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Titel des Beitrags:
Card9-dependent IL-1? regulates IL-22 production from group 3 innate lymphoid cells and promotes colitis-associated cancer.

Abstract:
Inflammatory bowel diseases (IBD) are key risk factors for the development of colorectal cancer, but the mechanisms that link intestinal inflammation with carcinogenesis are insufficiently understood. Card9 is a myeloid cell-specific signaling protein that regulates inflammatory responses downstream of various pattern recognition receptors and which cooperates with the inflammasomes for IL-1? production. Because polymorphisms in Card9 were recurrently associated with human IBD, we investigated the function of Card9 in a colitis-associated cancer (CAC) model. Card9 mice develop smaller, less proliferative and less dysplastic tumors compared to their littermates and in the regenerating mucosa we detected dramatically impaired IL-1? generation and defective IL-1? controlled IL-22 production from group 3 innate lymphoid cells. Consistent with the key role of immune-derived IL-22 in activating STAT3 signaling during normal and pathological intestinal epithelial cell (IEC) proliferation, Card9 mice also exhibit impaired tumor cell intrinsic STAT3 activation. Our results imply a Card9-controlled, ILC3-mediated mechanism regulating healthy and malignant IEC proliferation and demonstrates a role of Card9-mediated innate immunity in inflammation-associated...
carcinogenesis.