MyD88-mediated signaling prevents development of adenocarcinomas of the colon: role of interleukin 18

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Introduction

• Although inflammatory bowel diseases (IBDs) are associated with a high risk of colon carcinogenesis, the mechanisms underlying this association have yet to be fully elucidated. Intestinal microbiota appear to be a key pathogenic trigger in the development of IBD, a fact which implicates a contribution of innate and adaptive immune responses in which Toll-like receptors (TLRs) may function as primary sensors of microbial colonization. Most of these receptors, as well as all the receptors for the proinflammatory

Study Details

- MyD88/-
- Mucosal damage
- Mice
- Interferon
- InDol
- WT and knockout
- Basal level
- Gene activation
- AOM/DSS
- Interferon response
- Colonic polyps
- Symptom duration: ~ 10 days

Methods

Mice.
Myd88−/−, Il1r1−/−, Il18−/−, and Il18r1−/− mice were maintained in a specific pathogen-free (including helicobacter and parvovirus) environment, and generally used between 6 and 10 wk of age. All strains were backcrossed to obtain at least 98% congenicity

AOM/DSS model of chronic colitis.
Mice 6–8 wk of age were injected i.p. with 10 mg/kg AOM in 0.2 ml saline. 1 wk after AOM administration

Gene expression analysis by microarrays and real-time quantitative RT-PCR.
Total RNA was extracted from colon sections and gene expression was analyzed by whole genome mouse microarray (Affymetrix)

Mutation analysis.
PCR products were purified on the Mag-Bind EZ Pure kit (Omega BioTek).

Results

• Our data correlating the presence of IL-17 and MIP-2
• during the enhanced pathological response suggest that, as in the LPS-induced lung inflammation model (Miyamoto et al., 2003), IL-17 drives MIP-2 that recruits neutrophils to the tissue.
• The association between IL-17 and the frequency of neutrophils within the lung lesions of the repeatedly vaccinated mice
• suggests that granulocyte accumulation is a consequence of enhanced IL-17 activity in the Mtb-infected lung

Summary of Data Collection

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Conclusion

• Although inflammatory bowel diseases (IBDs) are associated with a high risk of colon carcinogenesis, the mechanisms underlying this association have yet to be fully elucidated. Intestinal microbiota appear to be a key pathogenic trigger in the development of IBD