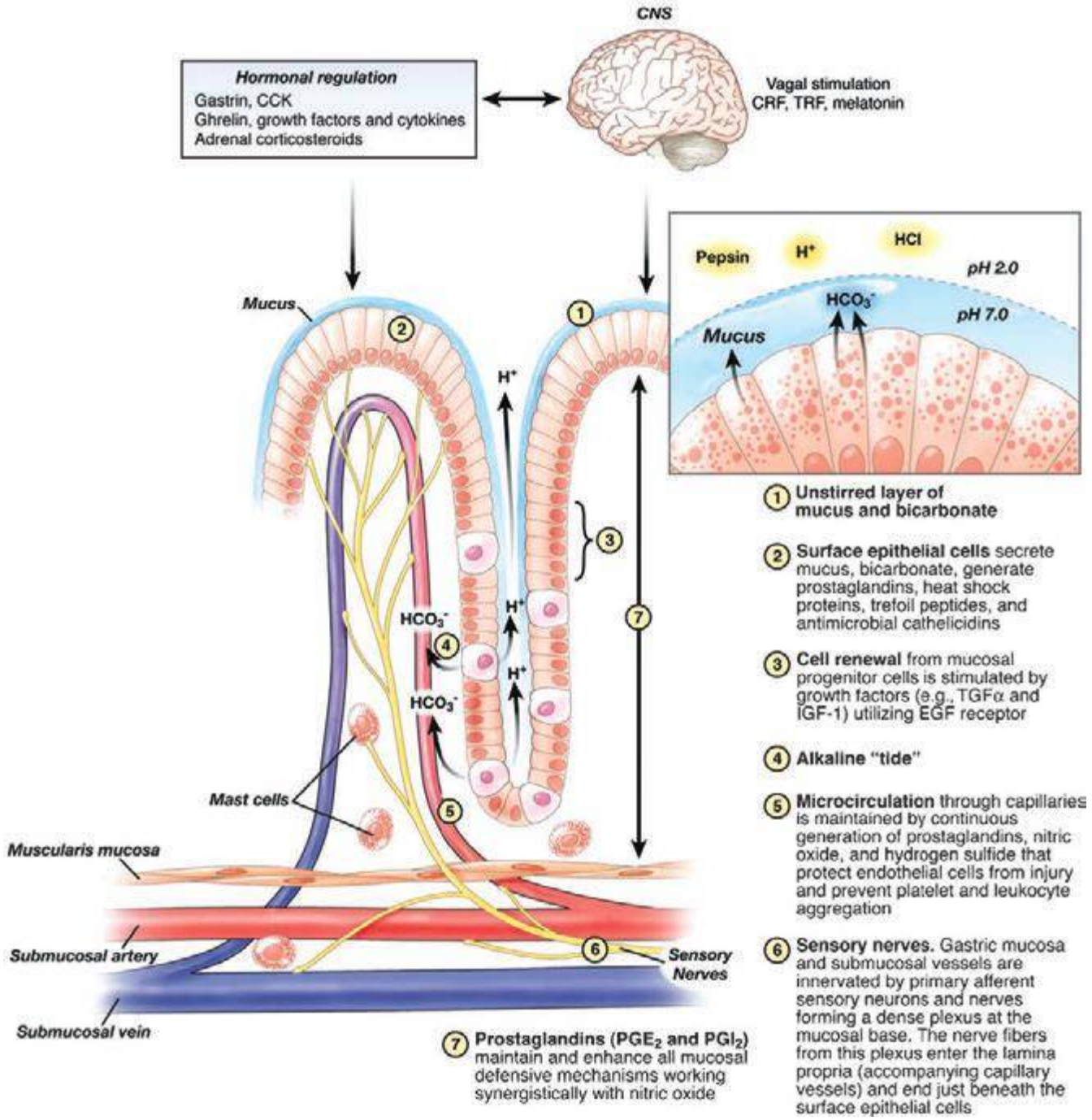

FIGURE 348-3 Components involved in providing gastroduodenal mucosal defense and repair. CCK, cholecystokinin; CRF, corticotropin-releasing factor; EGF, epidermal growth factor; HCl, hydrochloride; IGF, insulin-like growth factor; TGFα, transforming growth factor α; TRF, thyrotropin releasing factor. *(Modified and updated from Tarnawski A. Cellular and molecular mechanisms of mucosal defense and repair. In: Yoshikawa T, Arakawa T. Bioregulation and Its Disorders in the Gastrointestinal Tract. Tokyo, Japan: Blackwell Science, 1998:3–17.)*

stomach, may increase gastric acid secretion through stimulation of histamine release from ECL cells, but this remains to be confirmed.

The acid-secreting parietal cell is located in the oxyntic gland, adjacent to other cellular elements (ECL cell, D cell) important in the gastric secretory process (Fig. 348-5). This unique cell also secretes intrinsic factor (IF) and IL-11. The parietal cell expresses receptors for several stimulants of acid secretion, including histamine (H_2), gastrin (cholecystokinin B/gastrin receptor), and acetylcholine (muscarinic, M_3). Binding of histamine to the H_2 receptor leads to activation of adenylate cyclase and an increase in cyclic adenosine monophosphate (AMP). Activation of the gastrin and muscarinic receptors results in activation of the protein kinase C/phosphoinositide signaling pathway. Each of these signaling pathways in turn regulates a series of downstream kinase cascades that control the acid-secreting pump, H^+,K^+-ATPase. The discovery that different ligands and their corresponding receptors lead to activation of different signaling pathways explains the potentiation of acid secretion that occurs when histamine and gastrin or acetylcholine are combined. More importantly, this observation explains why blocking one receptor type (H_2) decreases acid secretion stimulated by agents that activate a different pathway (gastrin, acetylcholine). Parietal cells also express receptors for ligands that inhibit acid production (prostaglandins, somatostatin, and EGF). Histamine also stimulates gastric acid secretion indirectly by activating the histamine H_3 receptor on D-cells, which inhibits somatostatin release.

The enzyme H^+,K^+-ATPase is responsible for generating the large concentration of H^+. It is a membrane-bound protein that consists of two subunits, α and β. The active catalytic site is found within the α subunit; the function of the β subunit is unclear. This enzyme uses the