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**24-Nor-ursodeoxycholic acid improves intestinal inflammation**

**Zhu C, Boucheron N, Al-Rubaye O, *et al.* 24-Nor-ursodeoxycholic acid improves intestinal inflammation by targeting TH17 pathogenicity and transdifferentiation. *Gut* 2025; 74(7): 1079-1093. doi: 10.1136/gutjnl-2024-333297.**

There has been an increasing appreciation for the potential importance of bile acids and their effect on inflammatory pathways both in intestinal inflammation as well as cholestatic liver disease. As a result, there has been focus on bile acids as potential novel therapeutic targets for both liver and intestinal involvement, particularly in patients with primary sclerosing cholangitis (PSC). However, the mechanisms of bile acids and how they may affect inflammation have remained poorly described.

In this publication, Zhu *et al.,* sought to assess the effect of 24-Nor-ursodeoxycholic acid (norUDCA) on T-helper type 17 cells, and their role on inflammation. This was first assessed using an adoptive cell transfer mouse model. With further mechanistic studies to investigate using flow cytometry and several additional metabolomic assays. Key findings were then validated using a humanised NSG mouse model – where NSG refers to NOD/SCID/IL-2rγ (Non-Obese Diabetic/Severe Combined Immunodeficiency/Interleukin-2 receptor gamma) all being knocked out. Two weeks after transfer, mice were fed with either chow or norUDCA-supplemented diet for 2 weeks

NorUDCA suppressed TH17 effector function and enriched regulatory T cell (Treg) abundance. By mitigating intraepithelial TH17 pathogenicity, norUDCA decreased the generation of proinflammatory T helper cells. The effects of norUDCA appeared to be through metabolic conditioning of anti-inflammatory regulatory T cells, and also seemed to work in a humanised NSG model reconstituted with peripheral blood mononuclear cells from patients with PSC.

These data highlight the multiple functions and importance of bile acids. These findings also support targeting bile acids as a potentially attractive therapeutic avenue for both intestinal and hepatobiliary inflammation.