

P056 Increased susceptibility to colitis-associated cancer of mice lacking TIR8, an inhibitory member of the IL-1 receptor family

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TIR8 (also known as SIGIRR) is a member of the IL-1/Toll like receptor family with inhibitory activity on inflammatory reactions and high expression in intestinal mucosa. Here we report that Tir8-deficient mice **exhibited a dramatic intestinal inflammation** in response to Dextran sulfate sodium salt (DSS) administration in terms of weight loss, intestinal bleeding and mortality and showed increased susceptibility to carcinogenesis in response to azoxymethane and DSS. Increased susceptibility to colitis-associated cancer was associated to **increased permeability and local production of prostaglandin E₂, pro-inflammatory cytokines and chemokines**. Thus, these results are consistent with the hypothesis that TIR8, by negatively regulating intestinal inflammation, plays a non-redundant role in the control of the pro-tumor activity of **chronic inflammation in the gut**.