NGF—not just a nerve growth factor in the gut

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In the intestinal epithelium, complex regulation is necessary to downregulate and control inflammation. The focus has been on the role of transforming growth factor (TGF)-β and IL-10 in this regulatory process (6). In the paper of Ma et al. (7) in this issue of the American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, nerve growth factor (NGF) is added to the regulatory components of this system. NGF causes a dose-dependent increase of IL-10 secretion in intestinal epithelial cells, and, reciprocally, IL-10 causes NGF upregulation in the epithelium.

This finding leads to a variety of new questions. What is the source of NGF in the gastrointestinal tract? In addition to epithelial cells, NGF is secreted by glial cells, fibroblasts, and a variety of immune cells, such as activated T cells, mast cells, and dendritic cells (5). Activated T cells can secrete neurotrophins such as NGF in a clonally restricted manner and show a Th1/Th2 polarized expression of high-affinity Trk receptors (2). This leads to an even higher level of complexity in the regulation.

To surmount this, it has been shown recently that NGF is secreted in part as a high molecular weight pro-NGF (4, 8). Pro-NGF binds to p75NTR with a five times greater affinity than mature NGF, whereas pro-NGF is ineffective in displacing mature NGF from Trk A (4). In neuronal cells, preferential activation of p75NTR leads to apoptosis, whereas preferential activation of Trk A confers survival of the cells (3). This proapoptotic effect of pro-NGF has been shown recently in oligodendrocytes (1). It was hypothesized that pro-NGF has the role to eliminate damaged cells by activating the proapoptotic function of p75NTR after injury. Pro-NGF is expressed in the colon and profoundly upregulated during inflammation (8, 9).

Therefore, we can summarize at this point that NGF downregulates immune function in the epithelium by secretion of IL-10, interacts with a variety of immune cells, and might be involved in the regulation of apoptosis of epithelial cells during inflammation. It will be a fascinating challenge to further elucidate the complex regulatory functions of the “nerve growth factor” NGF in the gastrointestinal tract.

REFERENCES