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Regulation of estrogenic and nuclear factor κ B functions by polyamines and their role in polyamine analog-induced apoptosis of breast cancer cells.

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We investigated the role of polyamines in the function of NF-κ B and estrogen receptor-α (ER α), two transcription factors implicated in breast cancer cell proliferation and cell survival, using MCF-7 breast cancer cells. It was found that spermine facilitated the binding of ER alpha and NF-κ B to estrogen response element (ERE)- and NF-κ B response element (NRE), respectively, and enhanced ER α-mediated transcriptional activation in transient transfection experiments. Spermine also increased the nuclear translocation of NF-κ B compared to the control. In contrast, treatment with polyamine analogs, BE-3-4-3 and BE-3-3-3, resulted in transcriptional inhibition of both ERE- and NRE-driven reporter plasmids. In addition, polyamine analogs inhibited the association of ER α and NF-κ B with CBP/p300 and were unable to facilitate nuclear translocation of NF-κ B. APO-BRDU assay demonstrated that polyamine analogs induced apoptosis, with a loss of the anti-apoptotic protein Bcl-2. These data show a gene regulatory function of polyamines involving transcriptional activation of ER α and NF-κ B, potentially leading to the up-regulation of genes involved in breast cancer cell proliferation. Our results with BE-3-4-3 and BE-3-3-3 suggest that down-regulation of ER α- and NF-κ B-regulated genes is a possible mechanism for the action of polyamine analogs in inducing apoptosis of breast cancer cells.