

## Letter To Editor

### Enteric Glial Cells and Inflammatory Bowel Disease : Friend or Foe

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Sir,

Inflammatory bowel disease (IBD; Crohn's disease (CD), ulcerative colitis (UC)) are chronic relapsing diseases that lead to structural damage to the intestine and destruction of the bowel wall. Clinically, IBD patients can suffer from intestinal and extraintestinal manifestations. Patients with IBD are at increased risk of neoplasia. There is increasing incidences of IBD in Asian population and it is no surprize that IBD can impede career aspirations, instill social stigma and impair quality of life in patients. Enteric glial cells (EGC) are the main constituents of enteric nervous system (ENS) and are phenotypically equivalent to astrocytes in the brain. These cells are far more in number as compared to the neurons in the ENS. However, they are poorly studied as compared to the neurons. These cells form extensive communication network with other cells of the gut, such as, neurons, glial cells, immune cells, or other cells in the gut microenvironment. So many scientists have now started thinking about the roles of enteric glial cells in the gut homeostasis and inflammatory disorders.

Enteric glial cells are essential in the control of gut functions. In the past few years, these cells have been found to be participating in almost all the functions of gut, including motility, mucosal secretion, intestinal epithelial barrier integrity and cytoprotection(1). Moreover, these cells have immunomodulatory roles, they can express MCH class II molecules (2) and secrete pro-inflammatory cytokines (IL-1, IL-6), nitric oxide(NO), S-Nitrosoglutathione (GNSO), glial-derived neurotrophic factor (GDNF) (3, 4), vascular endothelial growth factors (VEGF) and many other signalling molecules. Similarly, under inflammatory conditions there is activation of EGC with increased expression of

cytoskeletal glial fibrillary acidic protein (GFAP). In the biopsy samples from the inflamed region of the gut there was increase in the levels of GFAP and GDNF observed in patients with UC and relatively lower levels in patients with CD (5). Human-derived EGC responds to the pathogenic, but not probiotic bacteria by stimulating the release of NO via the involvement of both toll-like receptors (TLR) and S100B/RAGE pathways (4). These finding highlight the important role of glial cells as *primummovers* in triggering and amplifying the gut inflammation. Signalling molecules leading to activation of the TLR-S100B/RAGE-iNOS-NO deserve further exploration to study human EGC function in the regulation of gut motility. Also for ischemia-reperfusion injury, increased evidence associate distinct abnormality of the intestine muscles (6), ENS and EGC (7) which may be associated with disturbed motility patters associated with ischemia-reperfusion injury. A corollary is that protection of glia may be a significant therapeutic target for inflammatory disorders of gut.

The concept of enteric glial cells as regulators of intestinal homeostasis is slowly gaining acceptance as a central concept in neurogastroenterology. Yet the precise role of EGCs in gastrointestinal physiology and pathophysiology is not well understood. Calcium ion ( $Ca^{2+}$ ) is universally used throughout phylogeny and by all cell types for signal transduction. Release of various neurotransmitters can initiate changes in  $Ca^{2+}$  responses in glial cells, but it is not clear how the  $Ca^{2+}$  signalling of EGCs is altered during inflammatory disorders of the gut. Therefore, with the advancement in the newer methods to study  $Ca^{2+}$  signalling, experimental approaches providing mechanistic insights into the diverse mechanisms of intra-glial  $Ca^{2+}$  signalling are

needed to understand how enteric glia influence gastrointestinal physiology and identifying how

those roles are altered during gastrointestinal pathophysiology remain areas of intense research.

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