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Endometriosis is a gynecological disease in which endometrial glands and stroma are present outside the uterus. Pelvic pain, infertility and decreased quality of life are the main problems caused by this disease carrying epidemiological and social impact. Peritoneal endometriosis which is characterized by the presence of red, black and white pelvic endometriotic lesions is clearly a multifactorial pathology associated with a local inflammatory response in the pelvic cavity. *In vitro* studies suggest that the transcription factor nuclear factor-kappaB (NF- κ B) is implicated in the transduction of proinflammatory signals in endometriosis.

The aim of this study was to investigate the involvement and role of the NF- κ B pathway in endometriosis *in vivo*.

Firstly, NF- κ B activation and intercellular adhesion molecule (ICAM)-1 expression were investigated in thirty-six peritoneal endometriotic lesions from women. Constitutive NF- κ B activation, involving p65- and p50-containing dimers, was demonstrated in peritoneal endometriotic lesions by electrophoretic mobility shift assays and supershift analyses, as well as NF- κ B (p65) DNA-binding activity immunodetection assays. NF- κ B activation and ICAM-1 expression were significantly higher in red lesions than black lesions, while I κ B α (NF- κ B inhibitory protein) expression was constant, as shown by Western blot analyses.

Secondly, endometriosis was induced in nude mice by intraperitoneal injection of fluorescent labeled menstrual endometrium. Two NF- κ B inhibitors (BAY 11-7085 and SN-50) were injected intraperitoneally and endometriotic lesions were recovered on day 5. Both NF- κ B inhibitors induced a significant reduction in lesion development compared to control mice. NF- κ B activation and ICAM-1 expression of endometriotic lesions were significantly reduced in treated mice, and cell proliferation in BAY 11-7085-treated mice. Both inhibitors produced a significant increase in apoptosis of endometriotic lesions, as assessed by active caspase-3 immunostaining and the TUNEL method.

In conclusion, this is the first study to show constitutive NF- κ B activation in peritoneal endometriotic lesions collected from women and during the initial development of endometriotic lesions in an animal model. Differential levels of NF- κ B activation have been established between red and black lesions, providing more evidence on the distinct inflammatory status of these two types of peritoneal endometriotic lesions. In addition, this study offers further insight into the pathways implicated in NF- κ B activation in endometriotic lesions, showing the involvement of p50/p65 dimers and suggesting participation of the canonical pathway of NF- κ B activation. This study also demonstrates, for the first time, that NF- κ B inhibition reduces the initial development of endometriotic lesions by inhibiting the inflammatory response and cell proliferation, and inducing apoptosis of endometriotic lesions. The NF- κ B pathway therefore looks to be a promising therapeutic target for endometriosis prevention and treatment.