



START CENTER
STRATEGIC ANALYSIS,
RESEARCH & TRAINING CENTER

GUT HEALTH DIGEST

UNIVERSITY OF WASHINGTON STRATEGIC ANALYSIS, RESEARCH & TRAINING (START) CENTER

REPORT TO THE BILL & MELINDA GATES FOUNDATION

DECEMBER 1, 2016

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- 1. 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** [{abstract & UW comment}](#) [{full article}](#)
Therapeutics
 - A randomized double-blind placebo-controlled study testing the effect of a combined intervention (zinc, albendazole, and micronutrients) on EED and linear growth among children (12-35 months) in rural Malawi.
- 2. Effects of a gut pathobiont in a gnotobiotic mouse model of childhood undernutrition** [{abstract & UW comment}](#) [{full article}](#)
Gut Microbiome/Nutrition/Model Organism
 - A study using gnotobiotic mice with gut microbiomes colonized by fecal microbiota of either a healthy or stunted 24-month-old Bangladeshi child.
- 3. Dysbiosis is not an answer.** [{abstract & UW comment}](#) [{full article}](#)
Microbiome
 - Authors discuss how the idea of balance in the microbiome (i.e. dysbiosis leads to disease) may be a misguided organizing concept for microbiome research.
- 4. A Dietary Fiber-Deprived Gut Microbiota Degrades the Colonic Mucus Barrier and Enhances Pathogen Susceptibility.** [{abstract & UW comment}](#) [{full article}](#)
Gut Microbiome/Infection
 - A study using gnotobiotic mice and synthetic microbiome communities to investigate whether specific species within a fiber-derived gut microbiota cause damage by increasingly foraging for nutrition in the epithelial mucous layer.
- 5. Enterocyte Purge and Rapid Recovery Is a Resilience Reaction of the Gut Epithelium to Pore-Forming Toxin Attack** [{abstract & UW comment}](#) [{full article}](#)
Basic Science/Inflammation
 - A study of *Drosophila* enterocytes exposed to bacterial pore-forming toxins extrude much of their apical cytoplasm, purging themselves of damaged components and bacteria.
- 6. Linking the Human Gut Microbiome to Inflammatory Cytokine Production Capacity** [{abstract & UW comment}](#) [{full article}](#)
Gut Microbiome/Inflammation
 - A cross-sectional study that investigated the role of the gut microbiome in explaining inter-individual variation in stimulus-induced cytokine response in healthy humans
- 7. Epidemiology and Impact of *Campylobacter* Infection in Children in 8 Low-Resource Settings: Results From the MAL-ED Study** [{abstract & UW comment}](#) [{full article}](#)
Infection
 - A multi-site birth cohort study of 2145 children followed for 24 months to assess the associations between *Campylobacter* infection and linear growth, intestinal permeability, and local and systemic inflammation.



8. The microbiota and immune response during *Clostridium difficile* infection [{abstract & UW comment}](#) [{full article}](#)

Gut Microbiome /Infection/Inflammation

- A review that outlines how the gut microbiome prevents host susceptibility to *Clostridium difficile* infection and how it can modulate specific immune mediators (e.g. IL-23 and IL-17A) to influence disease outcome.

9. Shifts in *Lachnospira* and *Clostridium* sp. in the 3-month stool microbiome are associated with preschool age asthma [{abstract & UW comment}](#) [{full article}](#)

Gut Microbiome

- This study used a novel method to quantify taxon-specific intestinal dysbiosis by assessing bacterial shifts as a ratio of *Lachnospira* and *C. neonatale*.

10. Culture of previously uncultured members of the human gut microbiota by culturomics [{abstract & UW comment}](#) [{full article}](#)

Basic Science Microbiome

- Research using microbial culturomics to identify 531 species in the human gut repertoire.



DETAILS OF ARTICLES

1. [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](#)

Wang AZ, Shulman RJ, Crocker AH, Thakwalakwa C, Maleta KM, Devaraj S, Manary MJ, Trehan I.
The Journal of Nutrition. 2016 Nov 2. pii: jn237735
PMID: 27807040

ABSTRACT

BACKGROUND: Environmental enteric dysfunction (EED) and linear growth stunting affect many rural agrarian children in the developing world and contribute to the persistently high rates of stunting that are observed worldwide. Effective interventions to consistently ameliorate EED are lacking.

OBJECTIVE: We tested whether a bundle of safe and affordable interventions would decrease EED and stunting over 12-24 wk in a cohort of rural Malawian children 12-35 mo old.

METHODS: This was a randomized, double-blind, placebo-controlled clinical trial in which the intervention group received a single dose of albendazole and 14 d of zinc at enrollment and after 20 wk. The intervention group also received a daily multiple micronutrient powder throughout the 24 wk of study. The primary outcomes were improvements in EED, as measured by the urinary lactulose-to-mannitol ratio (L:M ratio) from dual-sugar absorption testing, and linear growth. Urinary L:M ratios and anthropometric measurements were evaluated after 12 and 24 wk of intervention and compared with a placebo group that did not receive any of these interventions.

RESULTS: A total of 254 children were enrolled at a mean age of 24 mo; 55% were female. Their mean weight-for-age z score was -1.5, and their mean length-for-age z score was -0.9. After 12 and 24 wk of study, increases in the L:M ratio did not differ between the intervention group (0.071 and 0.088 units, respectively) and the placebo group (0.073 and 0.080 units, respectively) ($P = 0.87$ and 0.19 , respectively). Relative changes in length and weight also did not differ significantly between groups at any time point.

CONCLUSION: The combined usage of albendazole, zinc, and a daily multiple micronutrient powder did not decrease EED or stunting in this population of agrarian children 12-35 mo old in rural Malawi. Alternative interventions to improve these diseases should be investigated. This trial was registered at clinicaltrials.gov as [NCT02253095](#).

WEB: [10.3945/jn.116.237735](#)

IMPACT FACTOR: 3.74

CITED HALF-LIFE: >10.0

UW EDITORIAL COMMENT: This was a follow up study to previous work by the authors that found a modest amelioration of EED in rural Malawi children upon administration of zinc, albendazole, and multiple micronutrient separately. In this follow up study, the authors hypothesized that combining these three interventions would be even more efficacious against EED and stunting in a similar population of children. However as can be seen in Table 3, the authors did not find any statistically significant difference in the L:M ratio or linear growth measures between children in the intervention and control arms. Potential limitations of the study include the short length of follow up (about 24 weeks) and the high baseline intake of zinc, iron, and other nutrients in the study population. These limitations may have affected the ability of the study to detect a positive effect of the combined interventions.



2. [Effects of a gut pathobiont in a gnotobiotic mouse model of childhood undernutrition](#)
Wagner VE, Dey N, Guruge J, Hsiao A, Ahern PP, Semenkovich NP, Blanton LV, Cheng J, Griffin N, Stappenbeck TS, Ilkayeva O, Newgard CB, Petri W, Haque R, Ahmed T, Gordon JI
Science Translational Medicine. 2016 Nov;8(366):366ra164.
PMID: 27881825

ABSTRACT

To model how interactions among enteropathogens and gut microbial community members contribute to undernutrition, we colonized gnotobiotic mice fed representative Bangladeshi diets with sequenced bacterial strains cultured from the fecal microbiota of two 24-month-old Bangladeshi children: one healthy and the other underweight. The undernourished donor's bacterial collection contained an enterotoxigenic *Bacteroides fragilis* strain (ETBF), whereas the healthy donor's bacterial collection contained two nontoxigenic strains of *B. fragilis* (NTBF). Analyses of mice harboring either the unmanipulated culture collections or systematically manipulated versions revealed that ETBF was causally related to weight loss in the context of its native community but not when introduced into the healthy donor's community. This phenotype was transmissible from the dams to their offspring and was associated with derangements in host energy metabolism manifested by impaired tricarboxylic acid cycle activity and decreased acyl-coenzyme A utilization. NTBF reduced ETBF's expression of its enterotoxin and mitigated the effects of ETBF on the transcriptomes of other healthy donor community members. These results illustrate how intraspecific (ETBF-NTBF) and interspecific interactions influence the effects of harboring *B. fragilis*.

WEB: [10.1126/scitranslmed.aah4669](https://doi.org/10.1126/scitranslmed.aah4669)

IMPACT FACTOR: 16.26

CITED HALF-LIFE: 3.2

UW EDITORIAL COMMENT: Researchers used gnotobiotic mice to model the effect of diet-influenced microbiome composition on enteric bacterial infections. Figure 1 illustrates the species composition of the healthy and stunted microbiomes being studied, as well as the weight loss associated with infection per the healthy and stunted donor microbiomes, across different diets. Figure 4 shows that host metabolic abnormalities are associated with the stunted donor's community, which could inform therapeutic targets. The generalizability of these research findings is limited since the "healthy" and "stunted" microbiomes were harvested from two individual donors sourced from a small cohort. Additional microbiomes from other donors could be constructed in gnotobiotic mice to extend the applicability of the findings.

3. [Dysbiosis is not an answer](#)
Olesen SW and Alm EJ.
Nature Microbiology. 25 Nov 2016: Vol 1, Issue 363, pp. 363ec177
PMID: 27886190

ABSTRACT

Dysbiosis, an imbalance in the microbiota, has been a major organizing concept in microbiome science. Here, we discuss how the balance concept, a holdover from prescientific thought, is irrelevant to — and may even distract from — useful microbiome research.

WEB: [10.1038/nmicrobiol.2016.228](https://doi.org/10.1038/nmicrobiol.2016.228)

IMPACT FACTOR: n/a



CITED HALF-LIFE: n/a

UW EDITORIAL COMMENT: In this commentary, the authors argue that microbiome research needs to move beyond studies observing healthy and ill people as having different microbiomes because identifying “dysbiosis” in sick individuals may simply refer to the result of the disease rather than the cause. The authors also criticize the broad definitions of dysbiosis used in current literature because ambiguity in definition suggests that any measured difference in microbial composition is dysbiosis, regardless of whether it is the cause or effect of disease. Microbiome data may remain valuable for differential diagnoses of diseases with related symptoms and for informing what beneficial microorganism might be useful to improve host health, since therapeutics require causality but not full mechanistic understanding. Negative results about diagnostics or therapeutics in microbiome research are more useful than a positive result that just asserts dysbiosis.

4. [A Dietary Fiber-Deprived Gut Microbiota Degrades the Colonic Mucus Barrier and Enhances Pathogen Susceptibility](#)

Desai MS, Seekatz AM, Koropatkin NM, Kamada N, Hickey CA, Wolter M, Pudlo NA, Kitamoto S, Terrapon N, Muller A, Young VB, Henrissat B, Wilmes P, Stappenbeck TS, Núñez G, Martens EC.

Cell. 2016 Nov 17;167(5):1339-1353.e21

PMID: 27863247

ABSTRACT

Despite the accepted health benefits of consuming dietary fiber, little is known about the mechanisms by which fiber deprivation impacts the gut microbiota and alters disease risk. Using a gnotobiotic mouse model, in which animals were colonized with a synthetic human gut microbiota composed of fully sequenced commensal bacteria, we elucidated the functional interactions between dietary fiber, the gut microbiota, and the colonic mucus barrier, which serves as a primary defense against enteric pathogens. We show that during chronic or intermittent dietary fiber deficiency, the gut microbiota resorts to host-secreted mucus glycoproteins as a nutrient source, leading to erosion of the colonic mucus barrier. Dietary fiber deprivation, together with a fiber-deprived, mucus-eroding microbiota, promotes greater epithelial access and lethal colitis by the mucosal pathogen, *Citrobacter rodentium*. Our work reveals intricate pathways linking diet, the gut microbiome, and intestinal barrier dysfunction, which could be exploited to improve health using dietary therapeutics.

WEB: [10.1016/j.cell.2016.10.043](https://doi.org/10.1016/j.cell.2016.10.043)

IMPACT FACTOR: 28.7

CITED HALF-LIFE: 9.0

UW EDITORIAL COMMENT: To investigate whether specific species within a fiber-derived gut microbiota cause damage by increasingly foraging for nutrition in the protective mucous layer, researchers designed a synthetic microbiota for a gnotobiotic mouse model containing 14 species of commensal human gut bacteria, representative of five dominant phyla and possessing core metabolic capabilities of natural human microbiota. After stabilizing the synthetic microbiota with a standard fiber diet, the mice were fed one of three diets: fiber-rich, fiber-free, or prebiotic. Additional mice were fed diets that alternated between these diets to imitate the human diet, which may experience fluctuations in fiber from meal to meal. The prebiotic diet included a mixture of soluble glycans like those used in prebiotic formulations. Both chronic and intermittent fiber deficiency led to higher proportions of mucus-degrading bacteria. Colonic mucus measurements also revealed mucus thickness to be highest in the mice fed fiber rich



diets and transcriptomics revealed high activity of proteins that promote mucosal repair and defense in mice on fiber free diet, indicating a host response to mucus degradation. To confirm the link between a fiber-deprived gut with thinning mucus layers and increased pathogen susceptibility, authors infected the mice with *Citrobacter rodentium* and analyzed fecal samples for colonization. Fiber-free diet mice experienced higher pathogen burden, increased rates of weight loss, and significantly greater inflammation of colonic tissues.

5. [Enterocyte Purge and Rapid Recovery Is a Resilience Reaction of the Gut Epithelium to Pore-Forming Toxin Attack](#)

Lee KZ, Lestradet M, Socha C, Schirmeier S, Schmitz A, Spenlé C, Lefebvre O, Keime C, Yamba WM, Bou Aoun R, Liegeois S, Schwab Y, Simon-Assmann P, Dalle F, Ferrandon D.

Cell Host & Microbe. 2016 Nov; In Press.

PMID: 27889464

ABSTRACT

Besides digesting nutrients, the gut protects the host against invasion by pathogens. Enterocytes may be subjected to damage by both microbial and host defensive responses, causing their death. Here, we report a rapid epithelial response that alleviates infection stress and protects the enterocytes from the action of microbial virulence factors. Intestinal epithelia exposed to hemolysin, a pore-forming toxin secreted by *Serratia marcescens*, undergo an evolutionarily conserved process of thinning followed by the recovery of their initial thickness within a few hours. In response to hemolysin attack, *Drosophila melanogaster* enterocytes extrude most of their apical cytoplasm, including damaged organelles such as mitochondria, yet do not lyse. We identify two secreted peptides, the expression of which requires CyclinJ, that mediate the recovery phase in which enterocytes regain their original shape and volume. Epithelial thinning and recovery constitute a fast and efficient response to intestinal infections, with pore-forming toxins acting as alarm signals.

WEB: [10.1016/j.chom.2016.10.010](http://dx.doi.org/10.1016/j.chom.2016.10.010)

IMPACT FACTOR: 12.55

CITED HALF-LIFE: 4.0

UW EDITORIAL COMMENT: The authors describe a resilience mechanism in the *Drosophila* intestinal epithelium that protects against a pathogen invasion via a temporary thinning of the epithelium to alleviate the infectious stress on enterocytes. The authors conducted kinetic analysis of gut morphology after infection and observed epithelium thinning within three hours of infection, partial recovery within the next six hours, and full restoration of epithelium thickness by 24 hours. Thinning occurs as the result of pore formation and does not involve enhanced cell death or affect permeability of the digestive tract. Instead it appears to be due to cytoplasmic extrusion. Greater detail regarding the structural biology is provided in the article. While much of the research described in the article was conducted in a *Drosophila*, thinning and recovery of epithelium was also observed in insects (honeybees) and mammals (human epithelial Caco-2 cells, *in vitro*).

6. [Linking the Human Gut Microbiome to Inflammatory Cytokine Production Capacity](#)

Schirmer M, Smeekens SP, Vlamakis H, Jaeger M, Oosting M, Franzosa EA, Jansen T, Jacobs L, Bonder MJ, Kuriilshikov A, Fu J, Joosten LA, Zhernakova A, Huttenhower C, Wijmenga C, Netea MG, Xavier RJ.

Cell. 2016 Nov 3;167(4):1125-1136.e8

PMID: 27814509



ABSTRACT

Gut microbial dysbioses are linked to aberrant immune responses, which are often accompanied by abnormal production of inflammatory cytokines. As part of the Human Functional Genomics Project (HFGP), we investigate how differences in composition and function of gut microbial communities may contribute to inter-individual variation in cytokine responses to microbial stimulations in healthy humans. We observe microbiome-cytokine interaction patterns that are stimulus specific, cytokine specific, and cytokine and stimulus specific. Validation of two predicted host-microbial interactions reveal that TNF α and IFN γ production are associated with specific microbial metabolic pathways: palmitoleic acid metabolism and tryptophan degradation to tryptophol. Besides providing a resource of predicted microbially derived mediators that influence immune phenotypes in response to common microorganisms, these data can help to define principles for understanding disease susceptibility. The three HFGP studies presented in this issue lay the groundwork for further studies aimed at understanding the interplay between microbial, genetic, and environmental factors in the regulation of the immune response in humans.

WEB: [10.1016/j.cell.2016.10.020](https://doi.org/10.1016/j.cell.2016.10.020)

IMPACT FACTOR: 28.7

CITED HALF-LIFE: 9.0

UW EDITORIAL COMMENT: This was one of three studies from the Human Functional Genomics Project (HFGP) group that investigated how genetic, environmental, and microbiome-related factors may affect cytokine response profiles upon induction by various microbial antigens. This study explored the gut microbiome-stimulus-induced cytokine response association, and showed that the gut microbiome and its associated metabolites may explain some of the inter-individual variation in cytokine production observed in response to various microbial stimulations. As shown in Figures 2 and 4, the study found that inter-individual variation in stimulus-induced cytokine response is linked to both specific microbial organisms and functions.

7. [Epidemiology and Impact of *Campylobacter* Infection in Children in 8 Low-Resource Settings: Results From the MAL-ED Study](#)

Amour C, Gratz J, Mduma E, Svensen E, Rogawski ET, McGrath M, Seidman JC, McCormick BJ, Shrestha S, Samie A, Mahfuz M, Qureshi S, Hotwani A, Babji S, Trigoso DR, Lima AA, Bodhidatta L, Bessong P, Ahmed T, Shakoor S, Kang G, Kosek M, Guerrant RL, Lang D, Gottlieb M, Houpt ER, Platts-Mills JA.

Clin Infect Dis. 2016 Nov 1;63(9):1171-1179

PMID: 27501842

ABSTRACT

BACKGROUND: Enteropathogen infections have been associated with enteric dysfunction and impaired growth in children in low-resource settings. In a multisite birth cohort study (MAL-ED), we describe the epidemiology and impact of *Campylobacter* infection in the first 2 years of life.

METHODS: Children were actively followed up until 24 months of age. Diarrheal and nondiarrheal stool samples were collected and tested by enzyme immunoassay for *Campylobacter*. Stool and blood samples were assayed for markers of intestinal permeability and inflammation.

RESULTS: A total of 1892 children had 7601 diarrheal and 26 267 nondiarrheal stool samples tested for *Campylobacter*. We describe a high prevalence of infection, with most children (n = 1606; 84.9%) having a *Campylobacter*-positive stool sample by 1 year of age. Factors associated with a reduced risk of *Campylobacter* detection included exclusive breastfeeding (risk ratio, 0.57; 95% confidence interval, .47-



.67), treatment of drinking water (0.76; 0.70-0.83), access to an improved latrine (0.89; 0.82-0.97), and recent macrolide antibiotic use (0.68; 0.63-0.74). A high *Campylobacter* burden was associated with a lower length-for-age Z score at 24 months (-1.82; 95% confidence interval, -1.94 to -1.70) compared with a low burden (-1.49; -1.60 to -1.38). This association was robust to confounders and consistent across sites. *Campylobacter* infection was also associated with increased intestinal permeability and intestinal and systemic inflammation.

CONCLUSIONS: *Campylobacter* was prevalent across diverse settings and associated with growth shortfalls. Promotion of exclusive breastfeeding, drinking water treatment, improved latrines, and targeted antibiotic treatment may reduce the burden of *Campylobacter* infection and improve growth in children in these settings.

WEB: [10.1093/cid/ciw542](https://doi.org/10.1093/cid/ciw542)

IMPACT FACTOR: 8.74

CITED HALF-LIFE: 7.4

UW EDITORIAL COMMENT: In this study, the authors followed a cohort of 2145 children for 24 months, collected stool and blood samples to determine *Campylobacter* infection, measured markers of EED and inflammation, and gathered anthropometric and covariate data to measure linear growth and potential confounders. As illustrated in the graphs in Figure 1, the prevalence of *Campylobacter* varied considerably across the 8 study sites. About 50% of the children had a *Campylobacter*-positive stool sample by six months of age. The risk factors for *Campylobacter* infection are summarized in Table 1 and Figure 2, with exclusive breastfeeding providing significant protection against *Campylobacter* infection. The authors found an inverse association between *Campylobacter* infection burden and linear growth (Figure 4). The authors also reported statistically significant associations between *Campylobacter* infection and intestinal permeability and local and systemic inflammation (Figure 5). In the discussion section, the authors state that asymptomatic infections with enteropathogens are strongly associated with linear growth shortfalls and that their team is working on a manuscript on this topic.

8. [The microbiota and immune response during *Clostridium difficile* infection](#)

Buonomo EL, Petri WA Jr.

Anaerobe. 2016 Oct;41:79-84 PMID: 27736783

PMID: 27212111

ABSTRACT

Clostridium difficile is a gram-positive, spore forming anaerobe that infects the gut when the normal microbiota has been disrupted. *C. difficile* infection (CDI) is the most common cause of hospital acquired infection in the United States, and the leading cause of death due to gastroenteritis. Patients suffering from CDI have varying symptoms which range from mild diarrhea to pseudomembranous colitis and death. The involvement of the immune response to influence disease severity is just beginning to be investigated. There is evidence that the immune response can facilitate either protective or pathogenic phenotypes, suggesting it plays a multifaceted role during CDI. In addition to the immune response, the microbiota is pivotal in dictating the pathogenesis to CDI. A healthy microbiota effectively inhibits infection by restricting the ability of *C. difficile* to expand in the colon. Thus, understanding which immune mediators and components of the microbiota play beneficial roles during CDI will be important to future therapeutic developments. This review outlines how the microbiota can modulate specific immune mediators, such as IL-23 and others, to influence disease outcome.

WEB: [10.1016/j.anaerobe.2016.05.009](https://doi.org/10.1016/j.anaerobe.2016.05.009)



IMPACT FACTOR: 2.42

CITED HALF-LIFE: 5.1

UW EDITORIAL COMMENT: The review begins with a summary of evidence showing that the gut microbiota plays an active role in preventing host susceptibility to *Clostridium difficile* infection (CDI) and in resolving the infection when it occurs. One mechanism of protection is through colonization resistance where the gut microbiome outcompetes *Clostridium difficile* for space and nutrients. This protection through colonization resistance was demonstrated in a series of experiments using hamster models. Another mechanism of protection by the gut microbiome is through regulating primary and secondary bile salts which are involved in *C. difficile* outgrowth. The authors discuss the use of fecal microbiota therapy as one mechanism through which restoring gut microbiome can resolve an active CDI. The authors then go on to discuss the dual role of the immune response in a CDI and how the gut microbiome can influence the immune response towards a protective one.

9. [Shifts in *Lachnospira* and *Clostridium* sp. in the 3-month stool microbiome are associated with preschool age asthma](#)

Stiemsma LT, Arrieta MC, Dimitriu PA, Cheng J, Thorson L, Lefebvre DL, Azad MB, Subbarao P, Mandhane P, Becker A, Sears MR, Kollmann TR; Canadian Healthy Infant Longitudinal Development (CHILD) Study Investigators, Mohn WW, Finlay BB, Turvey SE
Clin Sci (Lond). 2016 Dec 1;130(23):2199-2207
PMID: 27634868

ABSTRACT

Asthma is a chronic disease of the airways affecting one in ten children in Westernized countries. Recently, our group showed that specific bacterial genera in early life are associated with atopy and wheezing in 1-year-old children. However, little is known about the link between the early life gut microbiome and the diagnosis of asthma in preschool age children. To determine the role of the gut microbiota in preschool age asthma, children up to 4 years of age enrolled in the Canadian Healthy Infant Longitudinal Development (CHILD) study were classified as asthmatic (n=39) or matched healthy controls (n=37). 16S rRNA sequencing and quantitative PCR (qPCR) were used to analyse the composition of the 3-month and 1-year gut microbiome of these children. At 3 months the abundance of the genus, *Lachnospira* (L), was decreased (P=0.008), whereas the abundance of the species, *Clostridium neonatale* (C), was increased (P=0.07) in asthmatics. Quartile analysis of stool composition at 3-months revealed a negative association between the ratio of these two bacteria (L/C) and asthma risk by 4 years of age [quartile 1: odds ratio (OR)=15, P=0.02, CI (confidence interval)= 1.8-124.7; quartile 2: OR=1.0, ns; quartile 3: OR=0.37, ns]. We conclude that opposing shifts in the relative abundances of *Lachnospira* and *C. neonatale* in the first 3 months of life are associated with preschool age asthma, and that the L/C ratio may serve as a potential early life biomarker to predict asthma development.

WEB: [10.1042/CS20160349](https://doi.org/10.1042/CS20160349)

IMPACT FACTOR: 5.02

CITED HALF-LIFE: 9.3

UW EDITORIAL COMMENT: This study analyzed the global gut microbial community composition in stool samples taken from infants at 3 months and 1 year of age for comparison between children diagnosed with asthma and healthy controls. Figure 1 illustrates the relative abundance of bacterial species [in operational taxonomic units; OTUs] between asthmatics and healthy children. This study



used a novel method to quantify taxon-specific intestinal dysbiosis by assessing bacterial shifts as a ratio of *Lachnospira* and *C. neonatale*. Evidence of bacterial dysbiosis was indicated by a reduction in the abundance of *Lachnospira* and an increase in the species *C. neonatale*. Both species have been biologically linked to asthma and allergic disease in previous studies.

10. [Culture of previously uncultured members of the human gut microbiota by culturomics](#)

Lagier JC, Khelaifia S, Alou MT, Ndongo S, Dione N, Hugon P, Caputo A, Cadoret F, Traore SI, Seck EH, Dubourg G, Durand G, Mourembou G, Guilhot E, Togo A, Bellali S, Bachar D, Cassir N, Bittar F, Delerce J, Mailhe M, Ricaboni D, Bilen M, Dangui Niekou NP, Dia Badiane NM, Valles C, Mouelhi D, Diop K, Million M, Musso D, Abrahão J, Azhar EI, Bibi F, Yasir M, Diallo A, Sokhna C, Djossou F, Vitton V, Robert C, Rolain JM, La Scola B, Fournier PE, Levasseur A, Raoult D.

Nat Microbiol. 2016 Nov 7;1:16203.

PMID: 27819657

ABSTRACT

Metagenomics revolutionized the understanding of the relations among the human microbiome, health, and diseases, but generated a countless number of sequences that have not been assigned to a known microorganism¹. The pure culture of prokaryotes, neglected in recent decades, remains essential to elucidating the role of these organisms². We recently introduced microbial culturomics, a culturing approach that uses multiple culture conditions and matrix-assisted laser desorption/ionization-time of flight and 16S rRNA for identification². Here, we have selected the best culture conditions to increase the number of studied samples and have applied new protocols (fresh-sample inoculation; detection of microcolonies and specific cultures of Proteobacteria and microaerophilic and halophilic prokaryotes) to address the weaknesses of the previous studies³⁻⁵. We identified 1,057 prokaryotic species, thereby adding 531 species to the human gut repertoire: 146 bacteria known in humans but not in the gut, 187 bacteria and 1 archaea not previously isolated in humans, and 197 potentially new species. Genome sequencing was performed on the new species. By comparing the results of the metagenomic and culturomic analyses, we show that the use of culturomics allows the culture of organisms corresponding to sequences previously not assigned. Altogether, culturomics doubles the number of species isolated at least once from the human gut.

WEB: [10.1038/nmicrobiol.2016.203](http://dx.doi.org/10.1038/nmicrobiol.2016.203)

IMPACT FACTOR: n/a

CITED HALF-LIFE: n/a

UW EDITORIAL COMMENT: Researchers sought to identify gaps in metagenomics knowledge. Figure 3 shows a phylogenetic tree of 247 new prokaryote species isolated by culturomics, a method to isolate ideal culture conditions for species identification using metagenomics. Detailed methods are provided for collection of samples and describing the varied high-throughput culture conditions that enabled detection of bacterial diversity.



ADDITIONAL ARTICLES OF INTEREST (NOVEMBER PUBLICATIONS)

[Antibiotic-mediated gut microbiome perturbation accelerates development of type 1 diabetes in mice](#)

[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](#)

[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.](#)

[Tuft Cells: New Players in Colitis.](#)

[Commendation for Exposing Key Advantage of Organ Chip Approach](#)

ARTICLES ON RELEVANT TOPICS (OTHER JOURNALS, NOT SPECIFICALLY AUTHORS OF INTEREST)

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

[Biomarkers of Environmental Enteropathy are Positively Associated with Immune Responses to an Oral Cholera Vaccine in Bangladeshi Children](#)

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

[Modeling human enteric dysbiosis and rotavirus immunity in gnotobiotic pigs.](#)

[PGE2 is a direct and robust mediator of anion/fluid secretion by human intestinal epithelial cells](#)

[Steroid Administration and Growth Impairment in Children with Crohn's Disease.](#)

[Eosinophils, probiotics, and the microbiome.](#)

