



# Involvement of Reactive Nitrogen Species and NF- B in colon cancer

*Einat Gochman, Abraham Z. Reznick, Jamal Mahajna*

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The reactive nitrogen species peroxynitrite is a product of the reaction of nitric oxide with superoxide. This powerful oxidant has been proposed to contribute to the pathology of a large variety of diseases associated with increased inflammation and cancer development by its ability to oxidize and nitrate a variety of macromolecules. The transcription factor NF- $\kappa$ B is a predominant player in inflammatory and carcinogenic processes and has been found to play a major role in the transition from chronic inflammation to cancer initiation. In this study the molecular mechanisms by which NF- $\kappa$ B is activated under nitrative stress in a human colon cancer cell line and in colitis and human colon cancer sections of patients were investigated. The in vitro studies showed a dynamic, kinetic, and intensity activation of NF- $\kappa$ B caused by peroxynitrite, lead to an aberrant and belated pathway compared to the canonical activation by TNF- $\alpha$ . It occurred in a simultaneous dual mechanism: IKK dependent, by which p38 MAPK was found to be involved, and IKK independent. The clinical studies supported these findings with high activation of NF- $\kappa$ B and its target genes in colitis and colon cancer sections.

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