcome the challenges faced by other therapies, such as faecal microbiome transplantation (FMT), probiotic and prebiotic therapy. With an emphasis on the importance of tailoring microbiome therapy to the individual, authors suggest an integrated approach to microbiome therapy that combines metabolites, FMT, probiotics, and prebiotics. Figure 1 gives a visual that compares the current approach versus the suggested integrated approach.

4. A methodologic framework for modeling and assessing biomarkers of environmental enteropathy as predictors of growth in infants: an example from a Peruvian birth cohort.
Colston JM, Peñataro Yori P, Colantuoni E, Moulton LH, Ambikapathi R, Lee G, Rengifo Trigoso D, Siguas Salas M, Kosek MN.
Am J Clin Nutr. 2017 Jun 7. pii: ajcn151886. [Epub ahead of print].

ABSTRACT
BACKGROUND: Environmental enteropathy (EE) impairs the gut's absorptive capacity and immune function and causes decelerations in statural growth that manifest gradually over time.
OBJECTIVE: To illustrate an approach for assessing emerging biomarkers of EE, we separately assessed the associations between 3 such markers and subsequent nutritional status.
DESIGN: Stool samples were routinely collected between January 2010 and November 2014 from a cohort of 303 Peruvian infants and analyzed for concentrations of the biomarkers α-1-antitrypsin (AAT), myeloperoxidase, and neopterin. For each marker, a mixed-effects linear regression model was fitted for length-for-age z scores (LAZs) obtained from anthropometric assessments that incorporated covariate predictors, polynomial terms for age, and product interaction terms to test associations over varying lag lengths. The biomarkers' contribution to the models was assessed with the use of the likelihood ratio test and partial R2 statistics.
RESULTS: Test statistics for the combined inclusion of the 4-model terms that involved the biomarker were highly statistically significant for AAT (28.71; $P < 0.0001$) and myeloperoxidase (62.79; $P < 0.0001$) over a 3-mo lag and moderately so for neopterin (13.97; $P = 0.0074$). AAT and myeloperoxidase seemed to interact strongly with age, with the magnitude and direction of the effect varying considerably over the first 3 y of life. The largest proportion of the variance explained by any biomarker (2.8%) and the largest difference in LAZ predicted between the 5th and 95th percentile (0.25) was by myeloperoxidase over a 2-mo lag.
CONCLUSIONS: Of the 3 fecal biomarkers studied, 2 that related to intestinal function-AAT and myeloperoxidase-were associated with small but highly statistically significant differences in future statural growth trajectories in infants in this cohort, lending further evidence to the EE hypothesis that increased gut permeability and inflammation adversely affects subsequent nutritional status. This association exhibited a complex interaction with age. This trial was registered at clinicaltrials.gov as NCT02441426.

WEB: 10.3945/ajcn.116.151886
IMPACT FACTOR: 4.56
CITED HALF-LIFE: 9.60

UW EDITORIAL COMMENT: Appropriate adjustments were made for calendar time, seasonality, sex, birth weight, maternal height, stool consistency (concentration of analytes), and infant feeding. The interaction between age and biomarker was also accounted for in the model, as the authors hypothesized that baseline inflammation rates may change as children age. To ensure adequate temporality for the association of biomarkers to predict LAZ, LAZ measures were correlated with biomarker levels from three months prior. This three-month lag time is clinically appropriate to allow for the effects of a nutritional intervention.

5. Organs-on-chips with integrated electrodes for trans-epithelial electrical resistance (TEER) measurements of human epithelial barrier function.
Olivier Y. F. Henry,ab Remi Villenave,a Michael J. Cronce,a William D. Leineweber,a Maximilian A. Benza and Donald E. Ingber.

Lab Chip. 2017 Jun 9. [Epub ahead of print].

ABSTRACT
Trans-epithelial electrical resistance (TEER) is broadly used as an experimental readout and a quality control assay for measuring the integrity of epithelial monolayers cultured under static conditions in vitro, however, there is no standard methodology for its application to microfluidic organ-on-a-chip (organ chip) cultures. Here, we describe a new microfluidic organ chip design that contains embedded electrodes, and we demonstrate its utility for assessing formation and disruption of barrier function both within a human lung airway chip lined by a fully differentiated mucociliary human airway epithelium and in a human gut chip lined by intestinal epithelial cells. These chips with integrated electrodes enable real-time, non-invasive monitoring of TEER and can be applied to measure barrier function in virtually any type of cultured cell.

WEB: 0.1039/c7lc00155j
IMPACT FACTOR: 4.07
CITED HALF-LIFE: 4.0

UW EDITORIAL COMMENT: The authors tested their TEER chip design using human intestinal epithelium and found some instability at lower frequencies but confirmed the design is effective for other types of epithelium. Figure 5C provides evidence that the measured TEER values are associated with the presence of tight junctions (decrease in percent impedance over treatment time, compared to the control cell chips).

6. New insights into environmental enteric dysfunction.
   Trehan I, Kelly P, Shaikh N, Manary MJ.
   Arch Dis Child. 2016 Aug;101(8):741-4. Epub 2016 Mar 1.

ABSTRACT
Environmental enteric dysfunction (EED) has been recognised as an important contributing factor to physical and cognitive stunting, poor response to oral vaccines, limited resilience to acute infections and ultimately global childhood mortality. The aetiology of EED remains poorly defined but the epidemiology suggests a multifactorial combination of prenatal and early-life undernutrition and repeated infectious and/or toxic environmental insults due to unsanitary and unhygienic environments. Previous attempts at medical interventions to ameliorate EED have been unsatisfying. However, a new generation of imaging and '-omics' technologies hold promise for developing a new understanding of the pathophysiology of EED. A series of trials designed to decrease EED and stunting are taking novel approaches, including improvements in sanitation, hygiene and nutritional interventions. Although many challenges remain in defeating EED, the global child health community must redouble their efforts to reduce EED in order to make substantive improvements in morbidity and mortality worldwide.

WEB: 10.1136/archdischild-2015-309534
IMPACT FACTOR: 0.19
CITED HALF-LIFE: n/a

UW EDITORIAL COMMENT: Figure 1 provides a list of pathways, transcripts, and host responses activated in EED. The review recaps EED morphology, transcriptome and metabolomic profiles, and the need for a standardized case definition and biomarkers for EED in order to more precisely assess the effectiveness of a variety of interventions.

7. Gastrointestinal inflammation by gut microbiota disturbance induces memory impairment in mice.
   Jang SE, Lim SM, Jeong JJ, Jang HM, Lee HJ, Han MJ, Kim DH.
   Mucosal Immunol. 2017 Jun 14. [Epub ahead of print].

ABSTRACT
In this study, we tested our hypothesis regarding mechanistic cross-talk between gastrointestinal inflammation and memory loss in a mouse model. Intrarectal injection of the colitis inducer 2,4,6-trinitrobenzenesulfonic acid (TNBS) in mice caused colitis via activation of nuclear factor (NF)-κB and increase in membrane permeability. TNBS treatment increased fecal and blood levels of lipopolysaccharide (LPS) and the number of Enterobacteriaceae, particularly Escherichia coli (EC), in the gut microbiota composition, but significantly reduced the number of Lactobacillus johnsonii (LJ). Indeed, we observed that the mice treated with TNBS displayed impaired memory, as assessed using the Y-maze and passive avoidance tasks. Furthermore, treatment with EC, which was isolated from the feces of mice with TNBS-induced colitis, caused memory impairment and colitis, and increased the absorption of orally administered LPS into the blood. Treatment with TNBS or EC induced NF-κB activation and tumor necrosis factor-α expression in the hippocampus of mice, as well as suppressed brain-derived neurotrophic factor expression. However, treatment with LJ restored the disturbed gut microbiota composition, lowered gut microbiota, and blood LPS levels, and attenuated both TNBS- and EC-induced memory impairment and colitis. These results suggest that the gut microbiota disturbance by extrinsic stresses can cause gastrointestinal inflammation, resulting in memory impairment.

WEB: 10.1038/mi.2017.49
IMPACT FACTOR: 5.53
CITED HALF-LIFE: 3.10

UW EDITORIAL COMMENT:
The findings in this study add to growing evidence of the gut-brain axis to explain the interactions between enteric microbiota and the central nervous system. Figure 5 provides a comparison of microbiota composition in mice exposed to a colitis-inducer and *L. johnsonii* (a beneficial bacteria).

8. Improving the detection of environmental enteric dysfunction: a lactulose, rhamnose assay of intestinal permeability in children aged under 5 years exposed to poor sanitation and hygiene.
   Faubion WA, Camilleri M, Murray JA, Kelly P, Amadi B, Kosek MN, Enders F, Larson J, Boe G, Dyer R, Singh R.
   BMJ Glob Health. 2016 Jul 4;1(1):e000066. eCollection 2016 Apr.

ABSTRACT
BACKGROUND: Environmental enteric dysfunction (EED) is an asymptomatic intestinal disorder affecting populations living in conditions of poor sanitation and hygiene. The study tested intestinal barrier function in infants with EED.
METHODS**:** We prospectively studied an advanced high-performance liquid chromatography mass spectrometry assay of urine collected after oral intake of the monosaccharide, L-rhamnose and the disaccharide, lactulose, in 112 children from three continents.
FINDINGS**:** Compared to the US cohort (n=27), the cohorts of children from Peru (n=19) and Zambia (n=85) were older with evidence of growth impairment. The median (range) of age (months) was 8.0 (2.0 to 13.0), 27.0 (15.0 to 29.0) and 21.0 (12.0 to 36.0), respectively. The median (range) of height for

age Z score was -0.1 (-1.8 to 2.4), -1.8 (-3.3 to -0.2) and -2.3 (-8.5 to 1.2), respectively. Among children with valid sugar data (n=22 USA, n=19 Peru, n=73 Zambia), there were no significant differences in the median rhamnose urine concentrations between the three groups. The median (range) lactulose concentration (µg/mL) was 6.78 (0.29 to 31.90), 47.60 (4.23 to 379.00) and 75.40 (0.67 to 873.00) in the US, Peruvian and Zambian cohorts, respectively (p<0.001). The lactulose/rhamnose ratio (LRR) was higher in cohorts from Peru (0.75, 0.15, 5.02) and Zambia (2.26, 0.08, 14.48) compared to the US (0.14, 0.06, 1.00) cohort (p<0.001). In a multivariate effect modification model, higher weight-for-age z scores were associated with lower post-dose lactulose when rhamnose excretion was constant (p=0.003). CONCLUSIONS**:** This non-invasive two saccharide permeability protocol measures changes in intestinal permeability in children with EED and permits the identification of individuals for interventional trials.

WEB: 10.1136/bmjgh-2016-000066
IMPACT FACTOR: 1.43
CITED HALF-LIFE: 2.60

UW EDITORIAL COMMENT: There are significant demographic differences among the study cohort groups (Table 1), namely differences in age and sex, which weakens the interpretation of differences in absorption as an indicator of differential intestinal permeability. Based on the demographic differences, differences in permeability might be expected regardless of EED condition. Furthermore, the variation observed between the two saccharides measured suggests that both need to be evaluated in order to have sufficient sensitivity for the detection of EED.

9. Parasitic protozoa and interactions with the host intestinal microbiota.
   Burgess SL, Gilchrist CA, Lynn TC, Petri WA Jr.
   Infect Immun. 2017 Jun 5. pii: IAI.00101-17. [Epub ahead of print].

ABSTRACT
Parasitic protozoan infections represent a major health burden in the developing world and contribute significantly to morbidity and mortality. These infections are often associated with considerable variability in clinical presentation. An emerging body of work suggests that the intestinal microbiota may help to explain some of these differences in disease expression. The objective of this minireview is to synthesize recent progress in this rapidly advancing field. Studies in humans, animal models and *in vitro* concerning the contribution of the intestinal microbiota to infectious disease will be discussed. We hope to provide an understanding of the human-protozoal pathogen-microbiome interaction and to speculate on how that might be leveraged for treatment.

WEB: 10.1128/IAI.00101-17
IMPACT FACTOR: 2.66
CITED HALF-LIFE: n/a

UW EDITORIAL COMMENT: This review suggests a role for mucosal parasites in microbiota interactions and recaps recent findings in murine models of host microbiome interactions and parasite infections. The authors also note that the gut microbiome can be difficult to study using metagenomics, since many microbiota are multiple morphologically identical but genetically distinct.

10. Early antibiotic exposure in low-resource settings is associated with increased weight in the first two years of life.

Rogawski ET, Platts-Mills JA, Seidman JC, John S, Mahfuz M, Ulak M, Shrestha S, Soofi SB, Yori PP, Mduma E, Svensen E, Ahmed T, Lima AAM, Bhutta Z, Kosek M, Lang D, Gottlieb M, Zaidi A, Kang G, Bessong P, Houpt ER, Guerrant RL; MAL-ED Network Investigators.
J Pediatr Gastroenterol Nutr. 2017 Jun 9. [Epub ahead of print].

ABSTRACT
OBJECTIVES: The potential growth-promoting effects of antibiotics are not well understood among undernourished children in environments with high pathogen exposure. We aimed to assess whether early antibiotic exposure duration and class were associated with growth to two years of age across 8 low-resource sites in the MAL-ED birth cohort study.
METHODS: We followed 1,954 children twice per week from birth to two years to record maternally-reported antibiotic exposures and measure anthropometry monthly. We estimated the associations between antibiotic exposure before 6 months of age and weight-for-age (WAZ) and length-for-age (LAZ) z-scores to two years. We assessed the impact of class-specific exposures and duration, and compared these results to effects of antibiotic exposures after 6 months of age.
RESULTS: Antibiotic use before 6 months of age was associated with increased weight from 6 months to 2 years, while associations with length were less consistent across sites and antibiotic classes. Compared to unexposed children, two or more courses of metronidazole, macrolides, and cephalosporins were associated with adjusted increases in WAZ of 0.24 (95% confidence interval (CI): 0.04, 0.43), 0.23 (95% CI: 0.05, 0.42), and 0.19 (95% CI: 0.04, 0.35) from 6 months to 2 years, respectively.
CONCLUSIONS: Antibiotic use in low-resource settings was most associated with the ponderal growth of children who had multiple exposures to antibiotics with broad spectrum and anaerobic activity in early infancy. Opportunities for rational and targeted antibiotic therapy in low resource settings may also promote short-term weight gain in children, though longer-term physical growth and metabolic impacts are unknown.

WEB: 10.1097/MPG.0000000000001640
IMPACT FACTOR: 1.48
CITED HALF-LIFE: 7.00

UW EDITORIAL COMMENT: The authors found important differences in outcomes depending on which antibiotics were used. For example, just one dose of metronidazole was associated with improved weight gain, while two or more doses of macrolides and cephalosporins were needed before the association was significant. Only fluoroquinolones were associated with increases in size at age two, suggesting that the effect of early life antibiotics is limited to short-term changes in microbiota and improved growth outcomes.

ADDITIONAL ARTICLES OF INTEREST

Targeting of microbe-derived metabolites to improve human health: The next frontier for drug discovery

Mechanisms Linking the Gut Microbiome and Glucose Metabolism

Intestinal Epithelial Sirtuin 1 Regulates Intestinal Inflammation during Aging in Mice by Altering the Intestinal Microbiota.

ARTICLE ARCHIVE (JAN 2016-PRESENT)

EED Biology & Review Articles

Age and Sex Normalization of Intestinal Permeability Measures for the Improved Assessment of Enteropathy in Infancy and Early Childhood: Results from the MAL-ED Study.

Infant Nutritional Status and Markers of Environmental Enteric Dysfunction are Associated with Midchildhood Anthropometry and Blood Pressure in Tanzania.

Biomarkers to Stratify Risk Groups among Children with Malnutrition in Resource-Limited Settings and to Monitor Response to Intervention

Association between Enteropathogens and Malnutrition in Children Aged 6-23 mo in Bangladesh: a Case-Control Study.

Causal Pathways from Enteropathogens to Environmental Enteropathy: Findings from the MAL-ED Birth Cohort Study.

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

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

Chronic consequences on human health induced by microbial pathogens: Growth faltering among children in developing countries.

The effects of micronutrient deficiencies on bacterial species from the human gut microbiota.

Gut microbiota interactions with the immunomodulatory role of vitamin D in normal individuals.

The association of serum choline with linear growth failure in young children from rural Malawi.

Starved Guts: Morphologic and Functional Intestinal Changes in Malnutrition.

Which dietary components modulate longitudinal growth?

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

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

Next-generation probiotics: the spectrum from probiotics to live biotherapeutics

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

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

Interleukin-23 Increases Intestinal Epithelial Cell Permeability In Vitro

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

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

Engineering bacterial thiosulfate and tetrathionate sensors for detecting gut inflammation.

Engineered Regulatory Systems Modulate Gene Expression of Human Commensals in the Gut

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

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

Leading microbiome-based therapeutic falters in Phase II trial

Faecal microbiota transplantation—A clinical view.

Optimization of metabolomics of defined in vitro gut microbial ecosystems

Community dynamics drive punctuated engraftment of the fecal microbiome following transplantation using freeze-dried, encapsulated fecal microbiota.

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The Role of the Immune System in Metabolic Health and Disease

Optimization of metabolomics of defined in vitro gut microbial ecosystems.

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Gut check

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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

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Antibiotics, Pediatric Dysbiosis, and Disease

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GEMS extend understanding of childhood diarrhoea

Infectious disease: something in the water

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Microbiome & Infection
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The shape of the microbiome in early life

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Dysbiosis in intestinal inflammation: Cause or consequence

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

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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

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Tummy Time: The Infant Microbiota–IgA Connection

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

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