



Category: Molecular Genetics

Involvement of mitochondrial intrinsic pathway in rhSP-D (recombinant human Surfactant Protein D) induced apoptosis of prostate cancer cells

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Abstract

Surfactant protein D (SP-D), an innate immune molecule, has an indispensable role in host defense and regulation of inflammation. We reported a novel anti-cancer role of a recombinant fragment of human SP-D (rhSP-D) in leukemic and breast tumor cell lines. A recent study revealed correlation of SP-D expression in Prostate cancer tissues with increased Gleason score and tumor volume. In the present study, we elucidated the role of rhSP-D in prostate cancer using LNCaP (androgen dependent), PC3 (androgen independent) cell lines and primary prostate cancer cells. In accordance with our previous finding, rhSP-D induced apoptosis in LNCaP and PC3 cell lines in a time and dose dependent manner. Isolated primary prostate cancer epithelial cells from explant cultures of tissue biopsies of prostate cancer patients were characterised for the presence of Cytokeratin (epithelial cell), CD10 (negative) and CD164 (positive) markers at protein and transcript level. Anti-prostate tumor effect of rhSP-D was established in the isolated primary prostate cancer epithelial cells. Importantly, primary normal prostate epithelial cells treated with similar concentrations of rhSP-D showed no adverse effect on viability. rhSP-D upregulated phospho p53 and transcripts of Bax and reduced Bcl2 transcripts, suggesting p53 mediated apoptosis in LNCaP cells. rhSP-D induced apoptosis in PC3 cells by lowering phospho ERK1/2 levels and increased BAD transcripts, a distinct mechanism of programmed cell death. Increased release of cytochrome c upon rhSP-D confirmed the activation of mitochondrial intrinsic apoptotic pathway in both the cell types. rhSP-D treatment downregulated transcripts of Bcl2 while upregulated PUMA transcripts, suggesting p53 mediated apoptosis primary prostate cancer cells. Also, positive TUNEL assay confirmed induction of apoptosis by rhSP-D in cancer tissue biopsies. Collectively, our findings reveal an integral role of SP-D in immune surveillance against prostate cancer mediated by two distinct mitochondrial apoptotic mechanisms.

References

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