The p50 NF-κB subunit is a prognostic regulator of colorectal cancer-associated inflammation

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In most tumors, tumor associated macrophages (TAMs) express an M2-skewed phenotype and are therefore associated with unfavorable prognosis. However, the impact of TAMs in colorectal cancer (CRC) development and outcome is still controversial. We first demonstrate, by parallel studies in colitis-associated cancer (CAC) and in genetically driven Apc^{Min} mouse models, that p50 NF-κB is essential for CRC development by restraining M1-dependent antitumor response. In absence of p50 mice developed fewer and smaller CRC lesions which express enhanced levels of M1/Th1 cytokines/chemokines including IL-12 and CXCL10, whose administration restrained CAC development *in vivo*. Moreover colons from $p50^{-/-}$ tumor bearers showed a reduced number of TAMs, as opposed to increased NK, NKT, $CD8^+$ T cells and apoptotic cancer cells. Consistently, in CRC patients, high burden of $p50^+$ TAMs was associated with decreased M1/Th1 inflammation and worse outcome indicating p50 as a new candidate for prognostic and target therapeutic intervention.