

**Exploring possible role of TGR5 and FXR in autoimmune neuropathy;** BETTY SOLIVEN,  
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Autoimmune diseases develop when the immune system mistakenly attacks the body's own tissue, which often results from an imbalance between activation of the immune response and the regulatory mechanisms. There is some evidence that microbial balance in our gut regulates our immune system via changes in short chain fatty acids, bile acids and other metabolites. Bile acids act on a variety of receptors including the so called TGR5 and FXR expressed on immune cells.

The objectives of this pilot project were: 1) to examine whether patients with GBS or CIDP would exhibit altered expression or function of these receptors in T and B lymphocytes, and 2) to delineate the role of these receptors in mouse lymphocytes. So far, data from 10 healthy controls and 10 CIDP patients suggest that cytokine responses in T lymphocytes and B lymphocytes are regulated by drugs that act on FXR and TGR5 in healthy controls. Interestingly, PBMCs from CIDP patients appear to exhibit diminished responsiveness to these drugs. The caveat is most of the CIDP patients had received either IVIg treatment, steroids or both, which complicate the interpretation of our findings. Additional studies are required to confirm these findings in treatment-naïve CIDP patients and to examine the mechanisms involved.

**References**

- Alshekhlee A, Basiri K, Miles JD, Ahmad SA, Katirji B. 2010. Chronic inflammatory demyelinating polyneuropathy associated with tumor necrosis factor-alpha antagonists, *Muscle & Nerve* 41(5):723-7.
- Beppu M, Sawai S, Misawa et al. 2015. Serum cytokine and chemokine profiles in patients with chronic inflammatory demyelinating polyneuropathy. *J Neuroimmunol.* 15;279:7-10.
- Fiorucci S, Distrutti E. 2015. Bile Acid-Activated Receptors, Intestinal Microbiota, and the Treatment of Metabolic Disorders. *Trends in Molecular Medicine* 21:702-14.
- Takigawa T, Miyazaki H, Kinoshita M et al . 2013. Glucocorticoid receptor-dependent immunomodulatory effect of ursodeoxycholic acid on liver lymphocytes in mice. *Am J Physiol GI and liver physiology* 305:G427-38.