

Beyond Inflammation: The Latest TL1A Pathway Insights and Clinical Advances

Florian Rieder, MD, and Maggie Neighbors, PhD

May 3, 2026

6:45 AM – 7:45 AM

Marriott Marquis Chicago

Great Lakes Ballroom EFG

This is an abbreviated presentation prepared by Genentech for a Genentech-sponsored symposium at Digestive Disease Week (DDW) 2026.

TL1A=tumor necrosis factor-like ligand 1A.



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Dr Florian Rieder

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Dr Maggie Neighbors

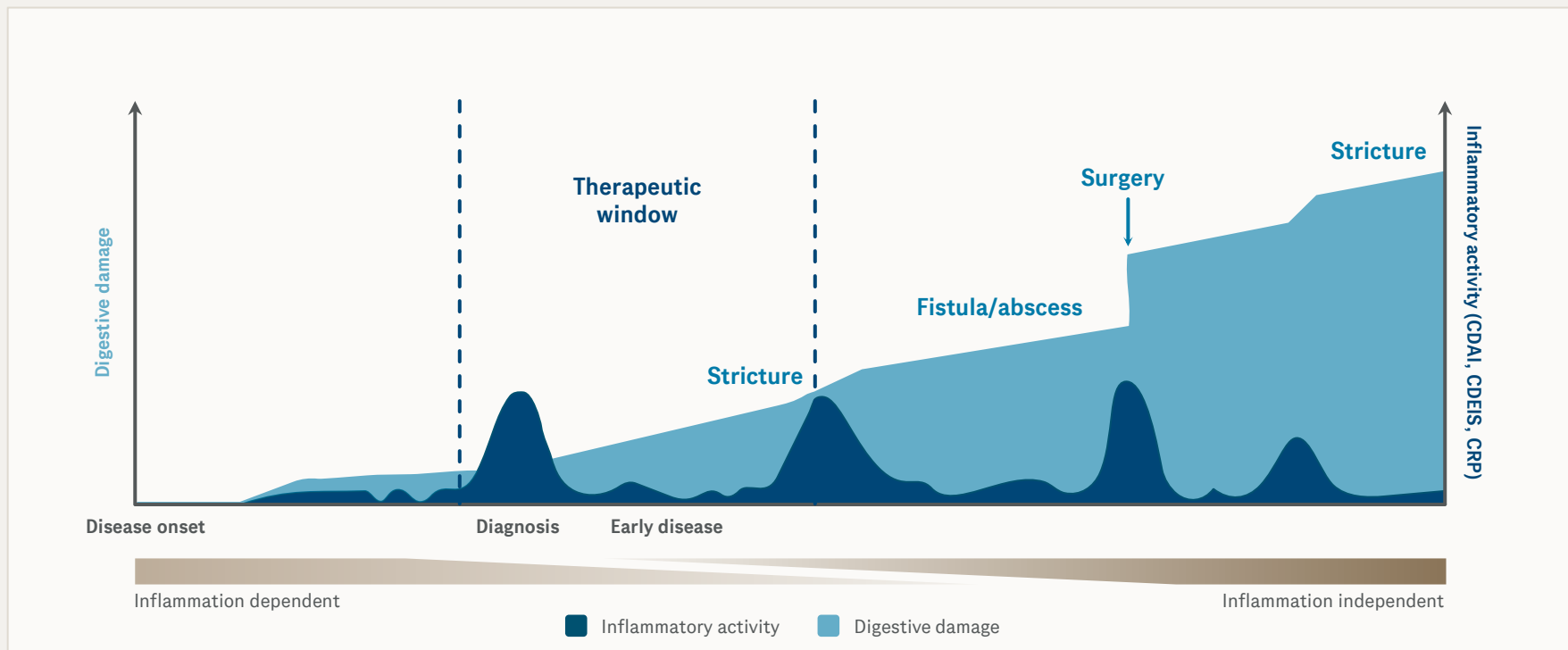
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Tissue Remodeling in Crohn's Disease and Ulcerative Colitis

Florian Rieder, MD



Crohn's Disease Follows a Familiar Path of Tissue Remodeling¹⁻³

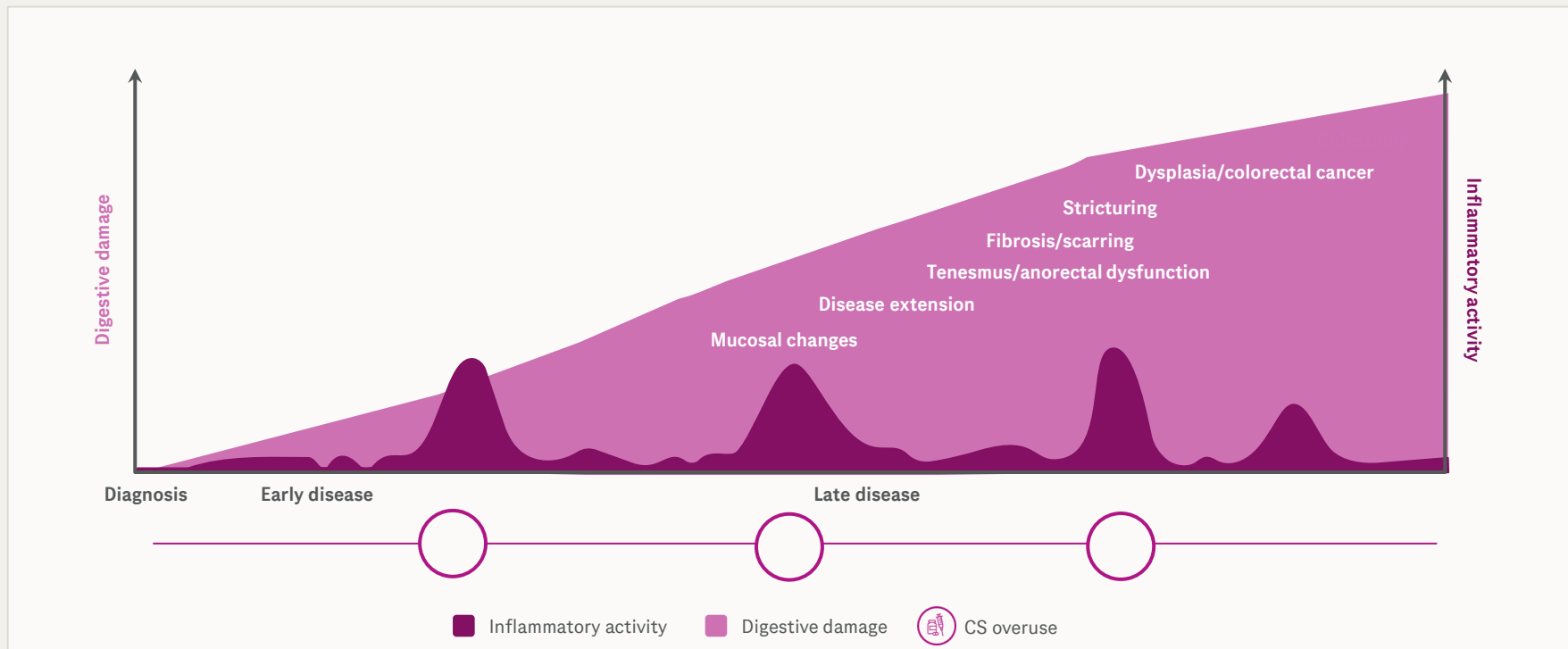


Progression of digestive damage and inflammatory activity in a theoretical patient with Crohn's disease. CDAI=Crohn's Disease Activity Index; CDEIS=Crohn's Disease Endoscopic Index of Severity; CRP=C-reactive protein.

Figure adapted from Pariente B, et al. *Inflamm Bowel Dis*. 2011;17:1415–1422, by permission of the Crohn's & Colitis Foundation.

1. Pariente B, et al. *Inflamm Bowel Dis*. 2011;17:1415–1422. 2. Colombel JF, et al. *Gastroenterol*. 2017;152:351–361. 3. Rieder F, et al. *Gut*. 2024;73:854–866.

Tissue Remodeling in Ulcerative Colitis Remains Poorly Understood¹⁻³

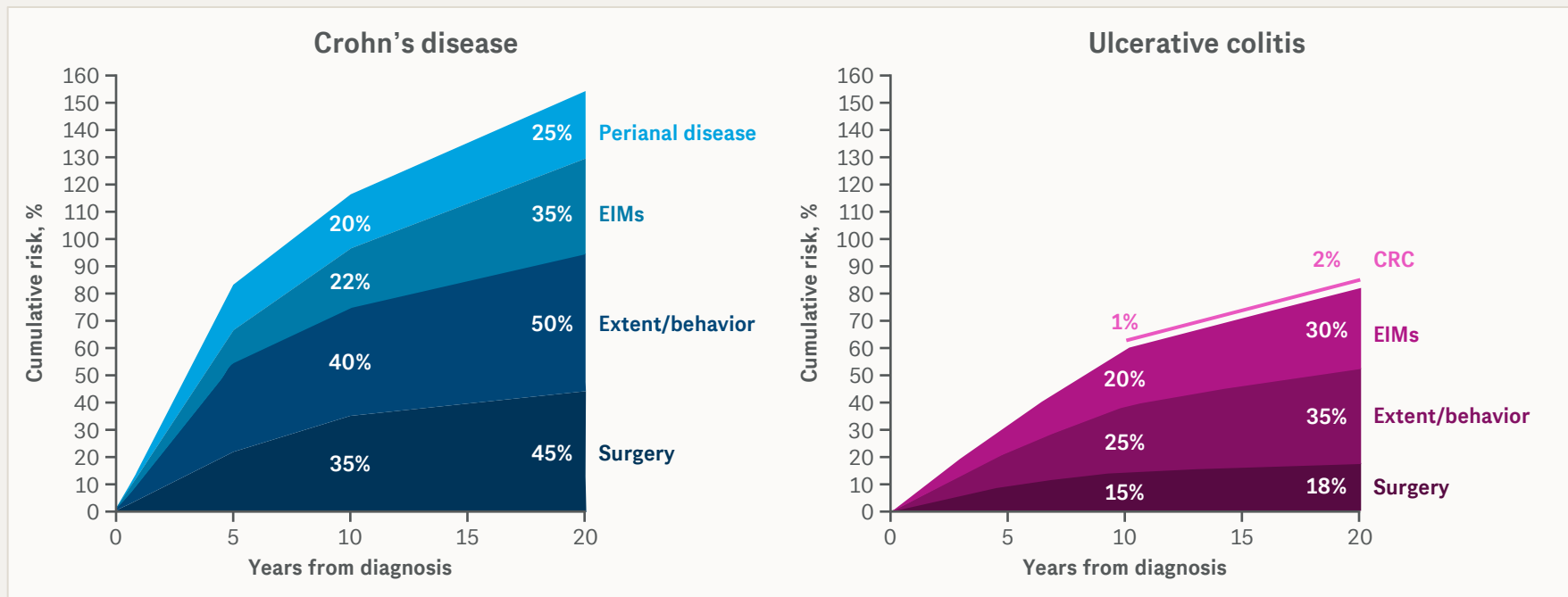


Progression of digestive damage and inflammatory activity in a theoretical patient with ulcerative colitis. Hypothetical graph for illustrative purposes only.

CS=corticosteroid.

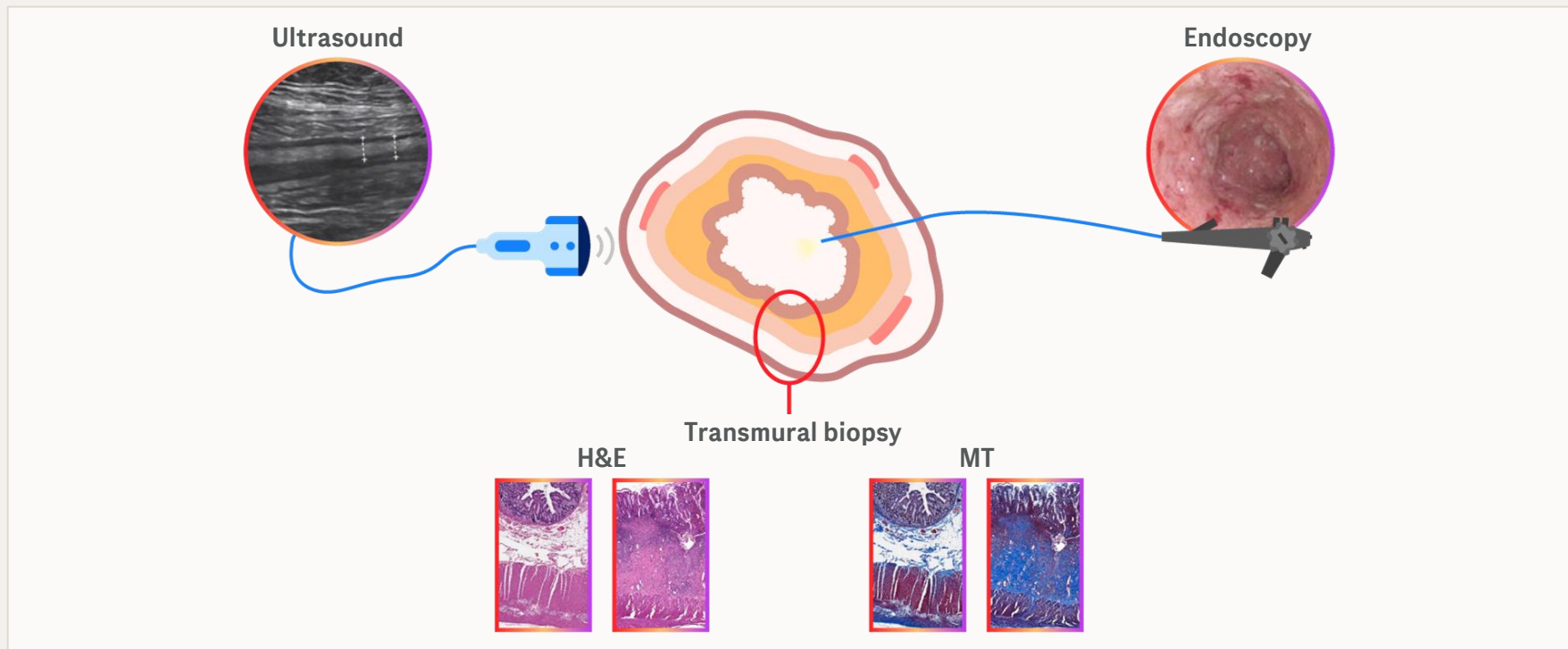
1. Solitano V, et al. *J Clin Med*. 2020;9:2646. 2. Torres J, et al. *Inflamm Bowel Dis*. 2012;18:1356–1363. 3. Fumery M, et al. *Clin Gastroenterol Hepatol*. 2018;16:343–356.e3.

Cumulative Risk of Comorbidities, Complications, and Interventions Increases with Disease Progression in CD and UC



CD=Crohn's disease; CRC=colorectal cancer; EIM=extraintestinal manifestation; UC=ulcerative colitis.
Figure adapted from Gros B, et al. *Gastroenterol Rep (Oxf)*. 2026;14:goag013.

There Are Investigational Techniques to Assess Tissue Remodeling^{1,2}



H&E=hematoxylin and eosin; MT=Masson's trichrome.

Figure reprinted from *Lancet Gastroenterol Hepatol*, vol 11(2), Eggermont E, et al., Ulcerative colitis: moving beyond the mucosal dogma, pages 163–174. Copyright 2026, with permission from Elsevier.

1. Eggermont E, et al. *Lancet Gastroenterol Hepatol*. 2026;11:163–174. 2. Gordon IO, et al. *Aliment Pharmacol Ther*. 2018;47:922–939.

Inflammatory Signaling Pathways Contributing to Tissue Remodeling

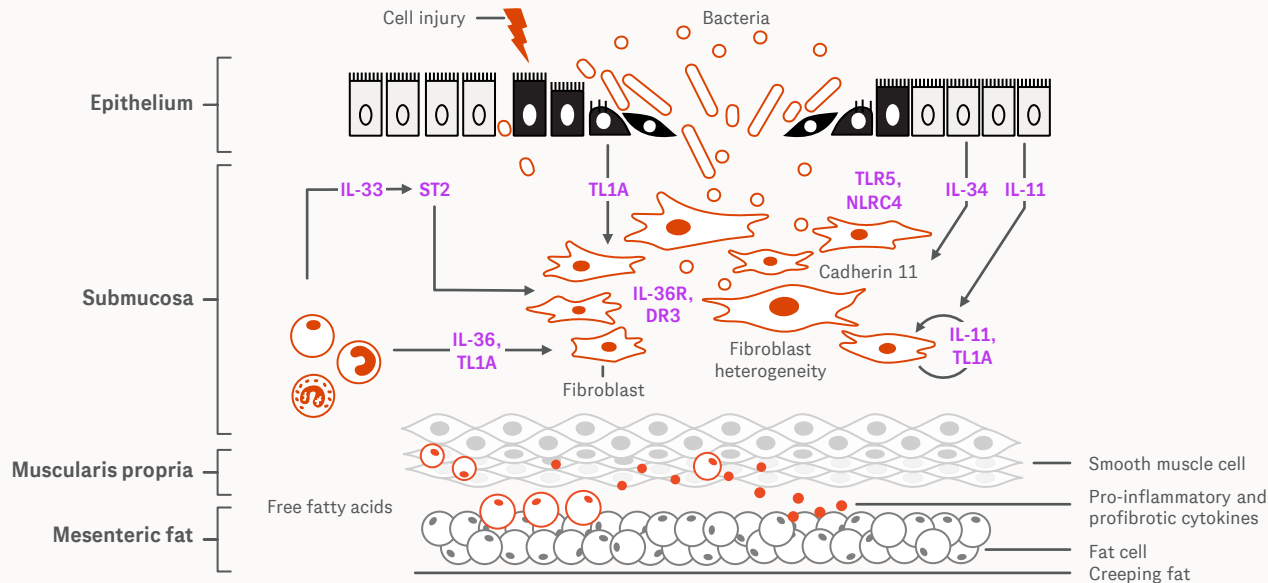


Image is for illustrative purposes only.

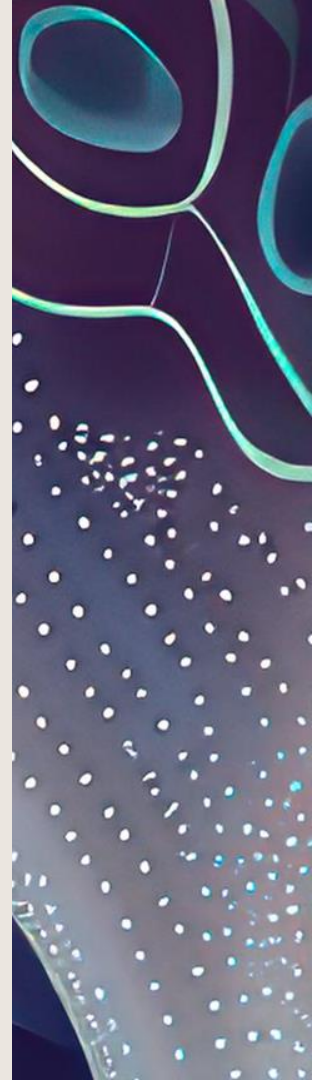
DR3=death receptor 3; IL=interleukin; NLR4=NOD-like receptor family CARD domain-containing protein 4; R=receptor; ST2=suppression of tumorigenicity 2; TLR5=Toll-like receptor 5.
Figure adapted from Rieder F, et al. Fibrosis: cross-organ biology and pathways to development of innovative drugs. *Nat Rev Drug Discov.* 2025;24:543–569. Copyright 2025, with permission from Springer Nature.

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TL1A and Its Potential Role in IBD

Maggie Neighbors, PhD and Florian Rieder, MD



Tumor Necrosis Factor–Like Ligand 1A (TL1A) Has Been Implicated in IBD

01 TL1A, the TNF-like ligand for DR3, was first described in 2002¹

02 TL1A has been linked to Crohn's disease via susceptibility-associated genetic variants²

04 Clinical trials of anti-TL1A agents began in the 2010s^{9–13}

03 Preclinical research supports the role of TL1A in mediating intestinal inflammation and fibrosis in the context of IBD^{3–7}

TNF=tumor necrosis factor.

1. Migone TS, et al. *Immunity*. 2002;16:479–492. 2. Yamazaki K, et al. *Hum Mol Genet*. 2005;14:3499–3506. 3. Bamias G, et al. *Gut*. 2025;74:652–668. 4. Takedatsu H, et al. *Gastroenterology*. 2008;135:552–567. 5. Shih DQ, et al. *PLoS One*. 2011;6:e16090. 6. Jia L-G, et al. *J Immunol*. 2016;197:377–386. 7. Bamias G, et al. *Transl Res*. 2017;180:118–130.e2. 8. <https://clinicaltrials.gov/study/NCT06589986>. Accessed September 2025. 9. <https://clinicaltrials.gov/study/NCT06588855>. Accessed September 2025. 10. <https://clinicaltrials.gov/study/NCT06819878>. Accessed September 2025. 11. <https://clinicaltrials.gov/study/NCT06819891>. Accessed September 2025. 12. Danese S, et al. *Clin Gastroenterol Hepatol*. 2021;19:2324–2332.e6. 13. Danese S, et al. *Lancet Gastroenterol Hepatol*. 2025;10:882–895.

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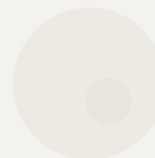
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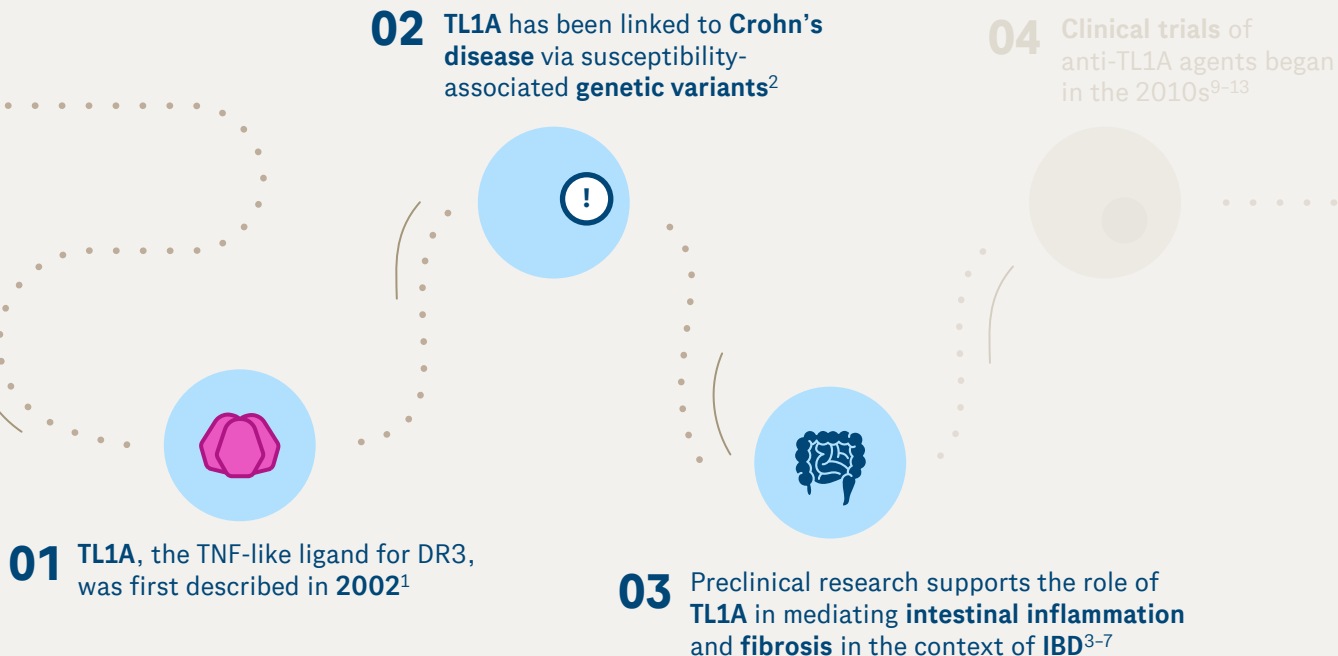
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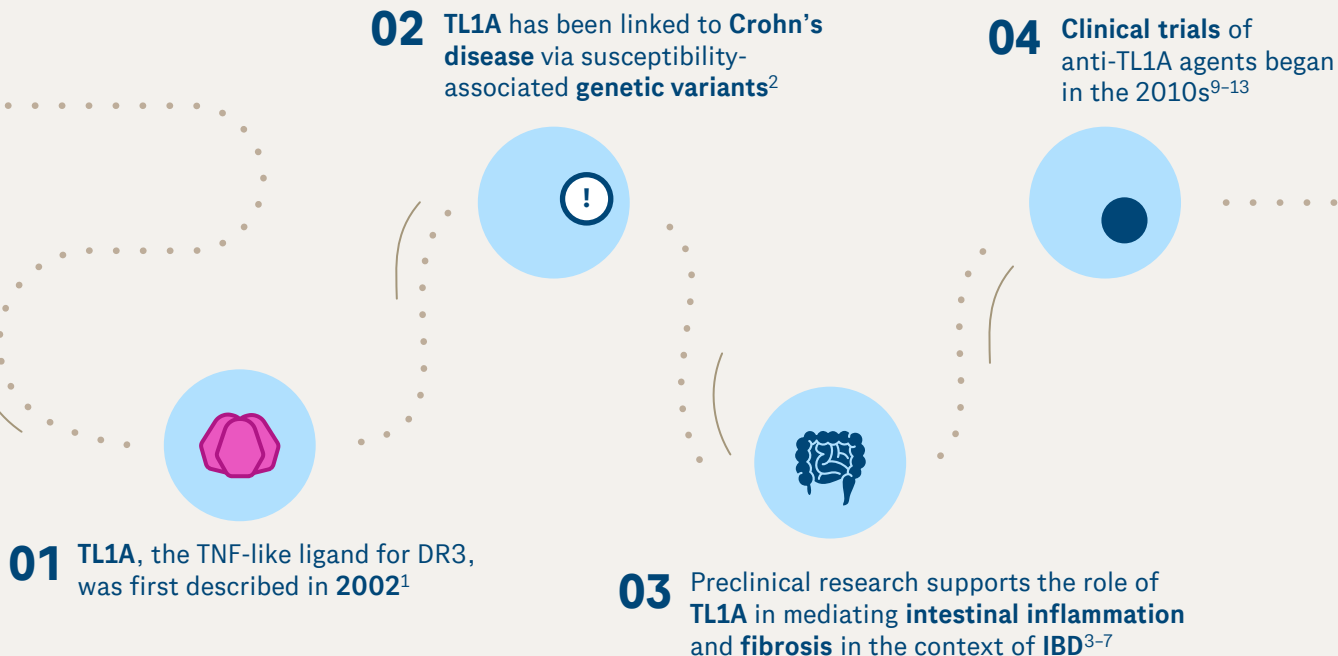
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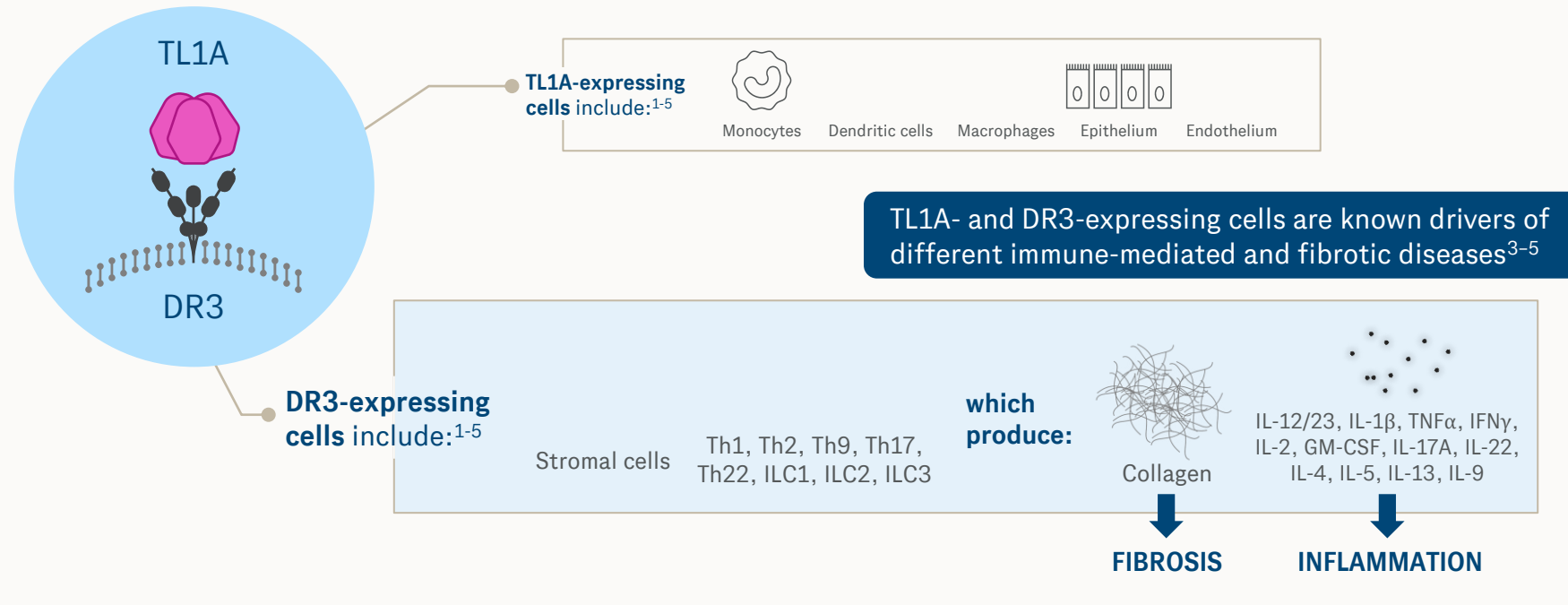
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TL1A-DR3 Axis Amplifies Pro-Inflammatory and Pro-Fibrotic Pathways



GM-CSF=granulocyte-macrophage colony-stimulating factor; IFN=interferon; ILC=innate lymphoid cell; Th=T helper cell.

1. Bamias G, et al. *Gut*. 2025;74:652–668. 2. Xu W-D, et al. *Front Immunol*. 2022;13:891328. 3. Pappu BP, et al. *J Exp Med*. 2008;205:1049–1062. 4. Wang S, et al. *Front Immunol*. 2024;15:1340467.

5. Solitano V, et al. *Med*. 2024;5:386–400.

The Potential Role of TL1A as an Amplifier in the Pathogenesis of IBD¹⁻⁷

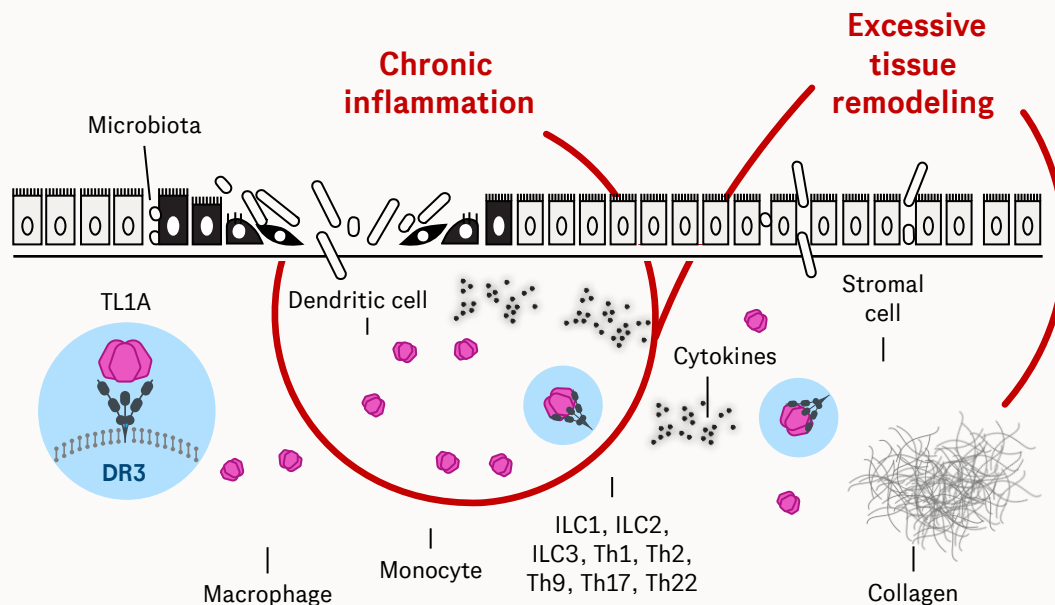


Image is for illustrative purposes only.

1. Solitano V, et al. *Med.* 2024;5:386–400. 2. Valatas V, et al. *Front Immunol.* 2019;10:583. 3. Bamias G, et al. *Gut.* 2025;74:652–668. 4. Xu W-D, et al. *Front Immunol.* 2022;13:891328. 5. Rieder F, et al. *Gut.* 2024;73:854–866.

Anti-TL1A Is an Emerging Treatment Strategy in IBD^{1,2}

Hypothesized anti-TL1A mechanism of action

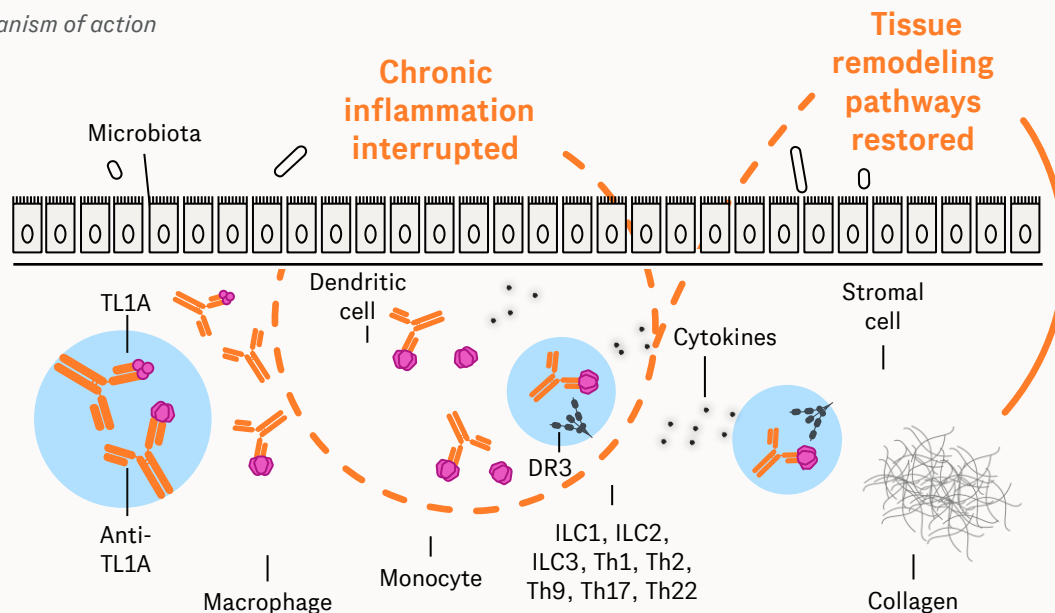


Image is for illustrative purposes only.

1. Hassan-Zahraee M, et al. *Inflamm Bowel Dis*. 2022;28:434–446. 2. Chang S, et al. Presented at: 21st Congress of the ECCO; February 18–21, 2026; Stockholm, Sweden. P0166.

Thank you.

A large, bold, black '50' where the zero is a thick-lined circle with a small white dot at the top right, resembling a stylized '0' or a planet.

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