Unfolding the Role of PKC Isoforms in Intestinal Physiology

Editorial

The protein kinase C (PKC) family has twelve isoforms [1], and the number of biological events driven by PKC isoforms is expanding. Some of the pathways the PKCs are involved encompass, but not restricted to: cell division, migration, apoptosis, protein trafficking, regulation of ion transport and barrier function [1-3]. Maintenance of intestinal barrier function is critical in order to preserve normal transepithelial transport as well as to prevent pathogens and toxins from entering the body [4]. For instance, PKCα, PKCβII, PKCδ, PKCε or PKCα have been shown to modulate intestinal barrier integrity during inflammation or cell injury [3], by phosphorylating tight junction proteins or cytoskeleton proteins [3,4]. Some of the previous mentioned PKC isoforms are also involved in the regulation of ion transport in the intestine. For example, PKCα is a well-known regulator of the Na/H exchanger, which participates in NaCl absorption in the intestine [5]. PKCε and PKCδ are implicated in the internalization of the Na-K-2Cl cotransporter 1, and thus decrease in fluid secretion in the colon [6]. In addition PKCδ has been also suggested to decrease Cl− secretion in the colon by blocking the K+-channel KCNQ1 [7].

As mentioned, the same isoform can be involved in very different biological processes. Thus, one important question arising from these observations: How is the same isoform driving specifically different biological events? Specificity is conveyed by the spatio-temporal distribution of the isoform, which is dependent on the association of the isoform with specific binding proteins such as receptor activated C kinase, A kinase anchoring protein or annexins [8,9]. The second mechanism being the target proteins phosphorylated by PKC isoform such as myristoylated, alanine rich C kinase substrate or adducin [9,10]. To date the proteins implicated in the specificity of the PKC isoform in intestinal biology (e.g., ion transport, barrier function) remains elusive. Much work is needed if we intend to understand how barrier function and ion transport are regulated by the PKC in normal and disease states in the intestine. Defining the scaffolding and target proteins of the PKC isoform may prove very useful targets to treat diseases such intestinal inflammation or cancer [11].

References