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Summary

SYSTEMS BIOLOGY ANALYSIS OF CYTOKINE SIGNALING IN INFLAMMATORY BOWEL DISEASE HIGHLIGHTS THE IMPORTANCE OF TYK2-DEPENDENT PATHWAYS

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Transcriptomic analysis of 4059 IBD biopsy samples reveals that TYK2-dependent pathways including type I interferon, IL-23, and IL-12 are enriched in UC and CD, remain incompletely addressed by current biologics, and are associated with treatment non-response.

KEY POINTS

- Seven TYK2-dependent gene signature modules (two type I interferon, three IL-23, two IL-12) were defined and analyzed across 4059 biopsy samples from 2993 patients in 15 UC and 38 CD studies.
- Type I interferon signatures were strongly enriched in both UC and CD; IL-23 enrichment was stronger in UC than CD; IL-12 enrichment was stronger in CD than UC.
- All three TYK2-dependent signature enrichments were associated with greater disease severity.
- Treatment with golimumab, infliximab, ustekinumab, or vedolizumab significantly reduced but did not completely ameliorate specific type I interferon and IL-12 modules.
- Enrichment of type I interferon, IL-23, and IL-12 signature modules was associated with non-response to golimumab, infliximab, and vedolizumab.
- The authors conclude that all three TYK2-dependent signalling pathways should be considered in the development of future IBD treatment options.

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