

GAMMA DELTA T CELL SELECTION BY BUTYROPHILIN-LIKE (BTNL) PROTEINS IS A CONSERVED TRAIT LIMITING IBD PROGRESSION

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Poster

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Restoration of colonic gamma delta intraepithelial lymphocyte CD103 expression in inflammatory bowel disease is associated with sustained remission, and a butyrophilin-like gene variant linked to deficient gamma four cells is associated with penetrating Crohn's disease.

KEY POINTS

- Complete restoration of gamma delta CD103 expression in treated IBD patients (n=7) was associated with significantly lower relapse over 5 years compared to those with ongoing dysregulation (n=12), with hazard ratio 6.54 (1.86–22.9) p=0.027, whereas CD8 CD103 restoration showed no association with sustained remission.
- A common 56kb copy number variant in the BTNL gene (minor allele frequency 0.310) that disrupts Vy4-BTNL3 interactions was significantly associated with penetrating Crohn's disease in a test set (n=1817) and replicated in an independent cohort (n=4491), with odds ratio 1.38 (1.13-1.68) p=0.0015, but not with IBD development.
- RNA sequencing demonstrated that colonic gamma delta cells expressing integrin CD103 have an intraepithelial transcriptomic programme, and CD103 expression is reversibly downregulated in gut inflammation and restored in healed ulcerative colitis.
- Homozygous carriage of the hypomorphic BTNL variant leads to lower proportions of Vy4 intraepithelial lymphocytes with altered phenotype resembling that seen in active inflammatory bowel disease.

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