Grain Legumes as a Means to Improve Gut Health and Child Survival

SO3.1 :: Improving the Nutrition of the Poor, Especially Young Women and Children Through Grain Legume Consumption
Outline

1. Importance of undernutrition
2. Conceptual mechanisms of the association between EED, gut microbiome and stunting
3. Potential role of grain legumes in gut health
4. The legumes and growth research project
UNDERNUTRITION

• Stunting affects 25% of children globally, 35% in Africa.
• Stunted children are more likely to:
  – not attend secondary school.
  – Have reduced incomes as adults by up to 22%
  – Have reduced life expectancy by 17%
• Stunting is a priority target for the Sustainable Development Goals (SDGs)
• A significant portion of stunting comes from EED which comes from marginal diet + Dysbiosis.
• Legumes have dietary protein + oligosaccharides which can correct Dysbiosis.
STUNTING

Lancet Nutrition Series

Feed the Future Innovation Lab for Collaborative Research on Grain Legumes
Environmental contamination

Ingestion of microbes

Altered microbiota composition and function

Villous atrophy

Altered gut structure and function
Impaired epithelial regeneration

Impaired enterocyte tight junction function

Intestinal permeability

Microbial translocation

Mucosal inflammation

Systemic inflammation

GH resistance

↓Absorptive surface area

Nutrient malabsorption

↑Nutrient requirement

Impaired Linear growth

Marginal diet

Nutrient malabsorption

↓ Nutrient requirement

Impaired Linear growth

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Adapted - SHINE Trial
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**ENVIRONMENTAL ENTERIC DYSFUNCTION**

**Pathways and Genes activated**
- NF-kappa B signaling pathway
- Toll-like receptor signaling pathway
- NOD-like receptor signaling pathway
- Chemokine signaling pathway
- TNF signaling pathway
- Osteoclast differentiation
- B-cell receptor signalling pathway
- FC gamma R-mediated phagocytosis
- NK cell mediated cytotoxicity
- T-cell receptor signalling pathway

**KEGG Signalling Pathways**
- NF-κB signaling pathway
- Toll-like receptor signaling pathway
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**GeneGO Canonical Pathways**
- Integrin inside-out signalling in neutrophils
- Inhibition of neutrophil migration by proresolving lipid mediators in COPD
- Transcription regulation of granulocyte development
- Lipoxin inhibitory action on fMLF induced neutrophil chemotaxis
- G-CSF induced myeloid differentiation
- Chemokines and adhesion

**Transcripts**
- ARRB2, CXCR2, LYN, CLEC7A
- NCF2, FCGR2A, FCGR3B, BCL2A1, SOCS3, IFITM1, FCER1G, PIK3AP1

**Host Response**
- Recruitment of diverse immunologically active cells
- Enhanced anti-viral defenses
- Chronic inflammation
- Compromised Mucus layer
- Compromised cell adhesion and increased permeability
- Apoptosis
Abnormal Gut Integrity Is Associated With Reduced Linear Growth in Rural Malawian Children. Weisz et al. *JPGN* 2012; 55: 747

In 2-15 month old Gambian infants, up to 43% of observed growth faltering can be explained on the basis of long-term intestinal lesions.

Fig 2—The relation between intestinal permeability (expressed as log$_e$ lactulose/mannitol ratio) and mean monthly (a) length and (b) weight growth of 119 rural Gambian infants.

Significance of regression coefficients, p < 0.001.

HOW MIGHT GRAIN LEGUMES FIT IN?

• Marginal benefit with prior interventions (Antibiotics, diets etc.)
• Diets enriched in legumes decrease markers of inflammation
• Major source of protein and micronutrients in populations where carbohydrate consumption predominates.
• Low circulating levels of amino acids associated with stunting

J Nutr 2012; 142: 334
Nitric Oxide 1997; 1: 476
Lipids 2010; 45: 765
Eur J Clin Nutr 2011; 65: 415
Dry Beans and Pulses 2012
JPGN 2007; 44: 487
EBIOME DOI 10.1016/j.ebiom.2016.02.030

Feed the Future Innovation Lab for Collaborative Research on Grain Legumes
THE LEGUME AND GROWTH PROJECT

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STUDY HYPOTHESIS

Children provided with a legume supplement will have greater linear growth and an improvement in biomarkers of EED, compared to those who receive standard food supplements.
STUDY DESIGN

• **Design**
  – Randomized single blind block randomized clinical trials in 2 rural communities in southern Malawi.

• **Interventions**
  – Bean or cowpea flour vs. 10% corn-soy blend
  – Beans provide 40% and 20% of non breast milk calories for <1 year and >1 year olds respectively.
## SCHEDULE OF TRIAL PROCEDURES

### Table 3: Study participation schedule for subjects enrolled in Study 1

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LACTULOSE MANITOL RATIO TEST

1. Starve from 10pm (water and breast milk are permitted)
2. At 6 am, drinks a 20 ml solution containing 1 g mannitol and 5 g lactulose
3. Apply urine bags
4. Transfer urine into container containing 10 mg merthiolate to prevent bacterial degradation of the excreted sugars.
5. After 3–3.5 hours, give water to facilitate urine collection.
6. The total amount of urine voided during the study is quantified and an aliquot flash frozen for analysis.
STUDY OUTCOMES

• Primary Outcomes
  – HAZ change
  – LM ratio

• Secondary Outcomes
  – $\Delta$ in novel biomarkers of EE (cytokines and interleukins)
  – $\Delta$ in intestinal microbiome

Sequencing of bacterial genomic DNA from fecal samples to determine changes in population taxonomy and their collective metabolic capacity.
CURRENT STATUS

- Enrollment completed
- High retention rate (<10%)
- Projected completion Sep for study 1 and December for study 2
ACKNOWLEDGEMENTS

Participating children and their parents
Research project staff
Community extension workers in the study areas