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# Modulation of ILC3 metabolism as a potential therapeutic target for colitis-dependent colorectal cancer

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Colorectal cancer (CRC) is a leading cause of death. Patients with inflammatory bowel disease (IBD) are more likely to develop CRC, although the factors that mediate the IBD-CRC transition remain unclear. Innate type 3 lymphocytes (ILC3s) are tightly involved in IBD pathogenesis and may be related to the transition from IBD to CRC. Moreover, the hypoxia-inducible transcription factor (HIF-1?) favors tumor growth in hypoxic environments and regulates ILC3 function.

To elucidate the function of HIF-1? in ILC3s during the transition from IBD to CRC, mice with HIF-1? deletion in ROR?t$^{+}$ cells (HIF-1?$^{?Rorc}$; CRE) were analysed. Additionally, RAG-1KO HIF-1?$^{?Rorc}$ mice (CRE), which produce no mature B or T cells, were used to ascertain HIF-1?'s specific role in ILC3s. Both models were subjected to chemical treatments with 3% DSS that induced colitis or with the carcinogen AOM followed by 2,5% DSS as a CRC model.

In both colitis and CRC models, CRE mice exhibited more severe tissue damage and significantly lower survival than their controls, throughout the treatment. Furthermore, in the colitis model, CRE mice presented a greater number of ILC3 NCR$^{+}$ lymphocytes.

Results reveal the protective role of the endogenous factor HIF-1? in ILC3 cells during the development of the colitis-associated CRC. Additionally, the higher number of ILC3 NCR+ lymphocytes in CRE mice suggests enhanced cell proliferation in the absence of the HIF-1? factor. However, further research is needed to delve into the mechanism through which ILC3s, without HIF-1?, affect CRC development and susceptibility.