START CENTER
STRATEGIC ANALYSIS,
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GUT HEALTH DIGEST

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

FEBRUARY 3, 2017

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LIST OF ARTICLES

1. **Systematic Characterization and Analysis of the Taxonomic Drivers of Functional Shifts in the Human Microbiome** {abstract & UW comment} {full article}
    - An analytical and computational framework that integrates taxonomic and functional comparative analyses to accurately quantify taxon-level contributions to disease-associated functional shifts.

2. **Structural Basis for Nutrient Acquisition by Dominant Members of the Human Gut Microbiome** {abstract & UW comment} {full article}
    - Description of the 3D atomic structure of the SusCD protein complex involved in bacterial nutrient uptake in the gut.

3. **Prior Dietary Practices and Connections to a Human Gut Microbial Metacommunity Alter Responses to Diet Interventions** {abstract & UW comment} {full article}
    - A mouse-model study demonstrating the influence of intestinal microbiome on nutritional interventions.

4. **Mechanisms of Cross-talk between the Diet, the Intestinal Microbiome, and the Undernourished Host** {abstract & UW comment} {full article}
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5. **Sufficient Protein Quality of Food Aid Varies with the Physiologic Status of Recipients** {abstract & UW comment} {full article}
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6. **Diet-Microbiome Interactions in Health Are Controlled by Intestinal Nitrogen Source Constraints** {abstract & UW comment} {full article}
    - A model of microbial use of nutrients at the community level predicts carbohydrate resources use is coupled tightly with nitrogen availability.

7. **Growth and Morbidity of Gambian Infants are Influenced by Maternal Milk Oligosaccharides and Infant Gut Microbiota** {abstract & UW comment} {full article}
    - A sub-study embedded in the Early Nutrition and Development Trial to determine whether specific types and structures of HMOs are sensitive to environmental conditions and associated with specific microbiota.

8. **Human Milk Oligosaccharides Influence Intestinal Epithelial Cell Maturation In Vitro** {abstract & UW comment} {full article}
    - A cell culture study of the effect of three human milk oligosaccharides on intestinal epithelial cell differentiation.

9. **Use of Antibiotics in Children Younger than Two Years in Eight Countries: a Prospective Cohort Study** {abstract & UW comment} {full article}
    - A study of frequency and factors associated with antibiotic use in early childhood as part of the MAL-ED study in eight countries.

10. **Environmental Enteric Dysfunction is Associated with Carnitine Deficiency and Altered Fatty Acid Oxidation**. {abstract & UW comment} {full article}
    - A cross-sectional study assessing biomarkers associated with gut permeability.

DETAILS OF ARTICLES

1. Systematic Characterization and Analysis of the Taxonomic Drivers of Functional Shifts in the Human Microbiome

Ohad Manor and Elhanan Borenstein.
Cell Host & Microbe. In Press, Corrected Proof, Epub: 19 January 2017.

ABSTRACT
Comparative analyses of the human microbiome have identified both taxonomic and functional shifts that are associated with numerous diseases. To date, however, microbiome taxonomy and function have mostly been studied independently and the taxonomic drivers of functional imbalances have not been systematically identified. Here, we present FishTaco, an analytical and computational framework that integrates taxonomic and functional comparative analyses to accurately quantify taxon-level contributions to disease-associated functional shifts. Applying FishTaco to several large-scale metagenomic cohorts, we show that shifts in the microbiome's functional capacity can be traced back to specific taxa. Furthermore, the set of taxa driving functional shifts and their contribution levels vary markedly between functions. We additionally find that similar functional imbalances in different diseases are driven by both disease-specific and shared taxa. Such integrated analysis of microbiome ecological and functional dynamics can inform future microbiome-based therapy, pinpointing putative intervention targets for manipulating the microbiome's functional capacity.

WEB: 10.1016/j.chom.2016.12.014
IMPACT FACTOR: 12.552
CITED HALF-LIFE: 4.0

UW EDITORIAL COMMENT: The authors demonstrate a novel computational framework that links the impact of individual taxa to disease-associated functional imbalances by decomposing each functional shift in in a microbial community down to the responsible taxon-level changes. Note that their analysis includes several assumptions: assumes each species has the same genomic content across samples (ignores strain-level variation) and assumes that removing a single species from the community leaves composition of other species intact (no ecological repercussions). This second assumption will likely be problematic for accurate predictions and thus additional research will be needed to better incorporate information about microbial interactions and ecological dynamics into the model.

2. Structural Basis for Nutrient Acquisition by Dominant Members of the Human Gut Microbiome.

Glenwright AJ, Pothula KR, Bhamidimarri SP, Chorev DS, Baslé A, Firbank SJ, Zheng H, Robinson CV, Winterhalter M, Kleinekathöfer U, Bolam DN, van den Berg B.

Nature. 2017 Jan 19;541(7637):407-411. PMID: 28077872. Epub 2017 Jan 11.

ABSTRACT
The human large intestine is populated by a high density of microorganisms, collectively termed the colonic microbiota, which has an important role in human health and nutrition. The survival of microbiota members from the dominant Gram-negative phylum Bacteroidetes depends on their ability to degrade dietary glycans that cannot be metabolized by the host. The genes encoding proteins involved in the degradation of specific glycans are organized into co-regulated polysaccharide utilization loci, with the archetypal locus sus (for starch utilisation system) encoding seven proteins, SusA-SusG. Glycan degradation mainly occurs intracellularly and depends on the import of oligosaccharides by an outer membrane protein complex composed of an extracellular SusD-like lipoprotein and an integral membrane SusC-like TonB-dependent transporter. The presence of the partner SusD-like lipoprotein is the major feature that distinguishes SusC-like proteins from previously characterized TonB-dependent transporters. Many sequenced gut Bacteroides spp. encode over 100 SusCD pairs, of which the majority have unknown functions and substrate specificities. The mechanism by which extracellular substrate binding by SusD proteins is coupled to outer membrane passage through their cognate SusC transporter is unknown. Here we present X-ray crystal structures of two functionally distinct SusCD complexes purified from Bacteroides thetaiotaomicron and derive a general model for substrate translocation. The SusC transporters form homodimers, with each β-barrel protomer tightly capped by SusD. Ligands are bound at the SusC-SusD interface in a large solvent-excluded cavity. Molecular dynamics simulations and single-channel electrophysiology reveal a 'pedal bin' mechanism, in which SusD moves away from SusC in a hinge-like fashion in the absence of ligand to expose the substrate-binding site to the extracellular milieu. These data provide mechanistic insights into outer membrane nutrient import by members of the microbiota, an area of major importance for understanding human-microbiota symbiosis.

WEB: 10.1038/nature20828
IMPACT FACTOR: 38.138
CITED HALF-LIFE: >10.0

UW EDITORIAL COMMENT: Researchers report they have purified and determined the first 3D atomic structure of the SusCD complex, which is the protein structure embedded in the bacterial cell envelope that takes up nutrients from the environment. Figure 1 provides illustrations of the overall structure of SusCD complexes. Unbiased molecular dynamics simulations were also performed, in the presence and absence of a modeled peptide, and some variations in the peptide conformations were observed. The authors attribute this inconsistency to the peptide chosen for the simulation (perhaps not stable in the binding site), which suggests the system is at least somewhat sequence-specific.

3. Prior Dietary Practices and Connections to a Human Gut Microbial Metacommunity Alter Responses to Diet Interventions

Nicholas W. Griffin, Philip P. Ahern, Jiye Cheng, Andrew C. Heath, Olga Ilkayeva, Christopher B. Newgard, Luigi Fontana, Jeffrey I. Gordon
Cell Host & Microbe. Volume 21, Issue 1, 11 January 2017, Pages 84–96.

ABSTRACT
Ensuring that gut microbiota respond consistently to prescribed dietary interventions, irrespective of prior dietary practices (DPs), is critical for effective nutritional therapy. To address this, we identified DP-associated gut bacterial taxa in individuals either practicing chronic calorie restriction with adequate nutrition (CRON) or without dietary restrictions (AMER). When transplanted into gnotobiotic mice,

AMER and CRON microbiota responded predictably to CRON and AMER diets but with variable response strengths. An individual's microbiota is connected to other individuals' communities ("metacommunity") by microbial exchange. Sequentially cohousing AMER-colonized mice with two different groups of CRON-colonized mice simulated metacommunity effects, resulting in enhanced responses to a CRON diet intervention and changes in several metabolic features in AMER animals. This response was driven by an influx of CRON DP-associated taxa. Certain DPs may impair responses to dietary interventions, necessitating the introduction of diet-responsive bacterial lineages present in other individuals and identified using the strategies described.

WEB: 10.1016/j.chom.2016.12.006
IMPACT FACTOR: 12.552
CITED HALF-LIFE: 4.0

UW EDITORIAL COMMENT: Echoing the findings of Thaiss et al. (2016), which were reported in the December digest, the authors report persistent changes in intestinal microbiota based on dietary practices. Taken together, the two studies provide significant evidence that dietary composition is a primary determinant of microbiota community structure. This study also suggests a hygiene-related mechanism for the development of metabolic diseases. The authors created several co-housing scenarios to intermix mice with varied microbiota and found that the exchange (in this case, mouse-to-mouse) of diet-responsive microbiota provided improved community-level diversity that may be relevant to understanding microbiome ecosystem dynamics.

4. Mechanisms of Cross-talk between the Diet, the Intestinal Microbiome, and the Undernourished Host

Velly H, Britton RA, Preidis GA.
Gut Microbes. 2016 Dec 5:1-15. Epub ahead of print. PMID: 27918230

ABSTRACT
Undernutrition remains one of the most pressing global health challenges today, contributing to nearly half of all deaths in children under five years of age. Although insufficient dietary intake and environmental enteric dysfunction are often inciting factors, evidence now suggests that unhealthy gut microbial populations perpetuate the vicious cycle of pathophysiology that results in persistent growth impairment in children. The metagenomics era has facilitated new research identifying an altered microbiome in undernourished hosts and has provided insight into a number of mechanisms by which these alterations may affect growth. This article summarizes a range of observational studies that highlight differences in the composition and function of gut microbiota between undernourished and healthy children; discusses dietary, environmental and host factors that shape this altered microbiome; examines the consequences of these changes on host physiology; and considers opportunities for microbiome-targeting therapies to combat the global challenge of child undernutrition.

WEB: 10.1080/19490976.2016.1267888
IMPACT FACTOR: 4.16
CITED HALF-LIFE: N/A

UW EDITORIAL COMMENT: Authors synthesize findings from several observational studies of the association between environmental enteric dysfunction, gut microbiota, and undernutrition. The authors note some research gaps, including the need for statistical techniques to handle the complex study designs and multi-dimensional longitudinal data sets collected from multiple subjects in a shared

household. The authors also note that despite convincing microbiome dysbiosis research, microbiome-targeting therapies have thus far demonstrated limited efficacy for EED. Mouse model research has suggested some success with probiotics, but the current lack of clinical evidence supporting their efficacy in humans remains a significant barrier.

5. Sufficient Protein Quality of Food Aid Varies with the Physiologic Status of Recipients.
Callaghan M, Oyama M, Manary M
Journal of Nutrition. 2017 Jan 18. pii: jn239665.

ABSTRACT
Protein quality scores use the amino acid (AA) requirements of a healthy North American child. AA requirements vary with physiologic status. We estimated AA requirements for healthy North American children, children with environmental enteric dysfunction, children recovering from wasting, and children with an acute infection. The protein quality of food aid products was then calculated to determine whether it was sufficient in all these groups, and we found that it may not be adequate for all of them. Physiologic status is important when assessing the protein quality of food aid. Rates of weight gain from 8 published trials treating children with moderate acute malnutrition were abstracted, and protein quality scores from the corresponding food aid products were calculated with the use of the digestible indispensable amino acid score (DIAAS). Two DIAAS values were calculated, one in healthy children aged 1-3 y as a reference population and the other in malnourished children aged 1-3 y as a reference population. These data were used to calculate the best fit regression line between weight gain and protein quality. The slope of the regression line was greater when malnourished children were used as a reference population than when healthy children were used (0.128; 95% CI: 0.118, 0.138 compared with 0.097; 95% CI: 0.090, 0.105 measured in $g \cdot kg^{-1} \cdot d^{-1} \cdot DIASS\ U^{-1}$). These findings suggest that adjusting AA requirements for physiologic status may more accurately estimate the minimum protein quality of food aid products.

WEB: 10.3945/jn.116.239665
IMPACT FACTOR: 3.265
CITED HALF-LIFE: 4.2

UW EDITORIAL COMMENT: The authors assert that standard methods of assessing protein quality do not adequately account for differences in consumer physiology, which may affect the determination of amino acid requirements used to assess the quality of food aid products. Table 1 illustrates the differential relationship between protein quality and rates of weight gain from studies of malnourished children compared to healthy children.

6. Diet-Microbiome Interactions in Health Are Controlled by Intestinal Nitrogen Source Constraints
Holmes AJ, Chew YV, Colakoglu F, Cliff JB, Klaassens E, Read MN, Solon-Biet SM, McMahon AC, Cogger VC, Ruohonen K, Raubenheimer D, Le Couteur DG, Simpson SJ.
Cell Metab. 2017 Jan 10;25(1):140-151. doi: 10.1016/j.cmet.2016.10.021. Epub 2016 Nov 23.

ABSTRACT
Diet influences health and patterns of disease in populations. How different diets do this and why outcomes of diets vary between individuals are complex and involve interaction with the gut microbiome. A major challenge for predicting health outcomes of the host-microbiome dynamic is reconciling the effects of different aspects of diet (food composition or intake rate) on the system. Here

we show that microbial community assembly is fundamentally shaped by a dichotomy in bacterial strategies to access nitrogen in the gut environment. Consequently, the pattern of dietary protein intake constrains the host-microbiome dynamic in ways that are common to a very broad range of diet manipulation strategies. These insights offer a mechanism for the impact of high protein intake on metabolic health and form the basis for a general theory of the impact of different diet strategies on host-microbiome outcomes.

WEB: 10.1016/j.cmet.2016.10.021
IMPACT FACTOR: 17.303
CITED HALF-LIFE: 4.6

UW EDITORIAL COMMENT:
The authors model microbial use of nutrients at the community level, predicting that the use of carbohydrate resources is coupled tightly with nitrogen availability. They also predict that this form of nitrogen regulation may play a role in the pathology of diseases that are associated with altered rates of nitrogen elimination through the intestine.

7. Growth and Morbidity of Gambian Infants are Influenced by Maternal Milk Oligosaccharides and Infant Gut Microbiota.

Davis JC, Lewis ZT, Krishnan S, Bernstein RM, Moore SE, Prentice AM, Mills DA, Lebrilla CB, Zivkovic AM.
Sci Rep. 2017 Jan 12;7:40466. PMID: 28079170

ABSTRACT
Human milk oligosaccharides (HMOs) play an important role in the health of an infant as substrate for beneficial gut bacteria. Little is known about the effects of HMO composition and its changes on the morbidity and growth outcomes of infants living in areas with high infection rates. Mother's HMO composition and infant gut microbiota from 33 Gambian mother/infant pairs at 4, 16, and 20 weeks postpartum were analyzed for relationships between HMOs, microbiota, and infant morbidity and growth. The data indicate that lacto-N-fucopentaose I was associated with decreased infant morbidity, and 3'-sialyllactose was found to be a good indicator of infant weight-for-age. Because HMOs, gut microbiota, and infant health are interrelated, the relationship between infant health and their microbiome were analyzed. While bifidobacteria were the dominant genus in the infant gut overall, Dialister and Prevotella were negatively correlated with morbidity, and Bacteroides was increased in infants with abnormal calprotectin. Mothers nursing in the wet season (July to October) produced significantly less oligosaccharides compared to those nursing in the dry season (November to June). These results suggest that specific types and structures of HMOs are sensitive to environmental conditions, protective of morbidity, predictive of growth, and correlated with specific microbiota.

WEB: 10.1038/srep40466
IMPACT FACTOR: 5.228
CITED HALF-LIFE: 2.1

UW EDITORIAL COMMENT: The findings of this study should be interpreted with caution as the associations observed are highly context dependent. The samples analyzed for this study were conducted as a sub-study embedded in a randomized trial, The Early Nutrition and Immune Development trial. Milk consumption per infant was not measured per infant and all associations were extrapolated from measurements taken at three time points (4, 16, and 20 weeks postpartum). Mothers

self-reported observed incidents of illness for their infants, which were used as a proxy for health outcomes. Additionally, only 85 of 99 samples contained enough fecal matter for microbiota analyses, therefore this study is limited in its small sample size.

8. Human Milk Oligosaccharides Influence Intestinal Epithelial Cell Maturation In Vitro.
Holscher HD, Bode L, Tappenden KA
J Pediatr Gastroenterol Nutr. 2017 Feb;64(2):296-301. PMID: 28114245

ABSTRACT
OBJECTIVES: Human milk oligosaccharides (HMOs) are reported to promote epithelial cell differentiation in vitro. The aim of the present study was to assess induction of epithelial cell differentiation by individual and combined administration of 3 HMOs.

METHODS: An in vitro epithelial model of the crypt-villus axis consisting of preconfluent HT-29, preconfluent Caco-2Bbe, and postconfluent Caco-2Bbe cells was used. Cultures were randomized to 17 treatments for 72 hours of incubation: low- and high-dose HMOs (3'sialyllactose [3'SL] at 0.2 and 1.0 g/L, 6'siallylactose [6'SL] at 0.4 and 1.0 g/L, and 2'fucosyllactose at 0.2 and 2.0 g/L), HMO combinations at both low and high doses, and controls (culture medium, 4 g/L pooled HMO, and lipopolysaccharide).

RESULTS: High doses of individual HMOs ($P < 0.05$), combined HMOs ($P < 0.05$), and pooled HMO decreased ($P < 0.001$) proliferation in preconfluent HT-29 cultures. Pooled means of individual low and high treatments with 3'SL and 6'SL, combinations of 2 or 3 high-dose HMOs, and total HMO significantly reduced ($P < 0.05$) proliferation in preconfluent Caco-2Bbe cells. HMOs increased differentiation in preconfluent HT-29 and Caco-2Bbe cells. 3'SL and 6'SL increased alkaline phosphatase activity but did not affect disaccharidase activity in postconfluent Caco-2Bbe cells. Apoptosis and necrosis were both decreased ($P < 0.001$) in postconfluent Caco-2Bbe cells treated with pooled HMO.

CONCLUSIONS: HMO treatments inhibited proliferation with some associated enhancement of epithelial differentiation. Effects of HMOs were additive but no specific combinations of HMOs were especially potent. These results suggest that commercially viable individual HMOs and specific combinations may promote intestinal epithelial cell maturation.

WEB: 10.1097/MPG.0000000000001274
IMPACT FACTOR: 2.4
CITED HALF-LIFE: 7.0

UW EDITORIAL COMMENT: The authors use in vivo observations to assess specific effects of HMOs on intestinal cells at varying stages of differentiation, with a range of HMO concentrations (including a level typical of human milk). Cells were grown to form a monolayer with cylindrical polarized morphology, tight cellular junctions, and apical microvilli. Since the study was conducted on epithelial cells in a lab system, the cells lacked their usual microbes and influences of the gut microbiome.

9. Use of Antibiotics in Children Younger Than Two Years in Eight Countries: a Prospective Cohort Study
Elizabeth T Rogawski, James A Platts-Mills, Jessica C Seidman, Sushil John, Mustafa Mahfuz, Manjeswori Ulak, Sanjaya K Shrestha, Sajid Bashir Soofi, Pablo Penataro Yori, Estomih Mduma, Erling Svensen, Tahmeed Ahmed, Aldo AM Lima, Zulfiqar A Bhutta, Margaret N Kosek, Dennis R

Lang, Michael Gottlieb, Anita KM Zaidi, Gagandeep Kang, Pascal O Bessong, Eric R Houpt, and Richard L Guerrant
Bull World Health Organ. 2017 Jan 1; 95(1): 49–61

ABSTRACT
Objective: To describe the frequency and factors associated with antibiotic use in early childhood, and estimate the proportion of diarrhoea and respiratory illnesses episodes treated with antibiotics.

Methods: Between 2009 and 2014, we followed 2134 children from eight sites in Bangladesh, Brazil, India, Nepal, Pakistan, Peru, South Africa and the United Republic of Tanzania, enrolled in the MAL-ED birth cohort study. We documented all antibiotic use from mothers' reports at twice-weekly visits over the children's first two years of life. We estimated the incidence of antibiotic use and the associations of antibiotic use with child and household characteristics. We described treatment patterns for diarrhoea and respiratory illnesses, and identified factors associated with treatment and antibiotic class.

Findings: Over 1 346 388 total days of observation, 16 913 courses of antibiotics were recorded (an incidence of 4.9 courses per child per year), with the highest use in South Asia. Antibiotic treatment was given for 375/499 (75.2%) episodes of bloody diarrhoea and for 4274/9661 (44.2%) episodes of diarrhoea without bloody stools. Antibiotics were used in 2384/3943 (60.5%) episodes of fieldworker-confirmed acute lower respiratory tract illness as well as in 6608/16742 (39.5%) episodes of upper respiratory illness. Penicillins were used most frequently for respiratory illness, while antibiotic classes for diarrhoea treatment varied within and between sites.

Conclusion: Repeated antibiotic exposure was common early in life, and treatment of non-bloody diarrhoea and non-specific respiratory illnesses was not consistent with international recommendations. Rational antibiotic use programmes may have the most impact in South Asia, where antibiotic use was highest.

WEB: 10.2471/BLT.16.176123
IMPACT FACTOR: 5.302
CITED HALF-LIFE: N/A

UW EDITORIAL COMMENT: The authors found a higher percentage of concordance between mother-reported antibiotic use and medical care records. The study provides a detailed description of antibiotic use across eight low-resource country settings, but is limited by some missing details about specific antibiotic courses, prophylactic versus treatment use, source of antibiotics, and details about appropriateness of antibiotic treatment. Overall, evidence suggests antibiotic overuse for treatment of non-bloody diarrhea and upper respiratory tract illnesses, and underuse for treatment of bloody diarrhea and lower respiratory tract illness.

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

Richard D. Semba, Indi Trehan, Ximin Lic, Ruin Moaddel, M. Isabel Ordiz, Kenneth M. Maleta, Klaus Kraemer, Michelle Shardell, Luigi Ferrucci, Mark Manary
EBioMedicine. E publish: 18 January 2017

ABSTRACT

Background: Environmental enteric dysfunction (EED), a condition characterized by small intestine inflammation and abnormal gut permeability, is widespread in children in developing countries and a major cause of growth failure. The pathophysiology of EED remains poorly understood.

Methods: We measured serum metabolites using liquid chromatography-tandem mass spectrometry in 400 children, aged 12–59 months, from rural Malawi. Gut permeability was assessed by the dual-sugar absorption test.

Findings: 80.7% of children had EED. Of 677 serum metabolites measured, 21 were negatively associated and 56 were positively associated with gut permeability, using a false discovery rate approach ($q < 0.05$, $p < 0.0095$). Increased gut permeability was associated with elevated acylcarnitines, deoxycarnitine, fatty acid β-oxidation intermediates, fatty acid ω-oxidation products, odd-chain fatty acids, trimethylamine-N-oxide, cystathionine, and homocitrulline, and with lower citrulline, ornithine, polyphenol metabolites, hippurate, tryptophan, and indolelactate.

Interpretation: EED is a syndrome characterized by secondary carnitine deficiency, abnormal fatty acid oxidation, alterations in polyphenol and amino acid metabolites, and metabolic dysregulation of sulfur amino acids, tryptophan, and the urea cycle. Future studies are needed to corroborate the presence of secondary carnitine deficiency among children with EED and to understand how these metabolic derangements may negatively affect the growth and development of young children.

WEB: 10.1016/j.ebiom.2017.01.026
IMPACT FACTOR: 1.37
CITED HALF-LIFE:

UW EDITORIAL COMMENT: The authors used a cross-sectional study design to assess biomarkers associated with gut permeability, meaning that the identified metabolites cannot be determined as causally linked to EED. The narrow geographical location of source population also reduces the generalizability of the metabolic abnormalities described due to differences in diet, environment, and other factors.

ADDITIONAL ARTICLES OF INTEREST (JANUARY PUBLICATIONS)

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

Discovery of Reactive Microbiota-Derived Metabolites that Inhibit Host Proteases

A microbial protein that alleviates metabolic syndrome

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

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

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.

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

ARTICLE ARCHIVE (JAN-DEC 2016)

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

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

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

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

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