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Summary

NOVEL TRANSCRIPTIONAL SIGNATURE OF CIRCULATING MONOCYTES DEFINES RESPONSE TO ADVANCED THERAPIES IN INFLAMMATORY BOWEL DISEASE

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Helios expression in circulating monocytes at baseline and after induction therapy distinguishes super-responders from non-responders to advanced IBD therapies, with Helios re-emerging in 34.14% of super-responder monocytes but remaining absent in non-responders.

KEY POINTS

- IBD patients had higher circulating monocyte counts at baseline compared to healthy controls ($p<0.001$), with levels decreasing significantly in super-responders but remaining elevated in non-responders at weeks 8-12.
- Helios expression was absent in IBD patient monocytes at baseline (47.31% in healthy controls) and re-emerged in 34.14% of super-responder monocytes by weeks 8-12 but remained undetectable in non-responders.
- Non-classical monocytes ($CD14^{-}CD16^{+}$) were increased in IBD patients at baseline versus healthy controls ($p<0.05$) and persisted in non-responders versus super-responders at weeks 8-12 ($p<0.05$).
- In vitro functional studies showed Ikaros silencing reduced pro-inflammatory markers, IL6 and IL1β secretion, and phagocytosis in response to LPS, while Helios silencing increased macrophage activation and pro-inflammatory markers in response to IL10.
- Macrophages treated with LPS+IFNγ or TPP upregulated Ikaros, STAT1, and CXCL10 ($p<0.01$), while Helios, TGM2, and MCR1 were upregulated in response to IL10 ($p<0.05$), confirming opposing roles in macrophage polarization.

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