We are IntechOpen, the world’s leading publisher of Open Access books
Built by scientists, for scientists

3,800 Open access books available
116,000 International authors and editors
120M Downloads

154 Countries delivered to
TOP 1% Our authors are among the most cited scientists
12.2% Contributors from top 500 universities

WEB OF SCIENCE™
Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com
Alteration of the Crypt Epithelial-Stromal Interface by Proinflammatory Cytokines in Crohn's Disease

Amira Seltana, Manon Lepage and Jean-François Beaulieu

Université de Sherbrooke
Canada

1. Introduction

The intestinal epithelium is a very dynamic tissue, being completely renewed over a 3-5 day period in the human. Epithelial cells in the intestine lie on a specialized layer of extracellular matrix material referred to as the basement membrane (BM). Intestinal epithelial cell interactions with BM molecules such as collagens, laminins, fibronectin and tenascin regulate crucial functions of the normal intestinal epithelial renewal process such as cell adhesion, migration, signalization and gene expression as well as anoikis. BM molecules can be secreted by epithelial cells but a number of them are exclusively synthesized and deposited by the subepithelial myofibroblasts. In this chapter, we will review alterations at the epithelial-stromal interface in Crohn's disease (CD) with a specific emphasis on epithelial cell and myofibroblast susceptibility to proinflammatory cytokines in the crypt region.

2. Epithelial BM molecules in the normal human intestine

The epithelial BM of the human intestine has been found to contain all the major components specific to most basement membranes as well as a number of non-exclusive BM components. There is good evidence that both types of BM components play an active role in intestinal epithelial cell biology through their interaction with specific cell membrane integrin and non-integrin receptors, which mediate cell adhesion, migration, cell cycle and gene expression. Current knowledge about epithelial BM composition in the normal human intestine is summarized below. More detailed information on BM molecules and their receptors in the intestine can be found elsewhere (Beaulieu 1997a, Beaulieu 2001, Lussier et al. 2000, Ménard et al. 2006, Teller&Beaulieu 2001).

2.1 Exclusive and non-exclusive BM components

As illustrated in Figure 1, exclusive BM components include the type IV collagens and laminins. These macromolecules are complex protein families composed of various sub-units. Detailed analysis of various genetic forms of type IV collagens and laminins revealed the presence of at least two distinct types of type IV collagen heterotrimers based on the expression of the α1(IV)/α2(IV) and α5(IV)/α6(IV) chains (Beaulieu 1992, Beaulieu et al.
Crohn’s Disease


A second interesting feature of the intestinal epithelial BM is the presence of a relatively large number of non-exclusive BM components, such as fibronectin, tenascin-C, osteopontin and type VI collagen that have been found to be integral epithelial BM components (Auferheide & Ekblom 1988, Beaulieu et al. 1991, Beaulieu 1992, Groulx et al. 2011, Simon-Assmann et al. 1990b) although they can be found also in the underlying interstitial matrix (Fig. 1).

The third interesting phenomenon relative to the epithelial BM in the intestine is the dual tissular origin of the BM components. Indeed, while the type IV collagen α5(IV) and α6(IV) chains as well as type VI collagen are expressed at least in part by epithelial cells, the major type IV collagen chains α1(IV) and α2(IV) are exclusively of stromal origin (Beaulieu et al. 1994, Groulx et al. 2011, Simon-Assmann et al. 1990a, Simoneau et al. 1998, Vachon et al. 1993), presumably synthesized by the subepithelial myofibroblasts (Fig. 1). Analysis of the tissular origin of the laminins also revealed dual epithelial/stromal origin for laminins LM-111 and LM-332 (epithelial), LM211 (stromal) and LM511 (both) (Perreault et al. 1998, Teller et al. 2007).

2.2 Spatial and temporal BM microenvironments

Spatial and temporal patterns of expression for BM components in the intact intestinal epithelium have been very informative in evaluating the potential role of individual macromolecules in the regulation of cell functions, most notably cell growth and differentiation, under a normal environment. Indeed, during development, the process of endodermal differentiation into a functional epithelium coincides with the morphogenesis of the villi and the crypts in both the small and large intestines. In the mature intestine, the

Fig. 1. The intestinal epithelial BM. The BM, which is located at the interface between the epithelial cells (e) and the subepithelial myofibroblasts (m), contains BM-specific macromolecules (e.g. type IV collagens and laminins) as well as non-exclusive BM components (e.g. tenascin-C and type VI collagen). Both types of components can originate from the epithelial cells and/or the subepithelial myofibroblasts (white arrows).

The third interesting phenomenon relative to the epithelial BM in the intestine is the dual tissular origin of the BM components. Indeed, while the type IV collagen α5(IV) and α6(IV) chains as well as type VI collagen are expressed at least in part by epithelial cells, the major type IV collagen chains α1(IV) and α2(IV) are exclusively of stromal origin (Beaulieu et al. 1994, Groulx et al. 2011, Simon-Assmann et al. 1990a, Simoneau et al. 1998, Vachon et al. 1993), presumably synthesized by the subepithelial myofibroblasts (Fig. 1). Analysis of the tissular origin of the laminins also revealed dual epithelial/stromal origin for laminins LM-111 and LM-332 (epithelial), LM211 (stromal) and LM511 (both) (Perreault et al. 1998, Teller et al. 2007).

2.2 Spatial and temporal BM microenvironments

Spatial and temporal patterns of expression for BM components in the intact intestinal epithelium have been very informative in evaluating the potential role of individual macromolecules in the regulation of cell functions, most notably cell growth and differentiation, under a normal environment. Indeed, during development, the process of endodermal differentiation into a functional epithelium coincides with the morphogenesis of the villi and the crypts in both the small and large intestines. In the mature intestine, the


Alteration of the Crypt Epithelial-Stromal Interface
by Proinflammatory Cytokines in Crohn’s Disease


In this book, several important points regarding Crohn's disease are discussed. In the first section, we focus on etiopathogeny of Crohn's disease and the recent advances in our overall understanding of the disease - specifically, the role of the gut epithelium, alterations of the epithelial crypts, and the roles of the different cytokines in the pathophysiology of Crohn's disease. In the second section, a diagnosis of Crohn's disease is discussed. Another particular area of focus is in the diagnosis of intestinal tuberculosis, and the role of mycobacterium avium in Crohn's disease. In the third and final section, the management of Crohn's disease is discussed, with a focus on recent evidence-based medicine recommendations.

How to reference
In order to correctly reference this scholarly work, feel free to copy and paste the following:
