

expression and neurons to show signs of impaired development. **DISCUSSION/SIGNIFICANCE OF IMPACT:** We expect that anemia has a differential impact on retinal vascular anatomy and neuronal function. While retinopathy severity may be improved, overall retinal function will be dampened. These findings and the mechanistic work of this study will generate targets for intervention to preserve improved retinopathy outcomes but rescue retinal function.

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### Gut-brain mechanisms of COVID-19 in wild type mice

Grant Talkington, Ismael Saifudeen and Gregory Jaye Bix  
Tulane University

**OBJECTIVES/GOALS:** SARS-CoV-2 infection has been shown to impact multiple organ systems, including the brain, and is associated with increased cognitive decline in vulnerable populations. The gut microbiome may play a significant role in modulating these effects, as shifts in microbiota composition have been linked to inflammation and systemic disease processes. **METHODS/STUDY POPULATION:** To explore these interactions, we conducted an acute COVID-19 study using 12-week-old C57 mice intranasally inoculated with  $1 \times 10^4$  PFU of the Mouse Adapted 10 (MA-10) strain of SARS-CoV-2. On day 5 postinfection, we performed 16S ribosomal RNA sequencing on fecal samples, analyzed using QIIME2 and DeSeq2, to assess microbiome alterations and identify changes in metabolic pathways associated with inflammatory responses. **RESULTS/ANTICIPATED RESULTS:** Analysis revealed notable shifts in the gut microbiome during the acute phase of COVID-19 infection, with significant alterations in metabolic pathways related to inflammation and immune regulation. These changes suggest that early gut microbiome disruptions may contribute to the host response in acute COVID-19. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Our findings indicate that acute SARS-CoV-2 infection leads to rapid alterations in the gut microbiome, which could underlie inflammatory and immune pathways impacting disease progression. These insights highlight the potential for microbiome-targeted therapies to mitigate acute COVID-19 morbidity and warrant further investigation.

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### Effects of butyrate supplementation in modulation of gut microbiome and its metabolites in new-onset rheumatoid arthritis

Rebecca Blank<sup>1</sup>, Alba Boix-Amoros<sup>2</sup>, Erin R. Reilly<sup>3</sup>, Kevin Bu<sup>2</sup>, Ian Cunningham<sup>1</sup>, Renuka R. Nayak<sup>4</sup>, Andrew Patterson<sup>3</sup>, Jose C. Clemente<sup>2</sup> and Jose U. Scher<sup>1</sup>

<sup>1</sup>Department of Medicine, Division of Rheumatology, New York University School of Medicine, New York, NY; <sup>2</sup>Department of Genetics and Genomic Sciences, and Precision Immunology Institute, Icahn School of Medicine at Mount Sinai; <sup>3</sup>Department of Biochemistry and Molecular Biology, The Pennsylvania State University, University Park, PA, USA and <sup>4</sup>Rheumatology Division, Department of Medicine, University of California, San Francisco, California, USA

**OBJECTIVES/GOALS:** The gut microbiome and its metabolites, such as short-chain fatty acids (SCFA), are dysregulated in rheumatoid arthritis (RA); however, the significance of this observation and

its implications in pathogenesis and therapeutics is unclear. Here, we explore the role of the SCFA, butyrate, in treatment efficacy in new-onset rheumatoid arthritis. **METHODS/STUDY POPULATION:** We designed a proof-of-principle study to determine the effects of butyrate supplementation in new-onset RA (NORA) patients that fulfilled 2010 ACR/EULAR RA criteria. We evaluated the effects of methotrexate (MTX) plus butyrate in NORA (n = 17; 1 gm butyrate, 3 times daily) compared to MTX alone (n = 19) over 4 months. MTX responders were defined by a change in disease activity score (DAS)-28 ESR of > 1.8 at 4 months. Fecal samples were collected at baseline and followed up for 16S rRNA sequencing and metabolite quantification by 1H NMR spectroscopy. Unpaired-t, paired-t, Wilcoxon and Fisher's exact test were performed as appropriate. **RESULTS/ANTICIPATED RESULTS:** MTX responders in the MTX-only group had a higher concentration of fecal butyrate than nonresponders at baseline (p = 0.045). Fecal butyrate concentration decreased over time in treatment responders in MTX group (p = 0.05), whereas butyrate concentration remained similar in MTX/butyrate group. Prior to treatment, both MTX and MTX/butyrate groups demonstrated similar levels of gut bacterial alpha diversity (Shannon index), yet only the MTX/butyrate group demonstrated a significant increase in alpha diversity by 4 months (p = 0.022). LeSe analysis demonstrated increased abundances of *Bacteroides*, *Clostridium*, and *Phascolarctobacterium* in responders in the MTX/butyrate group by 4 months. Ten (52.6%) patients in MTX and 11 (64.7%) in MTX/butyrate group were considered MTX responders by 4 months (p = 0.516). **DISCUSSION/SIGNIFICANCE OF IMPACT:** Butyrate supplementation increased gut microbial diversity in patients and led to increased abundance of *Bacteroides*, which has been implicated in efficacy of methotrexate, a first line medication in rheumatoid arthritis. Butyrate may have implications for the maximization of therapeutic effectiveness in rheumatoid arthritis.

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### Identification of gut barrier protective fruits and vegetables for Latin American infants

Brian Piccolo<sup>1</sup>, Leslie Tabor-Simecka<sup>1</sup>, Nicole Knox<sup>2</sup>, Ashley M. McAmis<sup>2</sup>, Ahmad Ud Din<sup>2</sup>, Andrew P. Neilson<sup>3</sup>, D. Keith Williams<sup>3</sup>, Jerry Simecka<sup>4</sup> and Mario G. Ferruzzi<sup>5</sup>

<sup>1</sup>Arkansas Children's Nutrition Center; <sup>2</sup>Arkansas Children's Nutrition Center Plants for Human Health Institute, North Carolina State University; <sup>3</sup>Arkansas Children's Nutrition Center; Department of Biostatistics, University of North; <sup>4</sup>Arkansas for Medical Sciences Department of Pharmaceutical Sciences, and <sup>5</sup>University of North Texas Health Science Center Arkansas Children's Nutrition Center; Department of Pediatrics

**OBJECTIVES/GOALS:** Early childhood obesity is a major concern for Latin American children in the U.S., with gut barrier dysfunction as a key risk factor. Diet plays a role in gut development, but few studies have focused on Latin American infants. Our objective is to identify culturally relevant introductory foods that promote in vitro gut barrier development and function. **METHODS/STUDY POPULATION:** Pooled human milk (2.5 mL) from 6-month postpartum Hispanic mothers was combined with fruit and vegetable baby food products (2.5 g) and subjected to a 3-phase in vitro digestion system that simulates oral, gastric, and intestinal digestion. Digested products were then anaerobically fermented for 24-hours