Integrated multi-scale strategies to investigate nutritional compounds on the gut microbiota and host health: A story of iron

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The gut is home to a complex ecosystem made of innumerable different bacteria, harbouring over 3 million genes which is about 100 fold the coding capacity of our own genome. Scientists are only beginning to map this largely uncharted territory with the goal of improving health and well-being and gaining understanding of many chronic diseases. The human gut microbiota composition and metabolic activities are impacted by the diet and reciprocally, host metabolism and metabolites also interact with the gut microbiota and diet shaping a complex interaction network driving gut health [1]. Evidence of microbial perturbations and even dysbiosis of the human gut microbiota have been reported for many diseases and disorders including diabetes, malnutrition and obesity. It is, therefore, crucial to better understand the relationships between host, diet and the gut microbiota, starting by investigating the specific effects of the main components of the diet.

Iron (Fe) deficiency is one of the most common nutritional deficiencies affecting especially children and women in developing countries. Therefore, WHO recommends as a counteracting strategy either Fe supplementation of vulnerable groups or Fe fortification of staple foods. However, Fe is poorly absorbed and 90-95% of ingested Fe passes into the colon where it can interact with the gut microbiota. Fe is a key co-factor in many enzymatic reactions and is necessary for most organisms including commensals of the gut and enteric pathogens. However the effects of Fe deficiency and supplementation on gut microbes and gut health are not well characterized. Fe supplementation or fortification studies have reported an increase in infectious diseases including gastrointestinal disease symptoms such as diarrhea and dysentery. Therefore, concerns have been raised about the safety of untargeted Fe supplementation at high doses especially in areas with an increased infectious disease burden.

There is still a limited understanding of the mechanisms underlying the effects of unbalanced microbiota. We developed integrated multi-scale strategies involving combination of advanced *in vivo* and *in vitro* studies in a systematic approach to elucidate the complex effects and mechanisms of nutritional compounds on gut microbiota and host health [2]. In this presentation the application of strategy and novel tools will be illustrated for the elucidation of mechanisms of dietary iron on the gut microbiota of infants and inflammation of humans living in different environment. Our data from *in vitro* (continuous colonic fermentation and cellular) and *in vivo* (conventional and gnotobiotic rats) models of Fe deficient diet and human studies suggest that Fe supplementation is safe in environment with low infectious disease. Furthermore iron resulted in increased activity of the gut microbiota and energy extraction from the diet, as shown by enhanced production of short chain fatty acids, especially butyrate, during iron repletion. In contrast Fe supplementation of infected and malnourished infant in Africa resulted in promotion of enteropathogens and inhibition of beneficial bacteria, exacerbated existing gut inflammation, and interacted with pathogen virulence. From our research, safer iron supplementation strategies for infants in developing countries were designed. This includes the formulation of multi-nutrient supplements targeting both gut health and iron sufficiency, and the screening and development of novel strains of bifidobacteria with high iron binding ability.

Keywords: gut microbiota, dietary iron, models, host interaction, pathogens, inflammation

References

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