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Intestinal mucosal innate immunity

R. N. CUNLIFFE and Y. R. MAHIDA

INTRODUCTION

The largest area of interaction between the human host and microorganisms occurs in the gastrointestinal (GI) tract, which is the home of an enormous indigenous or commensal bacterial flora. A highly complex host-microbial relationship has evolved at the GI mucosal surface but the nature of this relationship is incompletely understood. The importance of this relationship is illustrated by the fact that animals in whom the mucosal immune system is dysregulated develop chronic intestinal inflammation, only in the presence of the normal luminal microbial flora (see Chapter 10). In the normal GI tract, the mucosal immune system is able to interact with the indigenous bacterial flora without generating an inflammatory response. On the other hand it is able to mount an effective host response against pathogenic microorganisms when required. In the GI tract, as elsewhere in the body, defence against infection is mediated by innate and adaptive immune mechanisms.

ADAPTIVE IMMUNITY

Adaptive (or acquired) immune responses are specific for given microorganisms. In the GI tract they involve the cells of the gut-associated lymphoid tissue (GALT) and in particular result in the production of secretory IgA (sIgA) antibodies (see Chapter 2), which act in the epithelial

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fluid layer to inhibit attachment of microorganisms to epithelial cells – so called ‘immune exclusion’. In addition to providing a highly specific response, adaptive immunity is lasting in that antigen specific ‘memory’ B and T lymphocytes are preserved after an infection is eliminated and are able to mount a rapid host response when the same antigen is next encountered. The main disadvantage of the adaptive immune response is that it takes many days to develop but the generation time of most potential bacterial pathogens is much more rapid.

INNATE IMMUNITY

In contrast to the adaptive immunity, the innate immune response is either pre-existing or rapidly inducible, and is able to contribute to the elimination of invading microorganisms immediately upon exposure. Cells and molecules of the innate immune system recognise common conserved components of microorganisms such as lipopolysaccharide (LPS) and microbial carbohydrates (e.g. mannose), and are thus able to distinguish potentially infectious entities from host cells. Prior exposure to such molecules is not necessary for innate immune function, and upon re-exposure the same innate response will result since there is no memory effect (1,2).

Systemic innate immunity.
Phagocytic cells, the complement cascade and natural killer (NK) cells are components of innate immunity that function systemically. In the GI tract, these cells and molecules will be active in the lamina propria, and are able to migrate or diffuse through the epithelial cell layer to the mucosal surface and lumen, particularly once an inflammatory reaction has been generated.

The phagocytic cells, neutrophils and monocytes / macrophages are able to engulf bacteria, which are then killed within phagolysosomes by a variety of mechanisms. These can be oxygen-dependent utilising oxidants such as hydrogen peroxide and hypochlorite, or oxygen-independent utilising a variety of antimicrobial peptides and proteins (3) which will be considered in subsequent sections. A further important function of phagocytes is the release of chemokines and cytokines which serve to enhance the inflammatory response.

Complement comprises a cascade system of soluble plasma proteins that is able to bind microbial cells ultimately resulting in their cell lysis. Via the alternative pathway, the complement cascade is activated by recognition of bacterial cell surface components, and thus functions as part of the innate immune system.