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Food, Pro and Prebiotics: Effects Beyond the Gut

Intestinal microflora: negotiating health outcomes with the warring community within us

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Digestion of food and absorption of nutrients constitutes the primary role of the gastrointestinal tract (GIT) of mammals. An extremely large surface area created by the complex involution of crypts and villi, and lined with epithelial cells has evolved to facilitate these functions. Some of the 400 species of micro-organisms in the GIT that are adherent, have exploited and adapted to particular microniches in different compartments of this vast intestinal real estate while the rest abound as free living entities sequestered in mucus or complexed with digesta in the lumen. Whether localised or in transit, these bacteria are continuously competing for survival[1]. The ability to persist and propagate or be ultimately eliminated, is dependent to a large extent upon the armoury of each combatant. Susceptibility or immunity of each strain to the arsenal of bacteriocins or quorum sensing factors produced by another constitutes a community at war.

While only a thin layer of epithelial cells known as enterocytes separates the host from the warring factions, they must form an effective barrier against incursions and introgressions by intestinal microflora. Erosion of this barrier integrity by stress, inflammation or disease would lead to translocation of bacteria into the blood stream. If pathogenic, the host would die from septicaemia unless the micro-organisms are eliminated by the immune system. For this reason, the bulk of cells aligned behind the layer of intestinal epithelial cells are immune cells that include lymphocytes, monocytes, macrophages, polymorphonuclear leukocytes and dendritic cells.[2] These immune cells form a nexus of innate and acquired immune capability that constitutes a formidable barrier against intending or inadvertent translocators.

Immune responses are not initiated only when barrier integrity is compromised. TOLL receptors on the lumenal surface of basolateral enterocytes can signal the presence of "dangerous" or pathogenic microbes and therefore arm the immune system. Alternatively, danger signals including soluble molecules that transgress enterocytes despite a tight barrier junction, can be detected by TOLL receptors on macrophages and dendritic cells. Signalling provides the main pathway of immune activation when the barrier integrity is intact and is the main mechanism for countering a suppressed or tolerized default intestinal immune response. Suppression of immune responsiveness is mandated in the GIT to prevent undesirable responses against dietary antigens that can lead to allergic disorders like food intolerance.[3] The GIT has evolved its own hazard analysis and critical control points (HACCP) to balance reactivity with tolerance and this balance can be manipulated by diet, using nutraceutical supplements. Indeed, nutritional strategies can be used to derive health outcomes by manipulating warfare between bacteria and bacteria, as well as preparing defence of the host against intruders.

A mouse model of inflammatory bowel disease initiated by the enterocyte denuding agent dextran sodium sulphate (DSS) was used to explore the intimate tripartite relationship between the host, intestinal bacteria and diet. In this model, DSS reproducibly initiates an inflammatory response in the colon. It is believed that barrier integrity, once compromised by DSS, facilitates an inflammatory response against harmful enteric bacteria populations. Use of antibiotics that target these bacteria significantly reduces the severity of inflammatory pathology. Following the same principle, modulation of the good-bad bacteria balance by administration of probiotic bacteria[4,5] also significantly reduced the inflammatory response associated with DSS treatment. Another example of dietary manipulation of gut microflora was provided by a series of studies designed to examine the benefits of low glycemic index diets normally recommended for diabetics. In these studies, rats fed a LGI starch supplement for 10 weeks, developed colon pathology associated with an increase in haemolytic bacteria. These animals were also immunologically less responsiveness than controls not fed the supplement. Shifts in the population dynamics of enteric bacteria can also be modulated by supplements containing decoctions of various mushroom or herbal extracts. Some of these supplements possessed statin-like properties and were capable of changing recipient responses to immunological challenge.

With the advent of sensitive molecular tools such as PCR (Polymerase Chain Reaction) and t-RFLP (terminal-Restricition Fragment Length Polymorphism), both cultivable and non-culturable bacteria populations can be analysed. At the same time, the development of microarrays including PAM (Patterned Antibody Microarrays), will permit accurate dissection of the immune response to dietary change or supplementation. Armed with these tools, it

is now timely to critically re-address the role of diets and dietary supplements in generating desirable health outcomes that are no longer delimited by our perception of the foods we ingest as simply being nutritional.[3,6]

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