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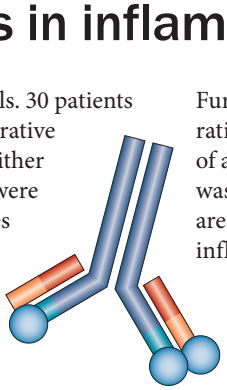
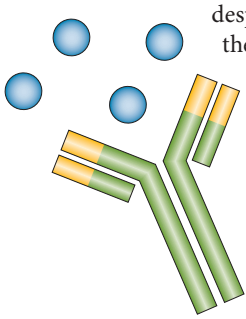
IBD

Tracking TNF and anti-TNF agents in inflamed gut tissue



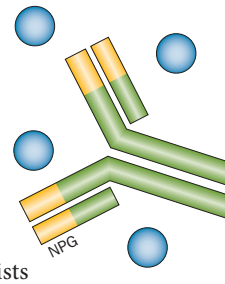
Higher levels of the cytokine TNF in inflamed mucosal tissue greater than local levels of anti-TNF agents could explain why some patients with IBD still have active disease despite treatment with TNF antagonists. "We had the concept that the more inflammation there is the more of the anti-TNF [agent] we need —as if the inflammation was a sump for the anti-TNF [drug]," explains author Maria Abreu.



Anti-TNF drugs are effective treatments for IBD, but some patients do not respond to therapy despite having detectable therapeutic serum levels of the drugs (an indicator of efficacy). In their study published in *Gut*, Abreu and colleagues questioned whether serum and intestinal levels of anti-TNF agents correlated with endoscopic disease activity and tissue TNF levels. 30 patients with Crohn's disease or ulcerative colitis who were receiving either infliximab or adalimumab were assessed, and biopsy samples were obtained from both inflamed and uninflamed intestinal tissue.

The researchers first confirmed that anti-TNF drug levels could indeed be measured accurately and reproducibly in intestinal tissue, which were positively correlated to serum levels of the drugs. Moreover, a positive correlation was observed between the level of mucosal inflammation and tissue TNF levels.

Crucially, during active inflammation, a discordance between serum and tissue levels of anti-TNF drugs was observed; this drug level mismatch (higher in serum, lower in tissue) was found in 73.3% of patients with active disease versus only 33.3% of patients in remission.



Furthermore, the ratio of tissue levels of anti-TNF drug to TNF was highest in uninflamed areas and lowest in severely inflamed areas.

More work is needed to clarify whether increasing the dose of TNF antagonists in patients with IBD could also increase drug levels in tissue to ameliorate disease. "It would be great ... if we could somehow measure local levels of TNF so that we could determine what the proper dose of anti-TNF [drug] should be—that is, measure the TNF burden in an individual patient," notes Abreu.

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Original article Yarur, A. J. *et al.* The association of tissue anti-TNF drug levels with serological and endoscopic disease activity in inflammatory bowel disease: the ATLAS study. *Gut* doi:10.1136/gutjnl-2014-308099