



Technical Note no. 11

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Host-microbe interactions

Animals, including humans, have evolved in environments densely populated with diverse microbes. Many of these microorganisms may have no meaningful interaction with the host, while with others, depending on the microbe and the host response, disease (of varying severity) may result (Couto Garcia et al., 2010). Interactions that do occur, generally do so at mucosal surfaces such as the mucosa of the intestine. Traditionally, host-microbe interactions are categorised as mutualistic, commensalistic, or parasitic.

The host has developed elaborate strategies to prevent microbes from making direct contact at mucosal surfaces, these include peristalsis to sweep microorganisms through the intestine along with digesta, secretions (mucus, antibodies, peptides, enzymes) onto epithelial cells and into the gut lumen, and strategically positioned immune cells within the epithelium or immediately below. Moreover, the resident microbiome competes, for example for nutrients, through production of antimicrobial compounds, occupying colonisation sites, etc., against microorganisms arriving from the external environment. Should these barriers be insufficient, the host needs additional mechanisms to detect and respond appropriately to the invader. Pattern recognition receptors (PRR), which recognise conserved microbial structures, are the primary mechanism by which the host can survey microbial activity and are expressed by various host cells, including immune and epithelial cells. There are various PRR families, including soluble and cell-associated (surface or intracellular) components (Juul-Madsen et al., 2014). Activation of PRR by ligand binding initiates signalling pathways that, typically, lead to the production of important immune-signalling molecules (e.g. cytokines and chemokines) and a protective innate 'pro-inflammatory' response that typically deals with the threat and initiates resolution processes and adaptive responses if necessary. However, various factors, such as crosstalk between signalling pathways, pathway activation thresholds, feedback loops, etc., generally help tailor the response to the stimulus (Dorrington and Fraser, 2019).

Inflammatory responses are one of the most highly conserved biological processes, supporting their critical importance for host defence (Ashley et al., 2012). Inflammatory responses can, however, become dysregulated leading to greater tissue pathology or chronic disorders. While there has been great interest in 'anti-inflammatory' strategies, these have often failed or shown inconsistent results (Neurath, 2017). Evidence and hypotheses are shifting towards inadequate very early innate, inflammatory responses failing to create the

necessary context to control the infection or injury and thus dysregulating the immune response (Kumar, 2018). Therefore, attention is turning towards priming immune cells and/or pro-resolving, “immunoresolvent” strategies (Quiros and Nusrat, 2019). Exogenous administration of different PRR ligands (e.g. β -glucans, CpG ODN, etc.,) have been shown to be beneficial for various chicken pathogens, such as coccidiosis, avian influenza virus, *Salmonella*, *Escherichia coli* and Newcastle disease Virus, when provided either prophylactically or as vaccine adjuvants (Cox et al., 2010; St. Paul et al., 2013) or to correct dysregulated cell signalling (Villena et al., 2014). Recently, a novel group of mediators, produced mainly by innate immune cells, that promote clearance of pathogens and activate resolution pathways, and restore tissue homeostasis have been identified (Dalli, 2017). More work is required in this area, but such approaches may provide important opportunities. In addition, short-chain fatty acids produced in the intestine may affect the types of immune cells generated (by influencing haematopoiesis following host absorption) and/or shift immune cell metabolism and function, known as immunometabolism (Dang and Marsland, 2019).

Conclusions and implications

Hosts are continually exposed to microorganisms and have, generally, evolved appropriate protective barriers and immune, including highly conserved inflammatory, responses to manage most challenges they may face. Interactions between hosts and their microbiomes involve complex signalling pathways mediated to a great extent by PRR. ‘Anti-inflammatory’ strategies evolved from concerns about dysregulated inflammatory responses but, due to unsatisfactory outcomes, are being superseded by immunoresolving, innate immune cell priming and/or immunometabolism approaches, which offer great potential to influence host (gut) health, performance and welfare.

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