Dig Dis Sci (2017) 62:2780
DOI 10.1007/s10620-017-4709-5

CONCISE COMMENTARY

Therapeutic Potential of the Gabaergic System in Ulcerative Colitis: Current Status and Perspectives

Maria Grazia Zizzo[1,2] · **Rosa Serio**[2]

Published online: 5 August 2017

An extensive body of literature supports the physiological and pathological importance of γ-amino butyric acid (GABA)ergic signalling in the gut. Although the functional significance of GABA in the gastrointestinal tract is still a matter of debate, GABA may contribute to the "neuroimmune dialogue" between the enteric nervous system and the intestinal mucosal immune system during inflammatory events [1] such as with the prototypic gut inflammatory disease, inflammatory bowel disease (IBD).

In this issue of *Digestive Diseases and Sciences*, Aggarwal et al. [2] provide data supporting the contribution of GABA and GABAergic signalling to the pathogenesis of ulcerative colitis (UC) in humans. The study reports reduced serum concentrations of GABA in the colonic mucosa of UC patients, correlated with dysbiosis of GABA-producing bacteria, suggesting that GABA may contribute to IBD pathogenesis and that its replacement may be therapeutic. These data support previous studies implicating intestinal bacteria in the initiation and amplification stages of IBD [3] and suggest that GABA-producing commensal bacteria could be exploited to compensate for the reduced GABA concentrations in UC patients. Nevertheless, the sources of GABA in the gut and in the GABAergic signalling system observed in the mucosa of UC patients are currently unknown; future investigations of the mucosal cellular subtypes involved in the production of GABA are needed to help identify these sources. Furthermore, since the occurrence and distribution of GABA in the enteric neurons regulating motor and secretory processes has already been reported, further structural and functional in-depth analysis of the GABAergic neurons in the gut of IBD patients is of interest.

The possible anti-inflammatory effects of GABA, including the pivotal contribution of the π subunit of the GABA-A receptor (GABPR), likely upregulated during low availability of ligand, are in need of further exploration. Despite the existence of fundamental observations concerning the therapeutic actions of GABA-A agonists and their possible clinical utility, clinical translation of fundamental data, however, is problematic, due to the potential severe adverse effects of GABA-A receptor modulators. Future studies of specific GABAergic agents, in particular those acting on the GABPR, are needed to extend and to provide therapeutic translation to the observations of Aggarwal et al.

References

1. Auteri M, Zizzo MG, Serio R. The GABAergic system and the gastrointestinal physiopathology. *Curr Pharm Des*. 2015;21:4996–5016.
2. Aggarwal S, Ahuja V, Paul J. Attenuated GABAergic signaling in intestinal epithelium contributes to pathogenesis of ulcerative colitis. *Dig Dis Sci*. (Epub ahead of print). doi:10.1007/s10620-017-4662-3.
3. Tamboli CP, Neut C, Desreumaux P, Colombel JF. Dysbiosis in inflammatory bowel disease. *Gut*. 2004;53:1–4.

✉ Rosa Serio
rosa.serio@unipa.it

[1] Dipartimento di Scienze e Tecnologie Biologiche Chimiche e Farmaceutiche (STEBICEF), Laboratorio di Fisiologia Generale, Università di Palermo, Viale delle Scienze, 90128 Palermo, Italy

[2] ATeN (Advanced Technologies Network) Center, Università di Palermo, Viale delle Scienze, 90128 Palermo, Italy