

Advancing IBD precision medicine: The next frontier

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Presentation

IBD

Mechanisms & Personalised Medicine

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The speaker presented research demonstrating that precision medicine in IBD requires understanding disease biology at the molecular level, including identification of FAP-positive fibroblasts driven by Twist1 in stricturing disease, GPX4 expression as a predictor of post-operative recurrence, and molecular endotypes in perianal Crohn's disease.

KEY POINTS

- The speaker identified FAP-positive fibroblasts as cells driving collagen deposition in stricturing Crohn's disease, activated by the transcription factor Twist1 through interaction with the myeloid compartment, and stated that Twist1 inhibition with harmine reduced collagen deposition in vitro.
- The speaker reported that GPX4 expression in the resection specimen at the time of surgery, when added to clinical features such as smoking and previous surgery, improved prediction of post-operative recurrence compared to clinical features alone.
- The speaker stated that molecular characterization of biopsies from rectum and fistula tracts in perianal Crohn's disease identified three distinct patient clusters with completely different underlying biology, with one cluster enriched for patients suitable for surgical or medical repair.
- The speaker reported that molecular endotypes in perianal Crohn's disease were linked to the future need for ileostomy, suggesting that biology could identify these patients upfront.
- The speaker is developing complex patient-derived intestinal organoid models co-cultured with endothelial cells, stromal compartment, microbiome, and immune system to unravel mechanisms of action and discover targets for specific phenotypes.
- In the Q&A, the speaker stated that progress in fibrosis and post-operative prediction is modest and believes there will never be a single gene or protein as a biomarker, emphasizing the need for increased complexity and larger sample sizes.

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