

Journal of Andrology, Vol 13, Issue 6 457-464, Copyright © 1992 by The American Society of Andrology

REVIEW

Androgen regulation of programmed death of normal and malignant prostatic cells

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Androgen-dependent normal prostatic glandular cells and androgen-dependent prostatic cancer cells can be induced to undergo cell death after androgen ablation. This death does not require the cells to proliferate and occurs as an energy-dependent process collectively referred to as "programmed cell death" in which the cells actively commit "suicide." Associated with this programmed cell death pathway is the enhanced expression of a series of genes and the fragmentation of the genomic DNA into nucleosomal oligomers. This genomic DNA fragmentation is the irreversible commitment step in the death of the cell and results from activation of Ca²⁺/Mg(2+)-dependent endonuclease activity within the cell nucleus. This activation is due to sustained elevation of intracellular free Ca²⁺ (Cai) induced after androgen ablation. Metastatic prostatic cancer within an individual patient is heterogeneous, including both androgen-dependent and -independent cancer cells. Thus, androgen ablation is rarely curative since it only induces the programmed death of the androgen-dependent cancer cells without activating this pathway in the androgen-independent cancer cells within the patient. Androgen-independent prostatic cancer cells do not activate this death process after androgen ablation, since this does not induce a sustained increase in Cai. A new approach to treat androgen-independent prostatic cancer cells has focused on the use of chemotherapeutic agents to induce a sustained increase in Cai. These studies demonstrate that if such a sustained elevation in Cai is maintained, even androgen-independent prostatic cancer cells undergo programmed cell death.

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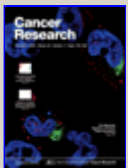
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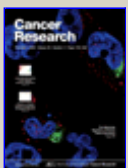
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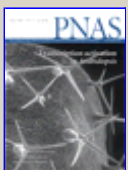
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