Nature Reviews Gastroenterology & Hepatology **9**, 489 (2012); published online 24 July 2012; doi:10.1038/nrgastro.2012.142

IBS

Distinct neuro–immune patterns defined in IBS subtypes

Distinct patterns of neuro–immune dysfunction exist in patients with IBS, with marked differences between IBS subtypes, according to new research published in *Gut*. "Not only is the immune profile different, but these alterations result in differential activation of sensory nerve endings innervating the colon," notes first author Patrick Hughes.

IBS is a chronic and debilitating gastrointestinal functional disorder, but little is known about the underlying mechanisms of disease. As alterations in the brain–gut axis and an aberrant immune response have already been implicated in the pathogenesis of IBS, Hughes *et al.* sought to characterize patients with different IBS subtypes in terms of immune profile and function.

The researchers enrolled 35 patients with IBS—15 with constipation-predominant IBS (C-IBS) and 20 with diarrhoea-predominant IBS (D-IBS)—and 36 age-matched healthy individuals as controls. Blood samples were then taken, peripheral blood mononuclear cells (PBMCs) isolated and PBMC supernatants collected for cytokine profile analysis and mechanosensitivity testing (by applying supernatants to mouse colonic afferent nerve endings).

> "...a single therapeutic treatment is unlikely to be useful for all classes of patients..."

Exploring the effects on colonic afferent nerves, the authors found that D-IBS supernatants made the nerve afferents more sensitive to mechanical stimuli, but not C-IBS supernatants. Unexpectedly, supernatants from healthy individuals actually inhibited mechanosensitivity in the nerves; a mechanism that, according to the new data, occurs in an opioid-dependent manner and via β-endorphin secretion.

Next, the immune profiles of the different PBMC supernatants were characterized. Importantly, levels of proinflammatory cytokines were increased in D-IBS supernatants (including IL-1β, IL-6 and tumour necrosis factor [TNF])—with TNF levels correlating with pain frequency and intensity in the patients—but not in C-IBS supernatants or controls.

"Immune-based therapies may provide benefit to patients with IBS, particularly those with D-IBS," concludes Hughes. However, he cautions that "a single therapeutic treatment is unlikely to be useful for all classes of patients with IBS, and potential treatments should be tailored to specific IBS types."

Katrina Ray

Original article Hughes, P.A. *et al.* Sensory neuro-immune interactions differ between irritable bowel syndrome subtypes. *Gut* doi:10.1136/gutjnl-2011-301856