

HEMATOPOIETIC STEM CELL GENE THERAPY AS A NOVEL THERAPEUTIC APPROACH FOR SEVERE NOD2-DEFICIENT CROHN'S DISEASE

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Poster

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Preclinical data demonstrate that OTL-104, an autologous hematopoietic stem cell gene therapy, restores NOD2 expression and function in models of NOD2-deficient Crohn's disease.

KEY POINTS

- OTL-104 uses a lentiviral vector expressing NOD2 under a macrophage-restricted promoter to restore NOD2-mediated cytokine responses in myeloid cells from NOD2-deficient CD patients to levels comparable with healthy donor cells
- In NOD2 knockout mice, transplantation of OTL-104-transduced hematopoietic stem/progenitor cells restores MDP-induced systemic inflammatory responses (IL-6, CXCL1) and myeloid cell recruitment
- Gene therapy-treated mice show normal hematopoiesis, stable vector copy numbers, and physiological NOD2 expression restored in intestinal lamina propria tissue-resident hematopoietic cells
- NOD2 deficiency is strongly associated with Crohn's disease and linked to aggressive, fistulizing, fibrostenotic phenotypes requiring multiple surgical resections and showing refractoriness to some therapies
- This preclinical work may inform development of gene therapy approaches for NOD2-deficient Crohn's disease patients

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