






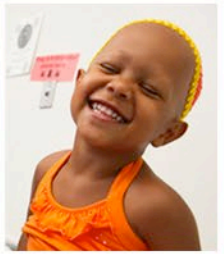


Liver-Gut-Microbiome Axis and Fatty Acid Absorption in Preterm Infants

Amy B. Hair, M.D.

Associate Professor of Pediatrics
Program Director of Neonatal Nutrition
Medical Director of TCH Milk Banks
Associate Director of NICU Intestinal Rehabilitation Team
Division of Neonatology
Department of Pediatrics
Baylor College of Medicine
Texas Children's Hospital

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Disclosure

- I have no conflicts of interest to disclose.

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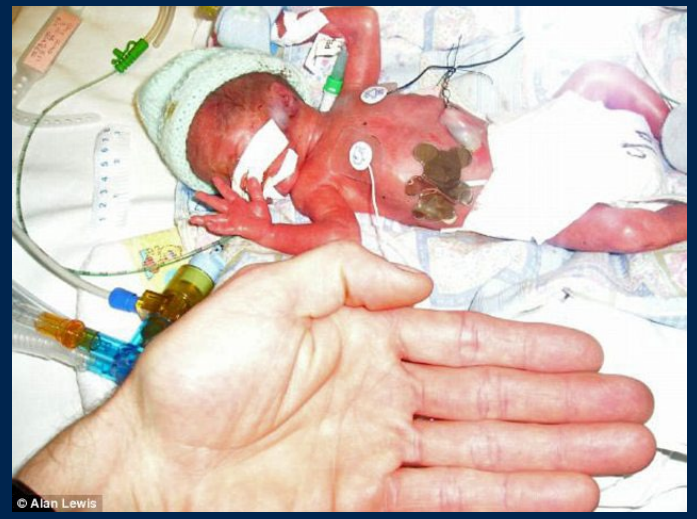
  Chan Zuckerberg Initiative, Gerber Foundation

Neonatal Nutrition Program at TCH



Neonatal Nutrition Program

- Neonatologists
- Neonatal Dietitians
- Trainees - Fellows, Residents, Medical Students, Graduate Students
- NNPs and Nurses
- Subspecialists - GI, Pedi Surgery, Cardiology, ID, CNRC, MFM, Radiology
- Multicenter Collaborations
- Research Team

NEC Awareness Day 2025
Research Team

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Neonatal Dietitian Team

Elizabeth Brodine
MS,RD,LD

Allyson Camp
MS,RD,CSP, LD

Amy Carter
MS,RD,LD

Agnes Mandy
RD,LD

Nidia Delgado-Woldegiogis
MS,RD,CSPCC,LD

Laura Lucas
MS,RD,LD,CNSC

Adriana Massieu
RD,LD,CNSC

Veronica Rubio
MS,RD,CSP,LD

*Slide courtesy of Dr. Reber and Laura Gollins

Neonatal Nutrition Research Group

- Dr. Premkumar
- Dr. Itriago
- Dr. Niemyjski

Research Team:

- Jessica Nguyen- Clinical Research Manager
- Nora Abu-Hamdan- Research Coordinator
- Wen-Wen Wu- Research Coordinator
- Priscilla Vasquez- Senior Research Coordinator

- Dr. Joe Hagan, ScD
- Dr. Thomas Lu, Dr. Andrew Beverstock, Dr. Lyca Intal
- NICU Dietitians
- Collaborators at TCH
  - Dr. Geoff Preidis, Dr. Moorthy, Kristina Tucker, Dr. Roddy, Dr. Wood, Dr. Vogel, Dr. Keswani, Dr. Meoded, Dr. Wes Lee, Dr. Pam Ketwaroo, Dr. Burrin, Dr. Ramani
- Laura Gollins, MBA, RDN, LD, CNSC, FAND, Clinical Program Coordinator

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Texas Children's Hospital Experience-16 years

RESEARCH ARTICLE Open Access

Human milk feeding supports adequate growth in infants ≤ 1250 grams birth weight

Amy B Hair*†, Keli M Hawthorne†, Katherine E Chetta† and Steven A Abrams†

Abstract

Background: Despite current nutritional strategies, premature infants remain at high risk for extrauterine growth restriction. The use of an exclusive human milk-based diet is associated with decreased incidence of necrotizing enterocolitis (NEC), but concerns exist about infants achieving adequate growth. The objective of this study was to evaluate growth velocities and incidence of extrauterine growth restriction in infants ≤ 1250 grams (g) birth weight (BW) receiving an exclusive human milk-based diet with early and rapid advancement of fortification using a donor human milk derived fortifier.

Methods: In a single center, prospective observational cohort study, preterm infants weighing ≤ 1250 g BW were fed an exclusive human milk-based diet until 34 weeks postmenstrual age. Human milk fortification with donor human milk derived fortifier was started at 60 mL/kg/d and advanced to provide 6 to 8 additional kilocalories per ounce (or 0.21 to 0.28 kilocalories per gram). Data for growth were compared to historical growth standards and previous human milk-fed cohorts.

Results: We consecutively evaluated 104 infants with mean gestational age of 27.6 ± 2.0 weeks and BW of 913 ± 181 g (mean ± standard deviation). Weight gain was 24.8 ± 5.4 g/kg/day with length 0.99 ± 0.23 cm/week and head circumference 0.72 ± 0.14 cm/week. There were 3 medical NEC cases and 1 surgical NEC case. 22 infants (21%) were small for gestational age at birth. Overall, 45 infants (43%) had extrauterine growth restriction. Weight velocity was affected by day of fortification ($p = 0.005$) and day of full feeds ($p = 0.02$). Our cohort had significantly greater growth in weight and length compared to previous entirely human milk-fed cohorts.

Conclusions: A feeding protocol for infants ≤ 1250 g BW providing an exclusive human milk-based diet with early and rapid advancement of fortification leads to growth meeting targeted standards with a low rate of extrauterine growth restriction. Consistent nutritional policies using this approach may be considered for this population.

Keywords: Neonate, Growth, Nutrition, Human milk, Growth failure, Necrotizing enterocolitis

Improved feeding tolerance and growth are linked to increased gut microbial community diversity in very-low-birth-weight infants fed mother's own milk compared with donor breast milk

Steven L Ford,[1] Pablo Lohmann,[1] Geoffrey A Preidis,[4] Pamela S Gordon,[2] Andrea O'Donnell,[1] Joseph Hagan,[1] Alamelu Venkatachalam,[3] Miriam Balderas,[3,5] Ruth Ann Luna,[3,5] and Amy B Hair[1]

Beyond Necrotizing Enterocolitis Prevention: Improving Outcomes with an Exclusive Human Milk–Based Diet

Amy B. Hair,[1] Allison M. Peluso,[1] Keli M. Hawthorne,[1] Jose Perez,[2] Denise P. Smith,[2] Janine Y. Khan,[3] Andrea O'Donnell,[4] Richard J. Powers,[5] Martin L. Lee,[6] and Steven A. Abrams[1]

Fatty acid concentrations in preterm infants fed the exclusive human milk diet: a prospective cohort study

Lindsay F. Holzapfel[1,2✉], Jana P. Unger[2], Pam Gordon[2,3], Heeju Yang[2], Joanne E. Cluette-Brown[4], Laura A. Gollins[2], Amy B. Hair[2,6] and Camilia R. Martin[5,6]

A preoperative standardized feeding protocol improves human milk use in infants with complex congenital heart disease

Jasmeet Kataria-Hale[1,2,3] · Dantin Jeramy Roddy[1,3,4] · Acacia Cognata[5] · Patrice Hochevar[1,2,3] · Jill Zender[1,3,4] · Paige Sheaks[1,3,4] · Scott Osborne[1,2,3] · Kristina Tucker[1,2,3] · Nancy Hurst[1,2,3] · Joseph Hagan[1,2,3] · Amy Hair[1,2,3]

Randomized Trial of Human Milk Cream as a Supplement to Standard Fortification of an Exclusive Human Milk-Based Diet in Infants 750-1250 g Birth Weight

Amy B. Hair, MD[1], Cynthia L. Blanco, MD[2], Alvaro G. Moreira, MD[2], Keli M. Hawthorne, MS, RD[1], Martin L. Lee, PhD[3], David J. Rechtman, MD[3], and Steven A. Abrams, MD[1]

Objective To evaluate whether premature infants who received an exclusive human milk (HM)-based diet and a HM-derived cream supplement (cream) would have weight gain (g/kg/d) at least as good as infants receiving a standard feeding regimen (control).

Study design In a prospective noninferiority, randomized, unmasked study, infants with a birth weight 750-1250 g were randomly assigned to the control or cream group. The control group received mother's own milk or donor HM with donor HM-derived fortifier. The cream group received a HM-derived cream supplement if the energy density of the HM tested <20 kcal/oz using a near infrared HM analyzer. Infants were continued on the protocol until 36 weeks postmenstrual age. Primary outcomes included growth velocities and amount of donor HM-derived fortifier used. The hypothesis of noninferiority was established if the lower bound of the one-sided 95% CI for the difference in weight velocities exceeded −3 g/kg/day.

Results There were no differences between groups in baseline demographics for the 78 infants studied except racial distribution ($P = .02$). The cream group (n = 39) had superior weight (14.0 ± 2.5 vs 12.4 ± 3.0 g/kg/d, $P = .03$) and length (1.03 ± 0.33 vs 0.83 ± 0.41 cm/wk, $P = .02$) velocity compared with the control group (n = 39). There were no significant differences in amount of fortifier used between study groups. The 1-sided 95% lower bound of the CI for the difference in mean velocity (cream-control) was 0.38 g/kg/d.

Conclusions Premature infants who received HM-derived cream to fortified HM had improved weight and length velocity compared with the control group. HM-derived cream should be considered an adjunctive supplement to an exclusive HM-based diet to improve growth rates in premature infants. *(J Pediatr 2014;165:915-20).*

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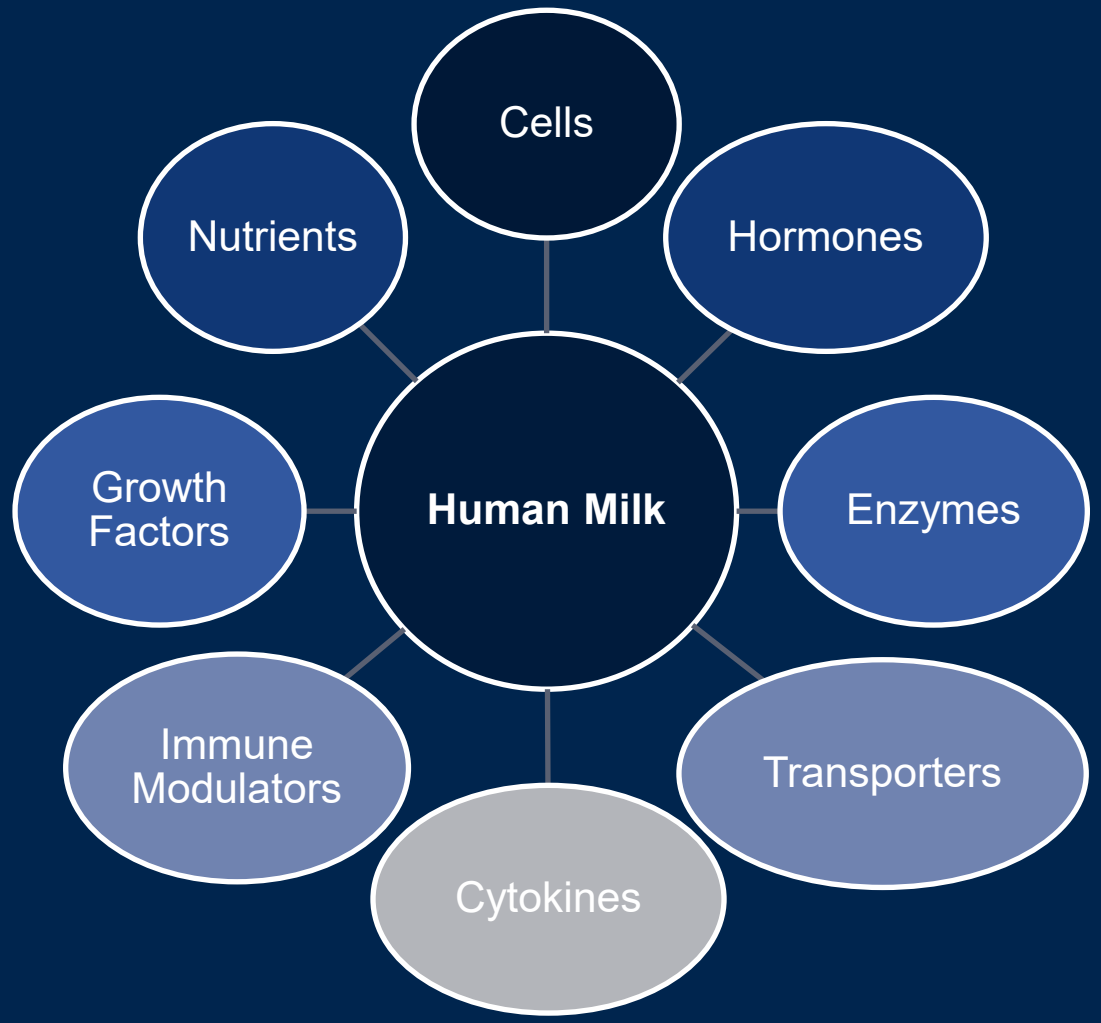
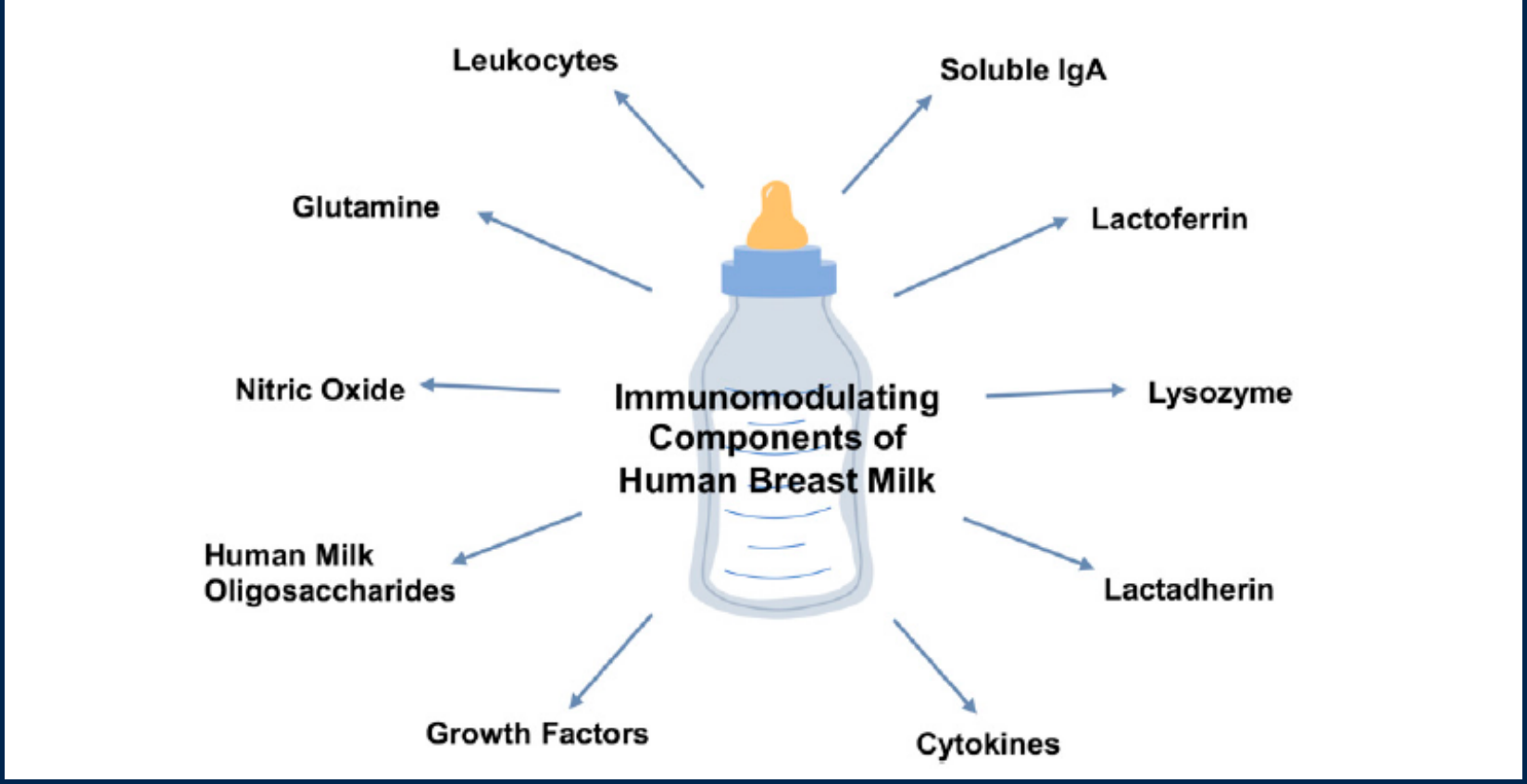
Human Milk is a Complex Tissue



Immunomodulatory Components of HM



Nolan, Parks and Good. Nutrients 2020.

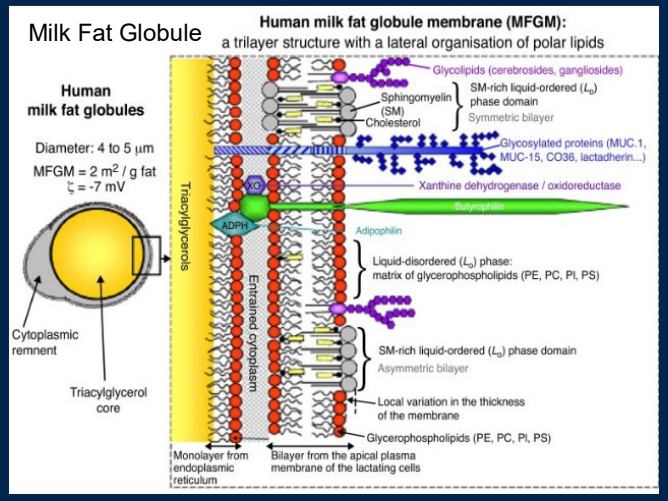
AAP Statement 2012 and 2022: “Breastfeeding and the Use of Human Milk”

- Lower rate of necrotizing enterocolitis
- Lower rate of sepsis
- Lower rate of retinopathy of prematurity
- Improved feeding tolerance
- Improved neurodevelopment
- Fewer hospital readmissions at 1-year post-discharge
- Lower rates of metabolic syndrome

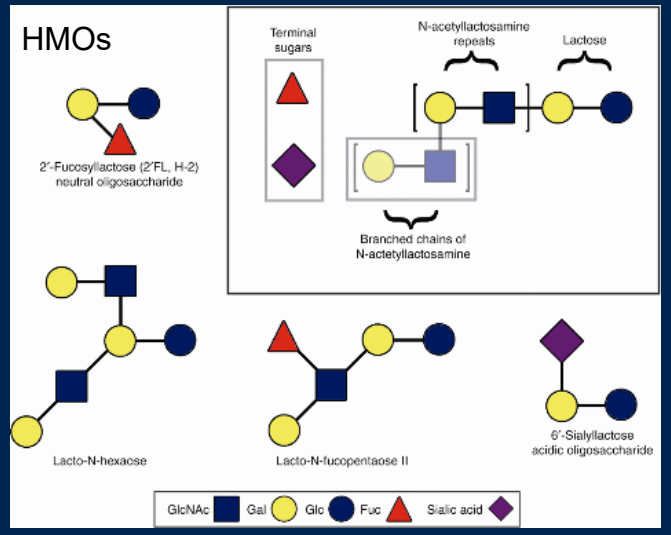
The American Academy of Pediatrics and ESPGHAN has recommended that all preterm infants receive human milk, and that **donor human milk** should be used if mother’s own milk is unavailable.

1. American Academy of Pediatrics. *Pediatrics*. 2012; 129(3): e827-e841. *Pediatrics*. 2022 Jul 1;150
2. ESPGHAN Committee on Nutrition, *J Pediatr Gastroenterol Nutr*. 2013 Oct;57(4):535-42.

Innovations: Human Milk



Lopez C, Ménard O. Colloids Surf B Biointerfaces. 2011 Mar;83(1):29-41.



Newburg and Grave. *Pediatr Res* **75,** 675–679 (2014).

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Optimizing Human Milk for Preterm Infants

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Caloric Variation of Human Milk

- Variation in Calories of Human Milk
  - Are we really giving the calories we think we are?
  - Are we delivering the calories?
  - Pasteurization and freezing
  - Donor milk is “term” milk
  - Preterm infants require additional protein, calcium and phosphorus added as a fortifier to human milk

https://www.flickr.com/photos/61056899@N06/5751301741

https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.parentingscience.com%2Fcalories-in-breast-milk.html&psig=AOvVaw1-025lc53GBSz6dmgbfhNP&ust=1619820330425000&source=images&cd=vfe&ved=0CAIQjRxqFwoTCJCyyYu8pPACFQAAAAAdAAAAABAD

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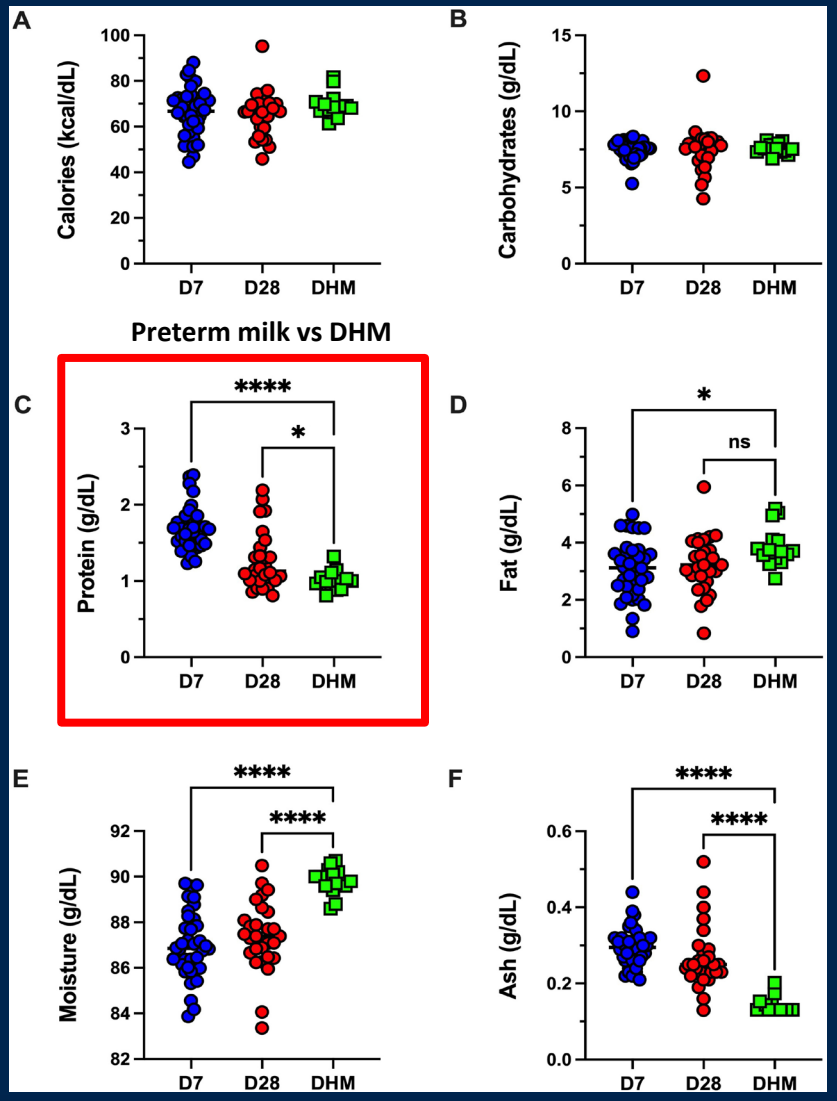
Comparison of Macronutrient Content in Preterm and Donor Human Milk



Gates, Hair, Salas, Thompson, Stansfield. *The Journal of Nutrition* 2023

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Table 1
Differences in nutrients and bioactive factors in maternal milk versus pasteurized donor HM[8,18,19,70]

Components	Functions	Maternal Milk	Pasteurized Donor Human Milk
Macronutrients, including: Protein Lipid	• Nutritional substrate for growth and development	• Protein content decreases with the duration of lactation. • Lipid content is the most variable of all macronutrients.	Reduced lipid content secondary to multiple freeze–thaw cycles and container changes. Reduction or destruction of digestive enzymes (amylases, proteases, lipases). • Higher protein content by holder method compared with vat or retort method. • Highest fat and calculated energy concentration in the vat method and lowest in the retort method.
Growth Factors, including: Epidermal Transforming Vasoactive endothelial	• Maturational, anti-inflammatory, and trophic effect on the gastrointestinal tract	• Content decreases markedly at 1-mo postbirth. • Slower decline seen in earliest gestation/less mature infants.	• Bioactivity varies by growth factor and is reduced by pasteurization.
Bioactive Proteins, including: Immunoglobulins Cytokines Milk Fat Globule Membrane	• Immune modulation • Anti-inflammatory and anti-infective • Gut barrier protection	• Most abundant in colostrum, with higher levels inversely associated with gestational age. • Selective elevation following pathogen exposure in infant environment.	Lower concentrations than maternal milk with little or no activity in some components. Concentrations of IgA, IgG, and IgM were lowest by retort method and highest by holder method • Lysozyme concentration was the highest by the vat method.
Oligosaccharides	• Prebiotic • Immune modulation • Antimicrobial	• Highest content in colostrum and transitional milk. • Individual variability in number and type.	Oligosaccharide pattern of donor human milk varies from that of maternal milk but largely preserved in pasteurization and storage • Higher oligosaccharide concentration in Holder method compared with vat or retort method.

Bergner EM, Taylor SN, Gollins LA, Hair AB. Human Milk Fortification: A Practical Analysis of Current Evidence. Clin Perinatol. 2022;49(2):447-460.

Human Milk Lab Studies

- Human Milk Analysis Multicenter Study
- Human Milk Analysis Using NIRS Analyzer
- Analysis of Nutrient Loss in Feeding Delivery Systems
  - Tubes, materials, syringes

THE JOURNAL OF PEDIATRICS • www.jpeds.com ORIGINAL ARTICLES

Randomized Trial of Human Milk Cream as a Supplement to Standard Fortification of an Exclusive Human Milk-Based Diet in Infants 750-1250 g Birth Weight

Amy B. Hair, MD[1], Cynthia L. Blanco, MD[2], Alvaro G. Moreira, MD[2], Keli M. Hawthorne, MS, RD[1], Martin L. Lee, PhD[3], David J. Rechtman, MD[3], and Steven A. Abrams, MD[1]

- Donor human milk-derived cream supplement
- Human Milk Cream or Human Milk Fat is derived from the processing of donor human milk
- Caloric content is 2.5 kcal/mL
- Designed to be given after goal enteral protein (g/kg/day) is achieved with an exclusive human milk diet

Cream

Donor milk-derived Fortifier

Mother's Milk

Donor Milk

Hair, Blanco, Moreira et al, J Peds 2014.

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Utilizing Targeted Fortification to Evaluate the Effects of High Versus Standard Protein on Linear Growth and Body Composition in ELBW infants

Purpose:

1. To evaluate the effects of a standard versus high protein diet on growth and body composition in ELBW infants.
2. To evaluate body composition by DEXA/Pea Pod.

Hypothesis:

1. Infants receiving high protein will have increased linear growth at 36 weeks PMA compared to those receiving standard protein.
2. Infants receiving high protein will have increased lean mass compared to those receiving standard protein.

Hair et al, unpublished data.

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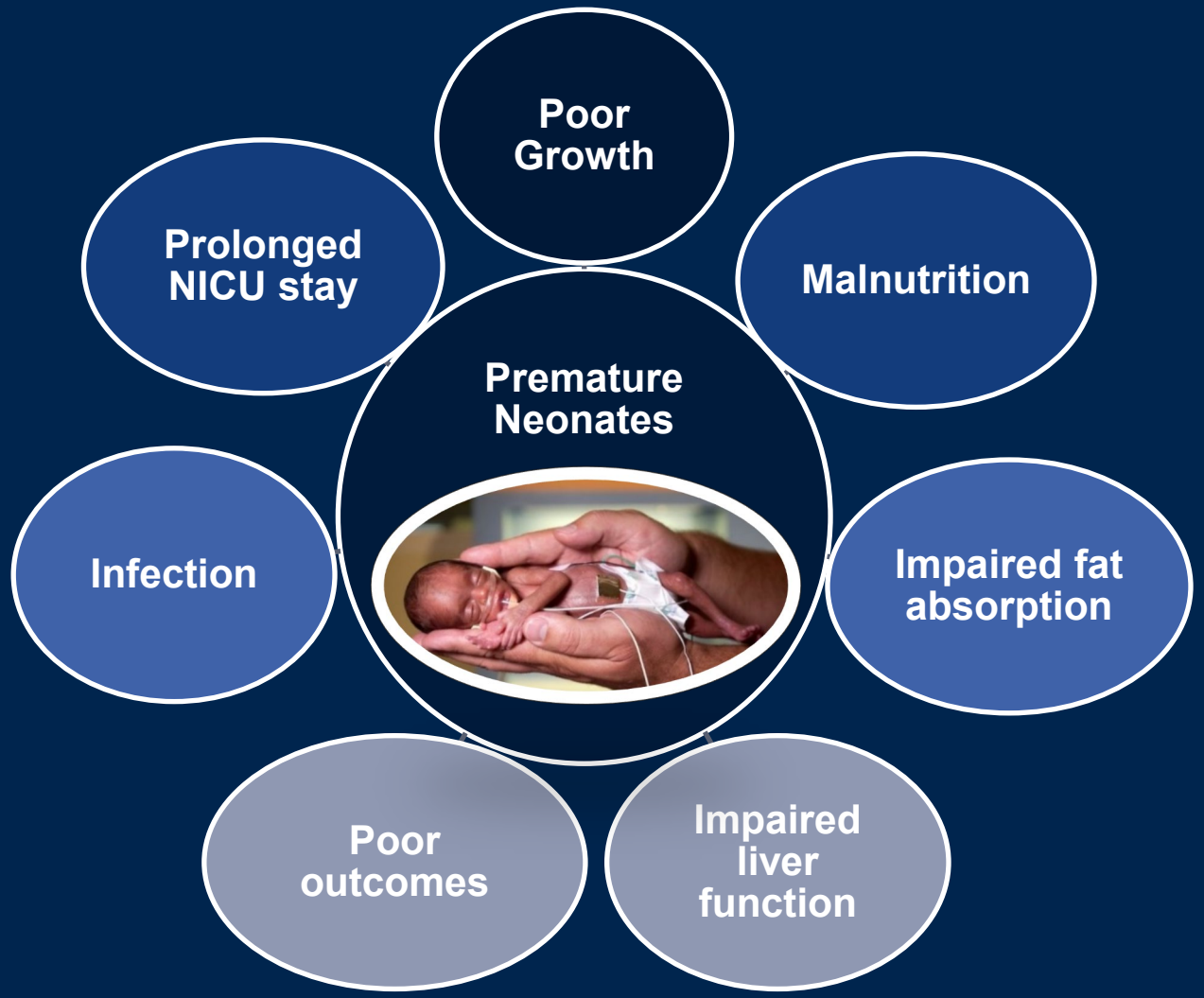
What are we missing?



Fatty Acid Levels in Preterm Infants

During First Week of Life:

↓ DHA rapidly

↓ AA rapidly

↑ LA rapidly

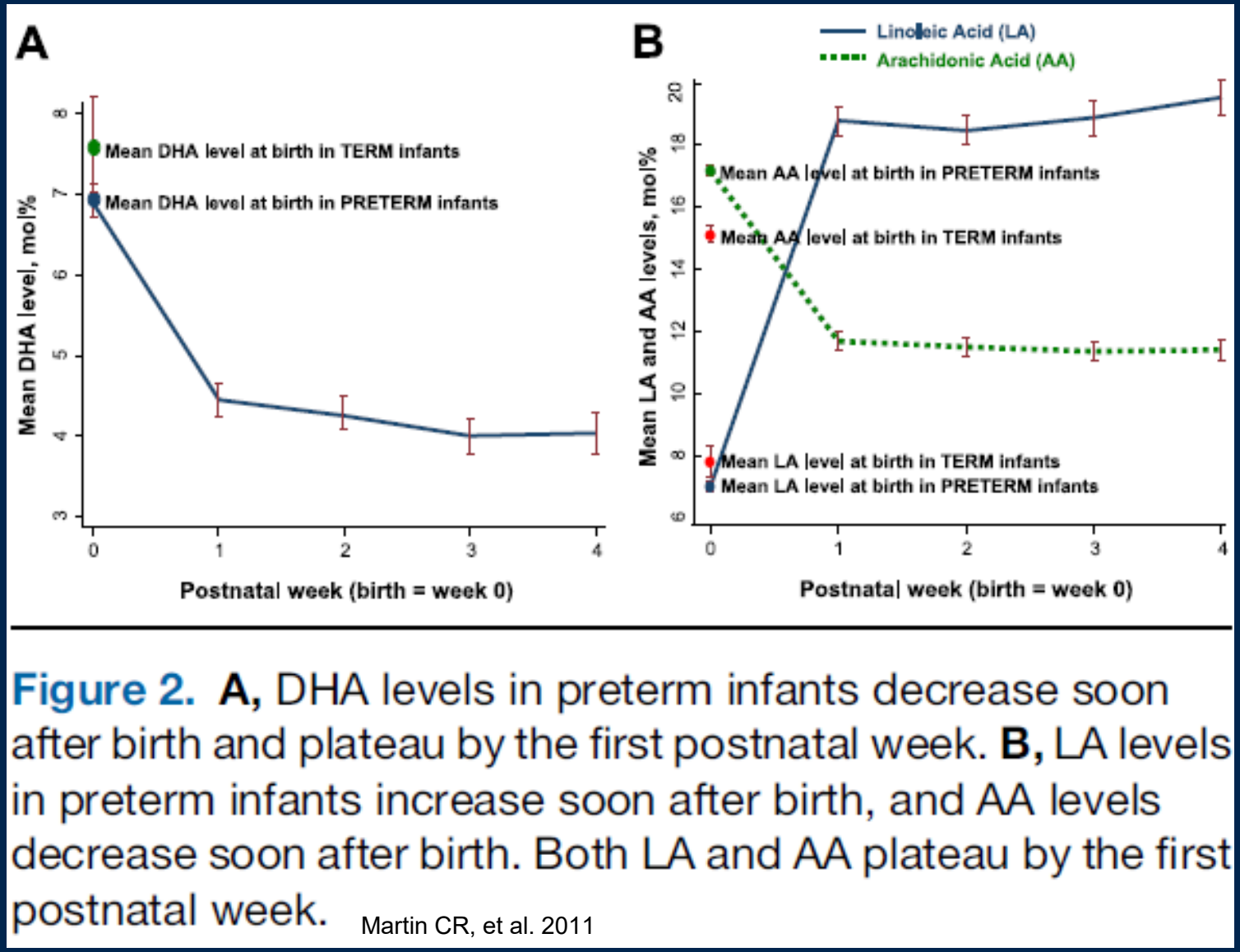


Figure 2. **A,** DHA levels in preterm infants decrease soon after birth and plateau by the first postnatal week. **B,** LA levels in preterm infants increase soon after birth, and AA levels decrease soon after birth. Both LA and AA plateau by the first postnatal week.

Martin CR, et al. 2011

Fatty Acid Absorption
Breastmilk vs. Formula

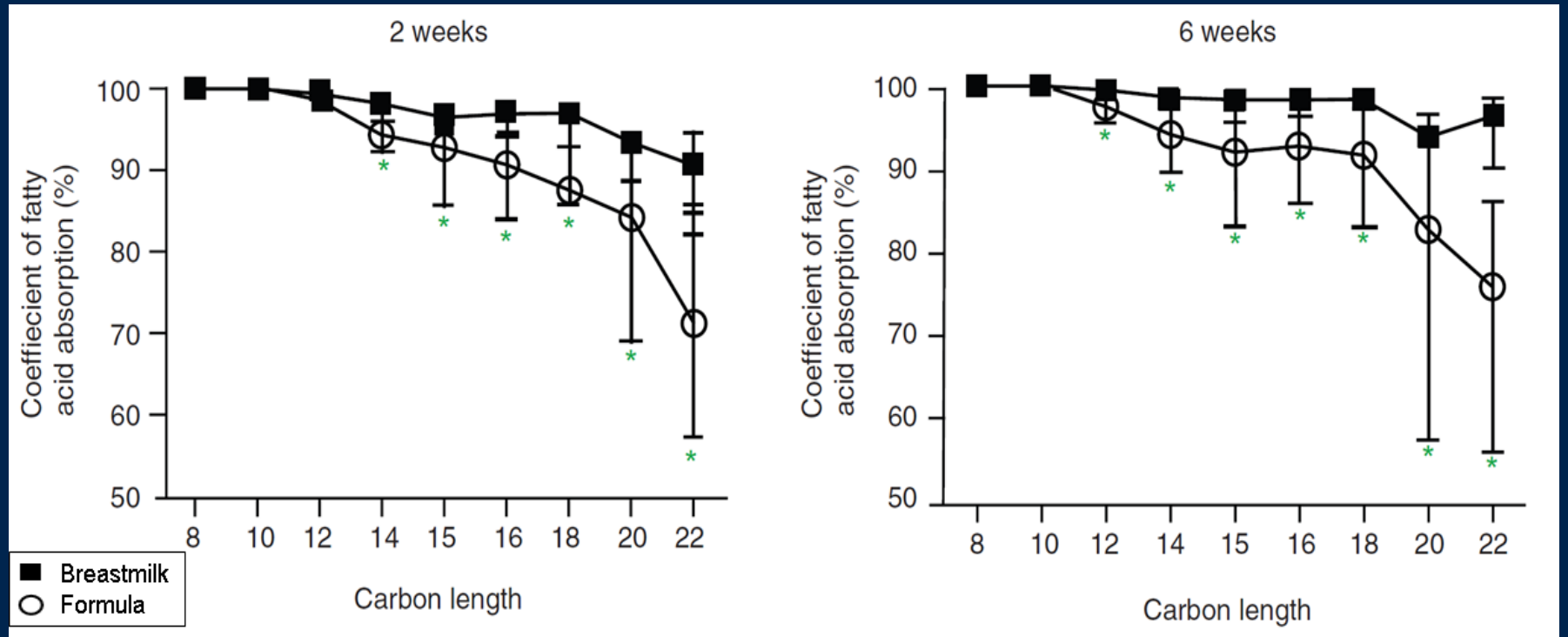


FIGURE 1. Fatty Acid Absorption in Preterm Infants. Absorption coefficients by fatty acids by carbon length, *P<0.05, Martin et al. 2016.

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Fatty Acid Levels In Infants <1250 grams Fed an Exclusive Human Milk Diet

Dr. Lindsay F. Holzapfel

Dr. Cami Martin

- Purpose
  - To measure blood levels of fatty acids in infants fed an exclusive human milk diet at different time points during their NICU stay.
  - To monitor growth and observe associations with common morbidities of prematurity such as chronic lung disease, retinopathy of prematurity, and infection risks.

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Fatty acid concentrations in preterm infants fed the exclusive human milk diet: a prospective cohort study

Lindsay F. Holzapfel[1,2]✉, Jana P. Unger[2], Pam Gordon[2,3], Heeju Yang[2], Joanne E. Cluette-Brown[4], Laura A. Gollins[2], Amy B. Hair[2,6] and Camilia R. Martin[5,6]

- Donor human milk-fed (n = 12) compared to mother's own milk-fed infants <1250 grams (n = 18) from birth to after 28 days of life, had an increased interval change of linoleic to docosahexaenoic acid ratio (5.5 vs. −1.1 mole percent ratio, p = 0.034).

- An exclusive human milk diet maintains birth docosahexaenoic (DHA) and eicosapentaenoic acid (EPA) concentrations. However, the postnatal deficit in arachidonic acid (AA) was not prevented.

Fecal Elastase in Preterm Infants to Predict Growth Outcomes

*†Lindsay F. Holzapfel, MD, MS, †Amy B. Hair, MD, ‡Geoffrey A. Preidis, MD, PhD, ‡Tripti Halder, BS, BED, †Heeju Yang, BS, †§Jana P. Unger, RD, LD, MS, ‖¶Steven Freedman, MD, PhD, and #Camilia R. Martin, MD, MS

- Preterm infants are born functionally pancreatic insufficient with decreased pancreatic production of lipase and proteases.

- Developmental pancreatic insufficiency (PI) may contribute to reduced nutrient absorption and growth failure.

Holzapfel LF, Hair AB, Preidis GA, Halder T, Yang H, Unger JP, Freedman S, Martin CR. Fecal Elastase in Preterm Infants to Predict Growth Outcomes. J Pediatr Gastroenterol Nutr. 2023 Feb 1;76(2):206-212.

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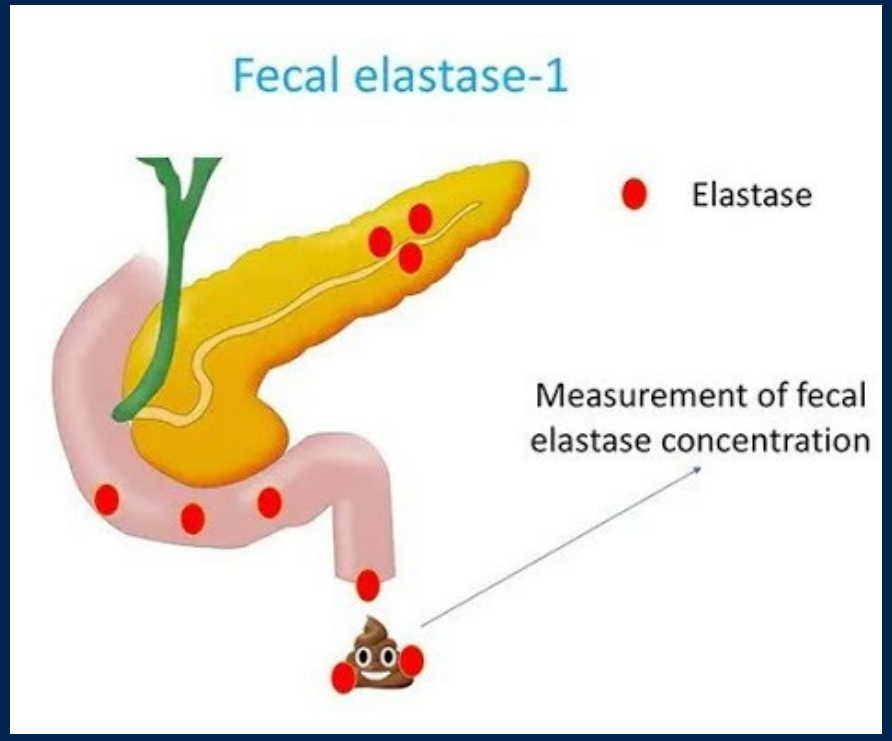
Pancreatic Insufficiency in Preterm Infants

- We sought to determine longitudinal fecal elastase (ELA1) levels in a cohort of preterm infants and whether levels are associated with growth outcomes.



https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.youtube.com%2Fwatch%3Fv%3DhSS_ZeJaCFs&psig=AOvVaw2BHQA0dkM7ppBfngVbqTST&ust=1763493544416000&source=images&cd=vfe&opi=89978449&ved=0CBYQjRxqFwoTCJiK2MTz-ZADFQAAAAAdAAAAABAI

Holzapfel LF, Hair AB, Preidis GA, Halder T, Yang H, Unger JP, Freedman S, Martin CR. Fecal Elastase in Preterm Infants to Predict Growth Outcomes. J Pediatr Gastroenterol Nutr. 2023 Feb 1;76(2):206-212.

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Pancreatic Insufficiency in Preterm Infants

- Prospective observational study of 30 infants 24-34 weeks gestational age and birth weight ≤1250 g fed the exclusive human milk diet, consisting of human milk with human milk-based fortifier.

- ELA1 was quantified by ELISA at two time points (Early vs Late)

- Early: 7.5 ± 1.8 DOL vs Late: 63.6 ± 24.1 DOL (after attainment of full, fortified feedings)

Holzapfel LF, Hair AB, Preidis GA, Halder T, Yang H, Unger JP, Freedman S, Martin CR. Fecal Elastase in Preterm Infants to Predict Growth Outcomes. J Pediatr Gastroenterol Nutr. 2023 Feb 1;76(2):206-212.

Fecal Elastase in Preterm Infants

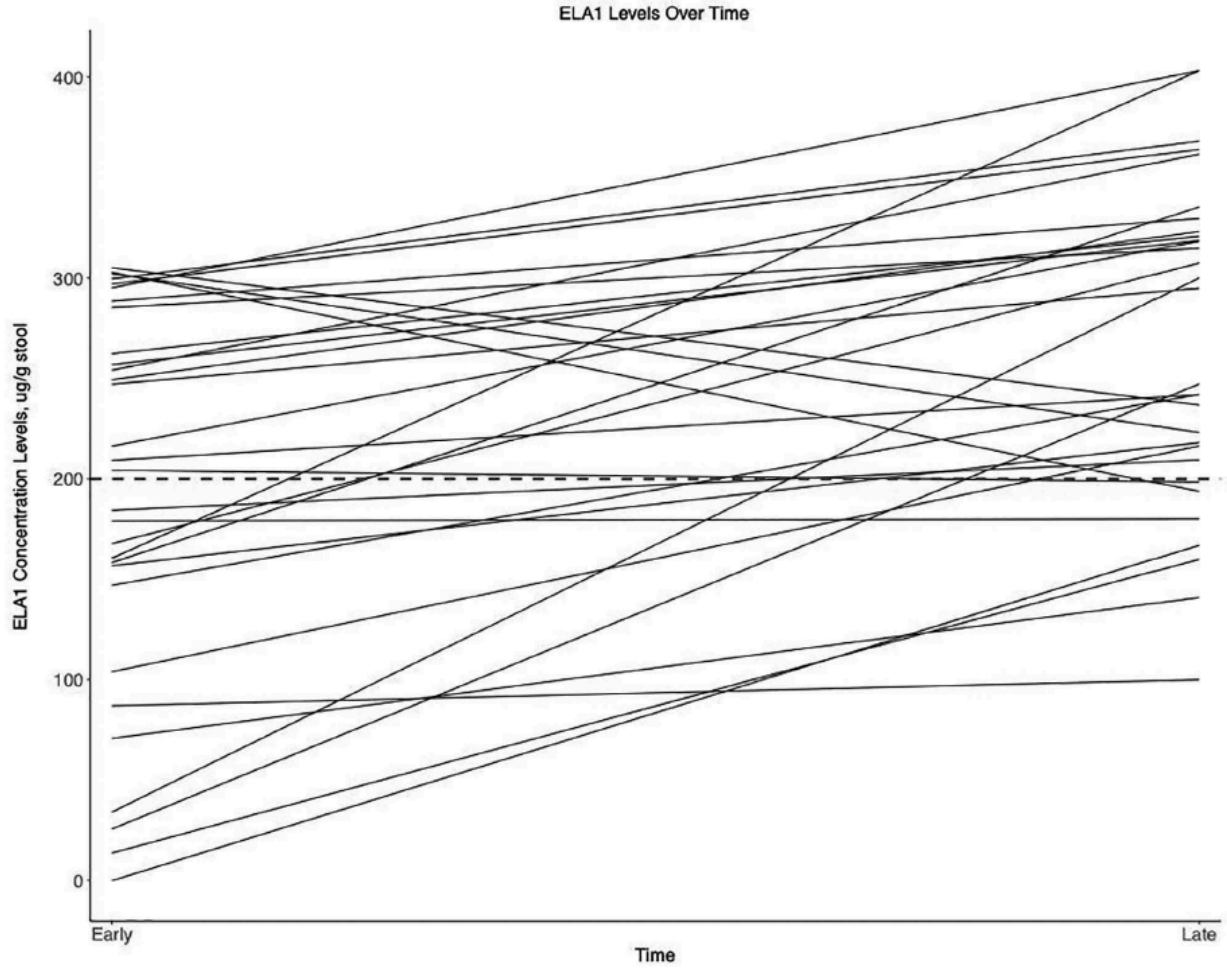

FIGURE 1. Longitudinal fecal elastase levels (ELA1) at Early (~1 week of age) versus Late (~2 months of age) time points. Pancreatic insufficiency, PI = ELA1 < 200 µg/g.

Holzapfel LF, Hair AB, Martin CR et al, J Pediatr Gastroenterol Nutr. 2023 Feb 1;76(2):206-212.

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Fecal Elastase in Preterm Infants

- Fecal ELA1 increases over time and with feedings of human milk fortified with human milk-based fortifier in preterm infants.
- Preterm infants have early, functional PI that improves over time.
- No difference in growth outcomes between pancreatic insufficient and pancreatic sufficient infants. PI infants did receive more calories.

Holzapfel LF, Hair AB, Preidis GA, Halder T, Yang H, Unger JP, Freedman S, Martin CR. Fecal Elastase in Preterm Infants to Predict Growth Outcomes. J Pediatr Gastroenterol Nutr. 2023 Feb 1;76(2):206-212.

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Challenges

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Improved feeding tolerance and growth are linked to increased gut microbial community diversity in very-low-birth-weight infants fed mother's own milk compared with donor breast milk

Steven L Ford,[1] Pablo Lohmann,[1] Geoffrey A Preidis,[4] Pamela S Gordon,[2] Andrea O'Donnell,[1] Joseph Hagan,[1] Alamelu Venkatachalam,[3] Miriam Balderas,[3,5] Ruth Ann Luna,[3,5] and Amy B Hair[1]

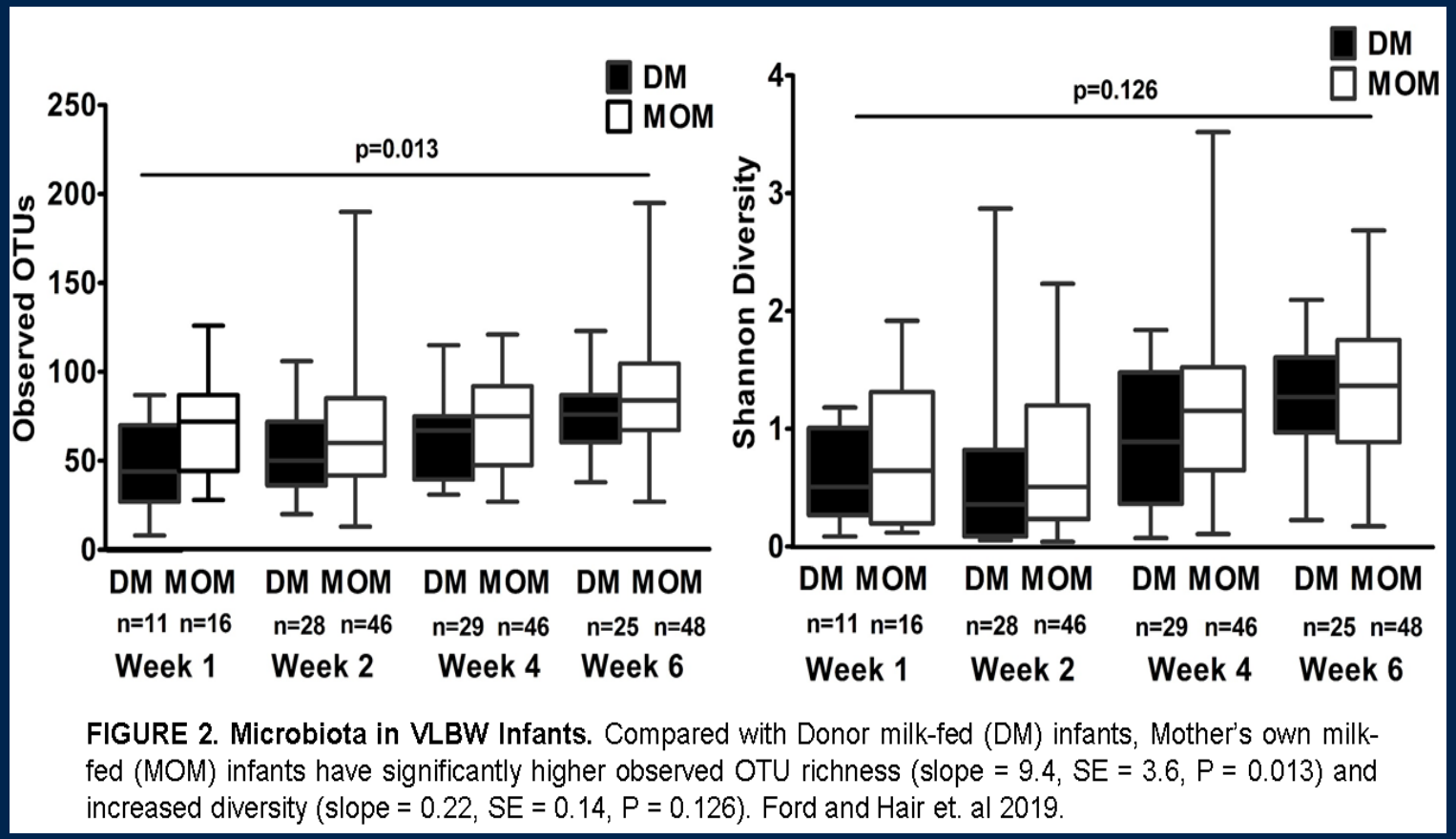

FIGURE 2. Microbiota in VLBW Infants. Compared with Donor milk-fed (DM) infants, Mother's own milk-fed (MOM) infants have significantly higher observed OTU richness (slope = 9.4, SE = 3.6, P = 0.013) and increased diversity (slope = 0.22, SE = 0.14, P = 0.126). Ford and Hair et. al 2019.

Steven Ford, MD

Geoff Preidis, MD, PhD

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Mother's own milk vs. Donor Human Milk Liver-Gut-Microbiome Immaturity

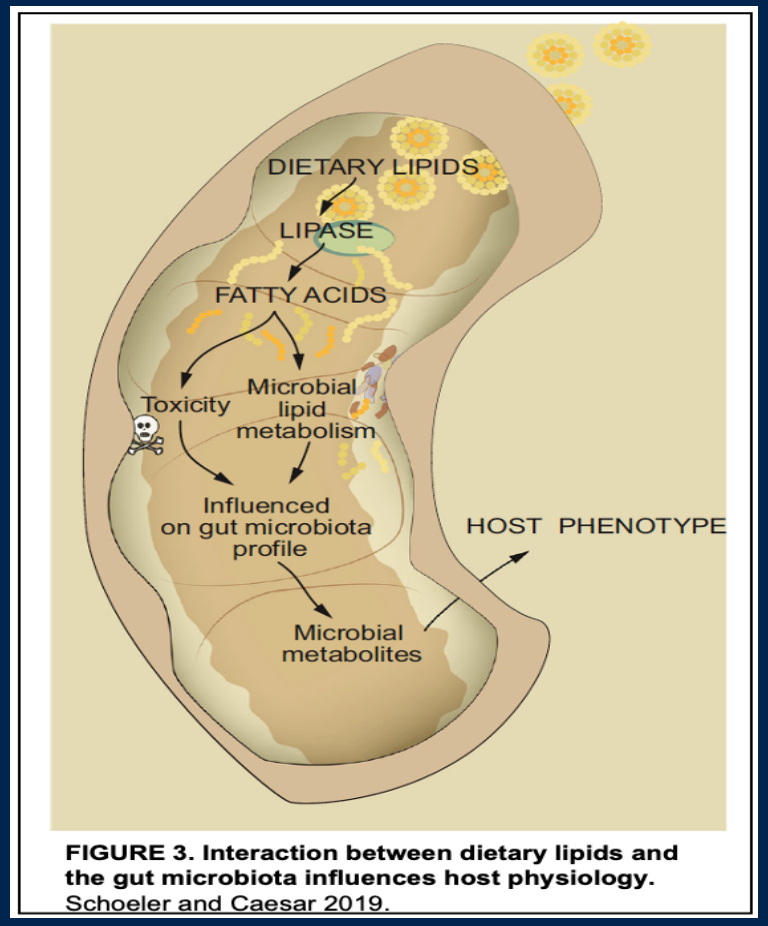

FIGURE 3. Interaction between dietary lipids and the gut microbiota influences host physiology. Schoeler and Caesar 2019.

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Liver-Gut-Microbiome Axis and Fatty acid Absorption in Preterm Infants

Geoff Preidis, MD, PhD

Cami Martin, MD, MS

Joe Petrosino, PhD

Ken Setchell, PhD

Cristian Coarfa, PhD

Pediatrics

Texas Children's Hospital®

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Role of Liver-Gut-Microbiome Axis In Fatty Acid Absorption in Preterm Infants

Altered Primary to Secondary Bile Acid Ratios

Deficient Microbial Bile Salt Hydrolase Enzymes

Impaired Hepatic Synthesis of Primary Bacteriostatic Bile Acids

Immature Liver and Altered Bile Acid Metabolism

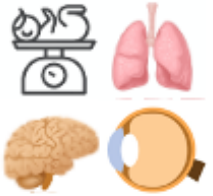
Immature Gut Microbiota

Overgrowth of Non-Beneficial Bacteria

Impaired Fatty Acid Absorption

Poor Health Outcomes

- Growth Failure
- Impaired development of brain and retina
- Increased risk of sepsis and lung disease
- Impaired cognition and motor skills



The ABSORB Study

LIVER-GUT-MICROBIOME AND FATTY ACID ABSORPTION IN PRETERM INFANTS

Role of Liver-Gut-Microbiome Axis In Fatty Acid Absorption in Preterm Infants

Altered Primary to Secondary Bile Acid Ratios

Deficient Microbial Bile Salt Hydrolase Enzymes

Impaired Hepatic Synthesis of Primary Bacteriostatic Bile Acids

Immature Liver and Altered Bile Acid Metabolism

Immature Gut Microbiota

Overgrowth of Non-Beneficial Bacteria

Impaired Fatty Acid Absorption

Poor Health Outcomes

- **Growth Failure**
- **Impaired development of brain and retina**
- **Increased risk of sepsis and lung disease**
- **Impaired cognition and motor skills**

AIM 1

Establish the longitudinal coefficient of fatty acid absorption of key fatty acids in a prospective VLBW cohort.

AIM 2

Quantify relative abundances of microbial bile acid modifying genes and activity and determine the impact on bile acids and fatty acid absorption coefficients.

The ABSORB Study

LIVER-GUT-MICROBIOME AND FATTY ACID ABSORPTION IN PRETERM INFANTS

The ABSORB Study

LIVER-GUT-MICROBIOME AND FATTY ACID ABSORPTION IN PRETERM INFANTS

Biospecimen	What is collected?	Birth (1st week of life)	2 weeks	6 weeks	36 weeks PMA
Stool	All stool output (diapers) for 72 consecutive hours 1 additional sample (diaper) following the 72 hours	X	X	X	X
Blood	0.5 mL*	X	X	X	X

*Diet at all time points

A systematic review of associations between gut microbiota composition and growth failure in preterm neonates

Larissa L. Neves[a], Amy B. Hair[b], and Geoffrey A. Preidis[a]

[a]Division of Gastroenterology, Hepatology, & Nutrition, Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston, TX, USA; [b]Division of Neonatology, Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston, TX, USA

Larissa Neves

Texas Children's Hospital®

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Growth and Microbiome in Preterm Infants

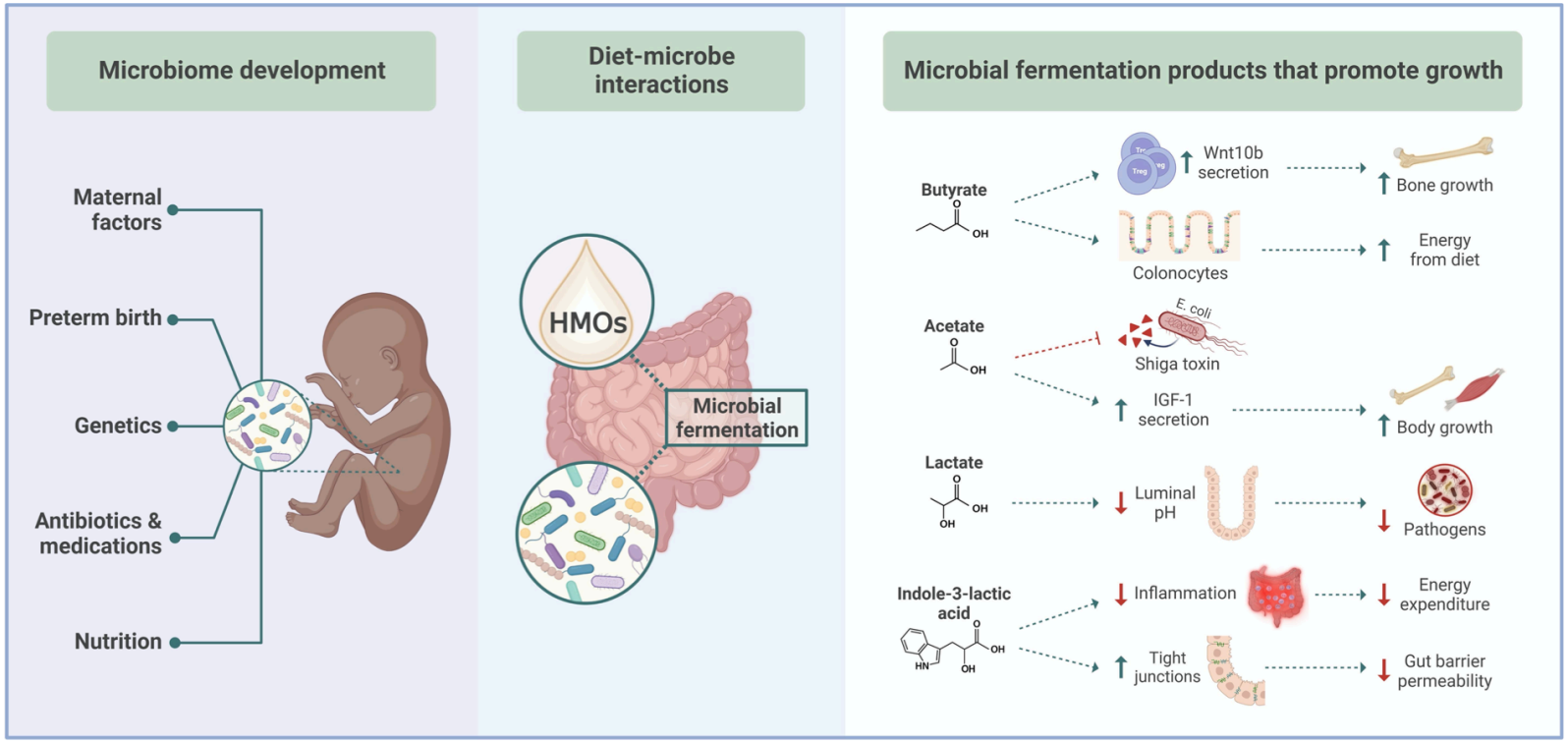

Figure 1. Mechanisms by which microbial fermentation of human milk oligosaccharides promote neonatal growth. Numerous factors shape the development of the neonatal gut microbiome. One of the most important factors – nutrition – provides substrates for gut microbes to perform beneficial functions that stimulate neonatal growth. Non-digestible HMOs are metabolized by bacterial enzymes to produce bioavailable energy, growth-promoting metabolites, and anti-inflammatory factors. HMO: human milk oligosaccharides; IGF-1: insulin-like growth factor-1; Wnt10b: Wnt family member 10b. Figure created with BioRender.Com.

Neves, Hair, and Preidis. Gut Microbes 2023

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Growth and Microbiome in Preterm Infants

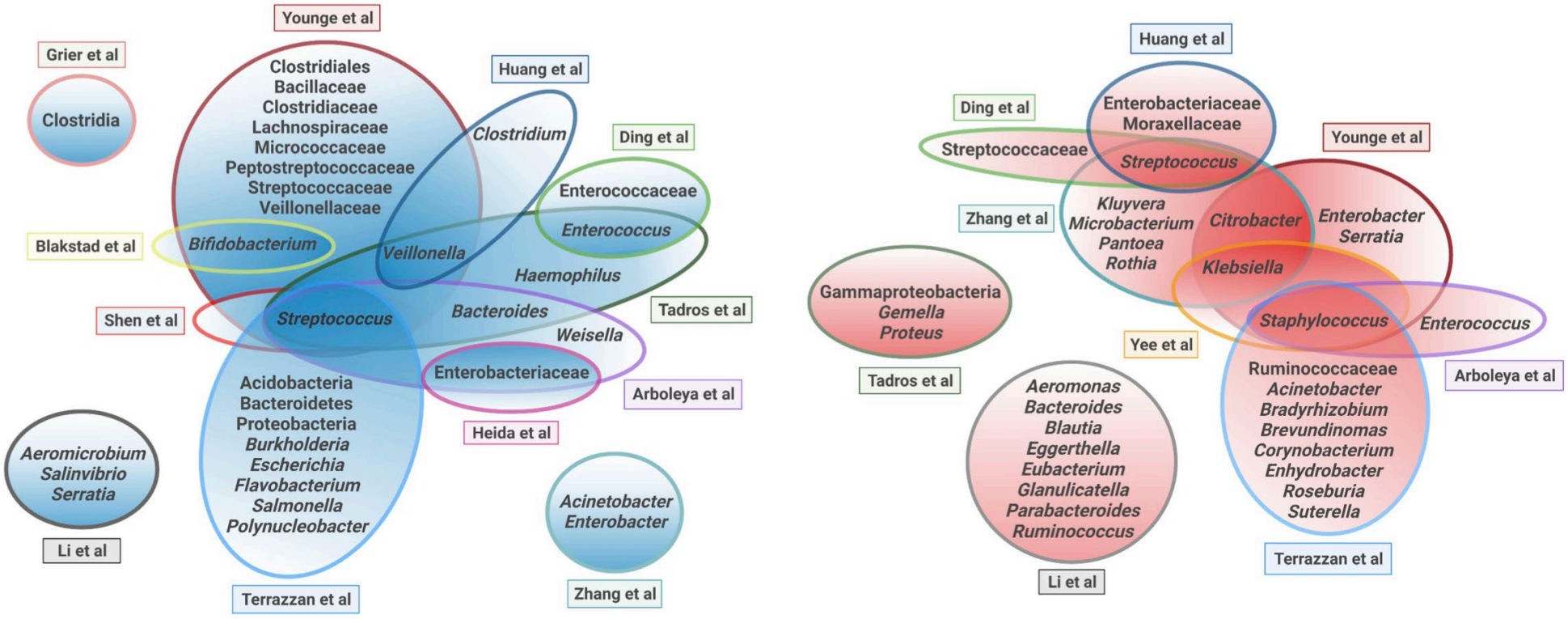

Figure 3. Microbial taxa positively or negatively associated with growth in studies of human preterm neonates. Blue Venn diagram (left) represents taxa positively associated with postnatal growth. Red Venn diagram (right) represents taxa negatively associated with postnatal growth. Figure created with BioRender.Com.

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Neonatal Growth and Associated Microbes

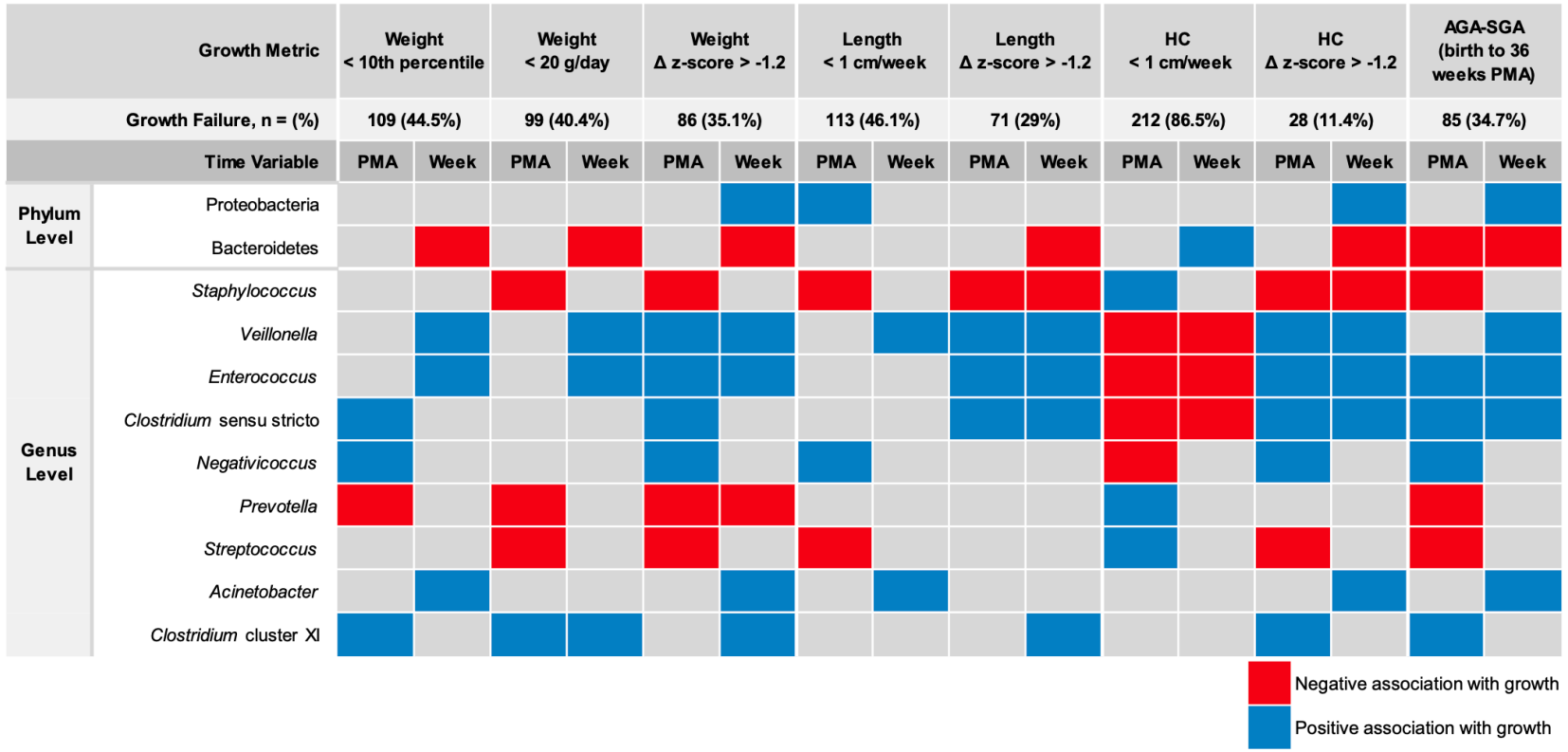

Figure 4. Phylum and genus level associations with postnatal growth based on 16 clinically relevant growth indices. in an exploratory secondary analysis of previously published microbiota sequencing from 245 longitudinally-sampled preterm infant stools, we sought to determine how changing the definition of neonatal growth might change the significantly associated microbes. We tested associations between relative abundance change over time and the binary outcome "appropriate growth" versus "growth failure" using eight clinically relevant definitions and analyzed each longitudinally according to PMA quartiles or postnatal week of life. Significant positive (blue) or negative (red) associations between taxa and postnatal growth are illustrated. *N* = (%) shows that the number of samples from infants classified as having growth failure changes dramatically with each of these 16 definitions. AGA-SGA: change in status from appropriate for gestational age at birth to small for gestational age (weight < 10th percentile) at 36 weeks PMA; HC: head circumference; PMA: post-menstrual age; Week: postnatal week of life.

Neves, Hair, and Preidis. Gut Microbes 2023

Cholestasis impairs gut microbiota development and bile salt hydrolase activity in preterm neonates

Lauren E. Lynch[a], Amy B. Hair[b], Krishnakant G. Soni[a], Heeju Yang[b], Laura A. Gollins[b], Monica Narvaez-Rivas[c], Kenneth D. R. Setchell[c,d], and Geoffrey A. Preidis[a]

[a]Division of Gastroenterology, Hepatology & Nutrition, Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston, TX, USA; [b]Division of Neonatology, Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston, TX, USA; [c]Division of Pathology and Laboratory Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA; [d]Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH, USA

Lauren Lynch

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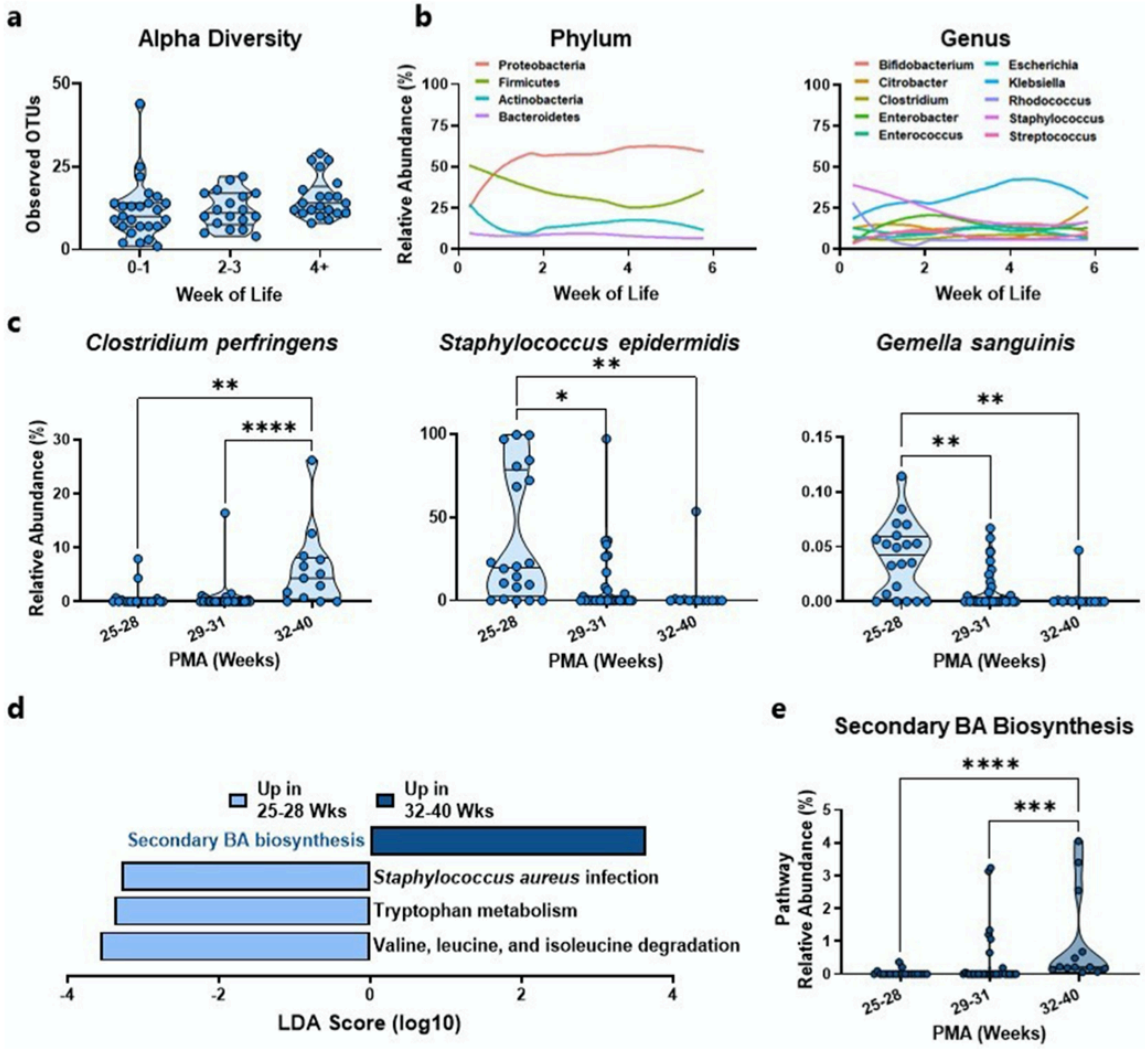


Figure 1. Development of the preterm gut microbiome in control neonates. (a) Observed OTUs increase with age over the first 6 weeks of life ($n = 18–25$). (b) The gut microbiome changes at both phylum and genus levels in the first 6 weeks of life ($n = 64$). (c) At the species level, *Clostridium perfringens* is most significantly increased and *Staphylococcus epidermidis* and *Gemella sanguinis* are most significantly decreased with increasing PMA ($n = 13–31$). (d) LEfSe analysis identified secondary bile acid biosynthesis as the most enriched pathway in control neonates 32–40 weeks PMA relative to control neonates 25–28 weeks PMA ($n = 20–31$). (e) The abundance of the secondary bile acid biosynthesis pathway increases with PMA ($n = 13–31$). BA, bile acid; LEfSe, linear discriminate analysis effect size; OTU, operational taxonomic unit; PMA, post-menstrual age. **** $P<0.0001$; *** $P<0.001$; ** $P<0.01$; * $P<0.05$.

Lynch, Hair, and Preidis. Gut Microbes 2023

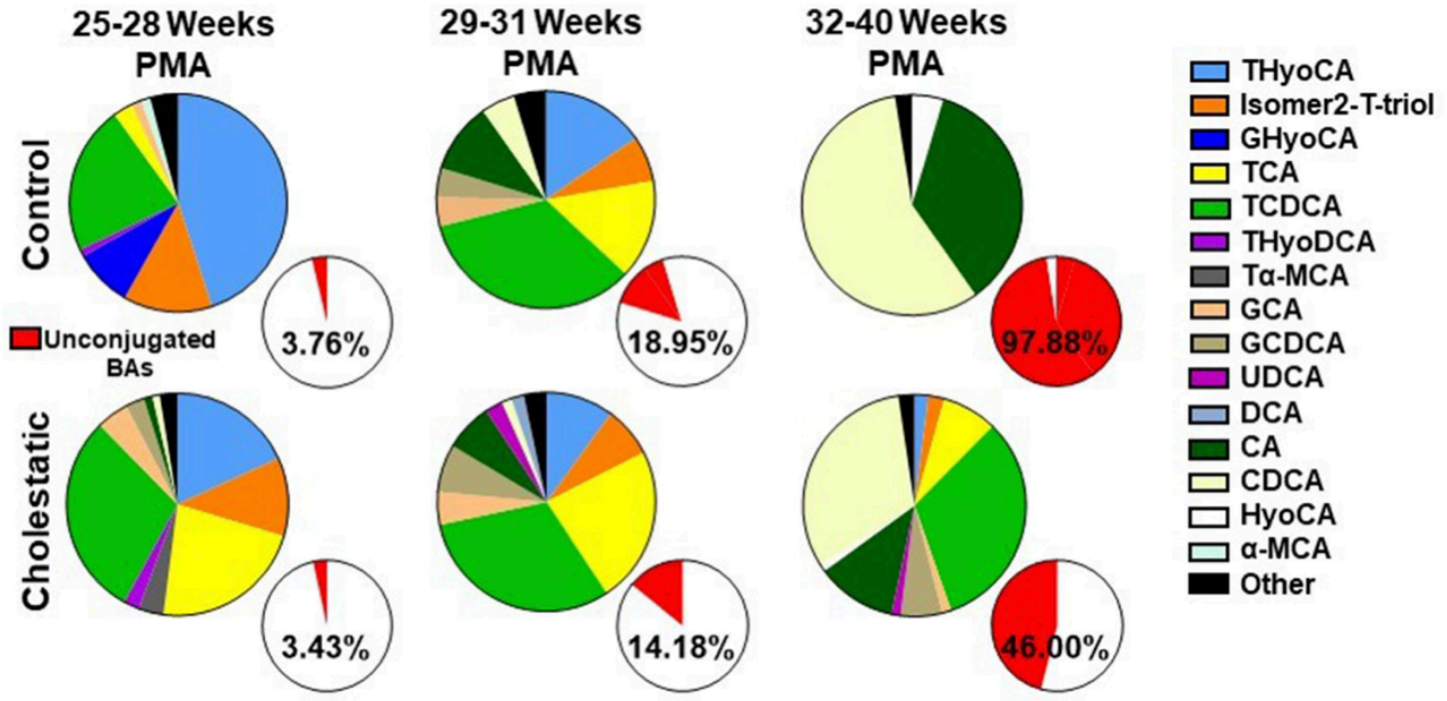


Figure 3. Fecal bile acid profiles are altered during cholestasis. Bile acid stereoisomers dominate in early development, then primary unconjugated bile acids increase in abundance in control neonates. Bile acid stereoisomers are less abundant and bile acid deconjugation is impaired in cholestatic neonates (excluding samples obtained during UDCA treatment) ($n = 14–26$). α-MCA, alpha-muricholic acid; CA, cholic acid; CDCA, chenodeoxycholic acid; DCA, deoxycholic acid; GCA, glycocholic acid; GCDCA, glycochenodeoxycholic acid; GHyoCA, glycohyocholic acid; HyoCA, hyocholic acid; Isomer2-T-Triol, taurine conjugate of an unidentified trihydroxy-cholanoic acid; PMA, post-menstrual age; Tα-MCA, tauro-α-muricholic acid; TCA, taurocholic acid; TCDCA, taurochenodeoxycholic acid; THyoCA, taurohyocholic acid; THyoDCA, taurohyodeoxycholic acid; UDCA, ursodeoxycholic acid.

Lynch, Hair, and Preidis. Gut Microbes 2023

CLINICAL RESEARCH ARTICLE

Check for updates

Human milk cream alters intestinal microbiome of preterm infants: a prospective cohort study

Grace O. Adeniyi-Ipadeola[1,2], Kristi L. Hoffman[3], Heeju Yang[4], Sara J. Javornik Cregeen[2,3], Geoffrey A. Preidis[5], Sasirekha Ramani[2] and Amy B. Hair[4]✉

Grace Adeniyi-Ipadeola

Kristi Hoffman

Sara Cregeen

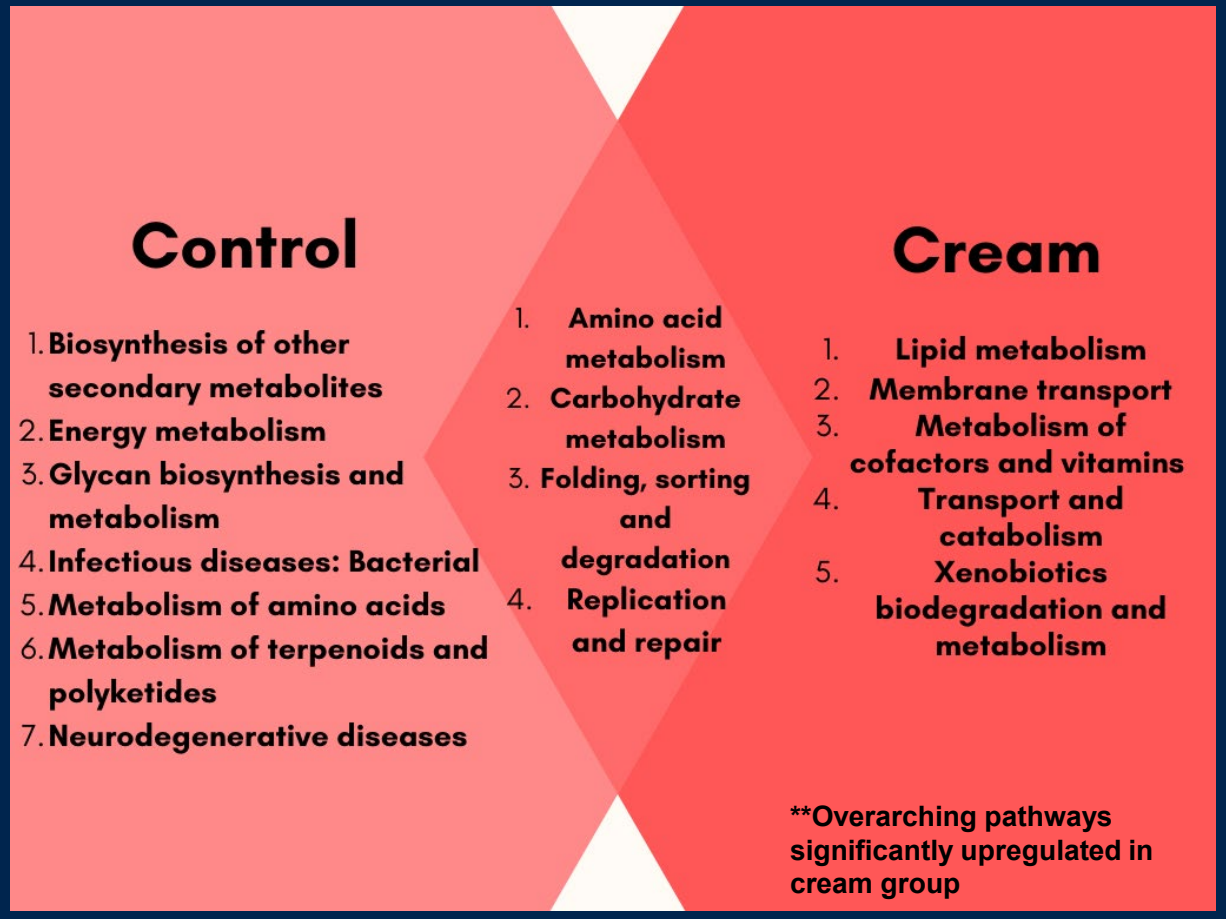
Sashi Ramani

Geoff Preidis

Texas Children's Hospital®

Baylor College of Medicine

Subset of Infants from the Cream RCT: Shared and distinct KEGG pathways of the bacterial metagenome in control and cream infants



Adeniyi-Ipadeola GO, Hoffman KL, Yang H, Javornik Cregeen SJ, Preidis GA, Ramani S, Hair AB. Human milk cream alters intestinal microbiome of preterm infants: a prospective cohort study. Pediatr Res. 2024 May;95(6):1564-1571. Epub 2024 Jan 16.

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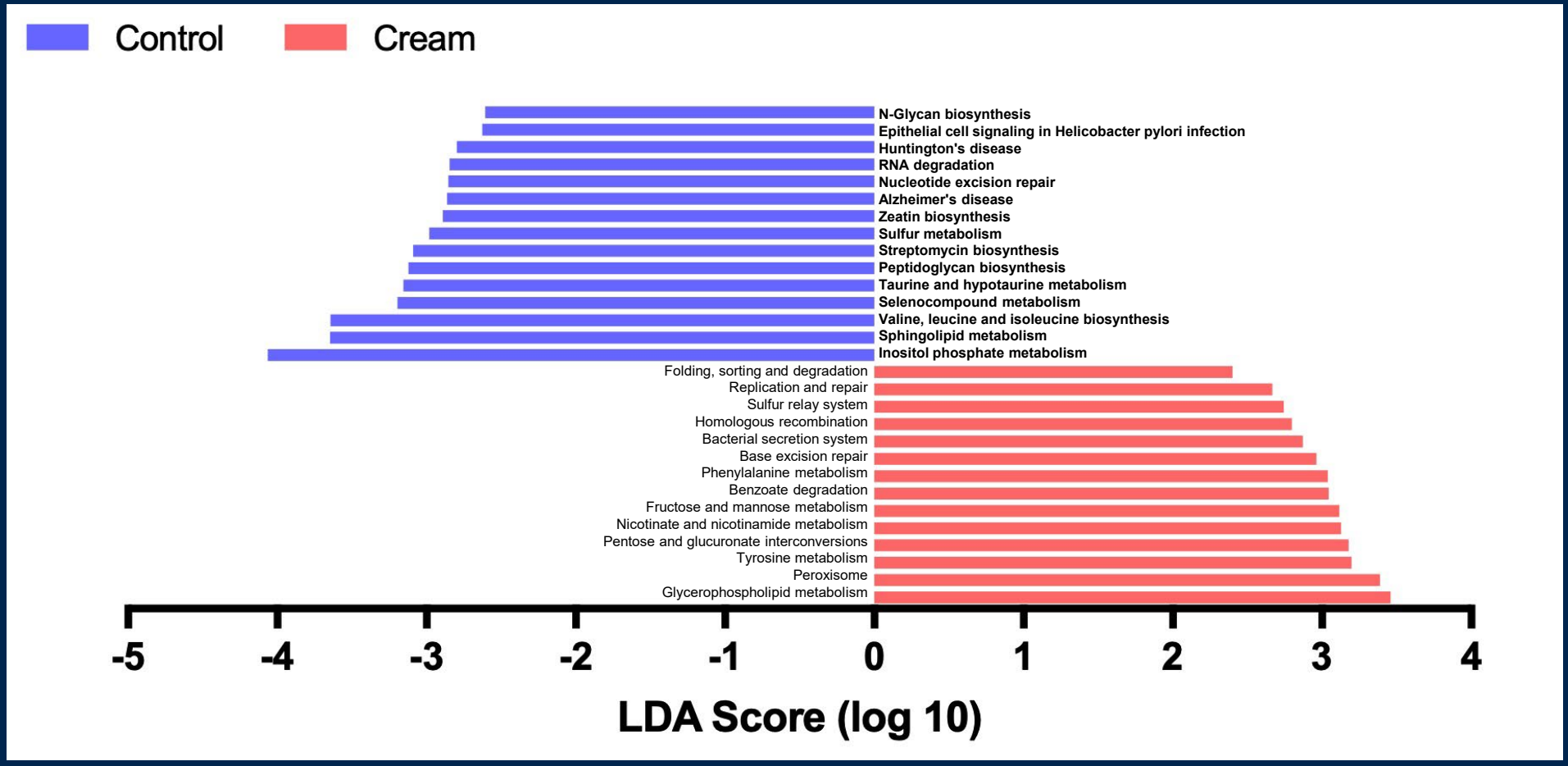
Significantly upregulated KEGG pathways



Horizontal bars represent the effect size for each pathway: blue color indicates pathways enriched in control group, and red color indicates pathways enriched in cream group. LDA score cutoff of 2 was used to discriminate pathways.

Adeniyi-Ipadeola, Hair, et. al. Pediatric Research 2024

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Challenges

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Current Large Studies

The ABSORB Study

LIVER-GUT-MICROBIOME AND FATTY ACID ABSORPTION IN PRETERM INFANTS

LET-FEED Trial

Limited versus Extended Trophic Feeding Trial

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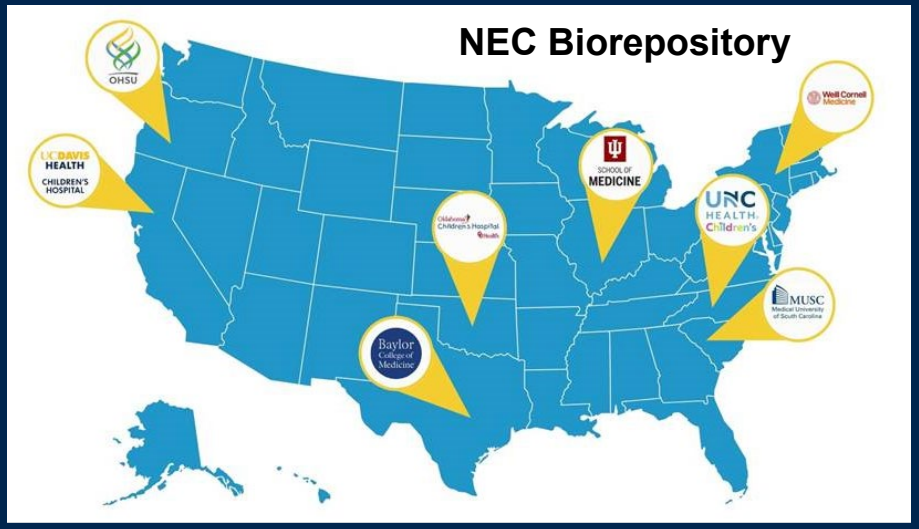

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Thank you!

Dr. Murali Premkumar – Associate Professor, Co-Director of NICU Intestinal Rehabilitation Team

NICU Intestinal Rehabilitation Attendings:
- Dr. Elena Itriago
- Dr. Emily Niemyjski

Neonatal Nutrition Program and Research Team:
- Laura Gollins – Clinical Program Coordinator
- Nora Abu-Hamdan- Research Coordinator
- Wen-Wen Wu- Research Coordinator
- Priscilla Vasquez- Senior Research Coordinator
- Jessica Nguyen- Clinical Research Manager
- Joe Hagan- Statistician

Neonatal Dietitians:
- Allyson Camp, Amy Carter, Nidia Delgado, Laura Lucas, Agnes Mandy, Adriana Massieu, Veronica Rubio

•Collaborators:
- Dr. Preidis, Dr. Misty Good, Dr. Cami Martin, Dr. Burrin, Dr. Roddy, Dr. Greg Valentine

National Institute of Diabetes and Digestive and Kidney Diseases

Eunice Kennedy Shriver National Institute of Child Health and Human Development

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