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JOURNAL ARTICLE

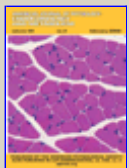
Androgen regulation of the human ornithine decarboxylase promoter in prostate cancer cells

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We studied the response of the human ornithine decarboxylase (ODC) promoter to androgen in human prostate cancer cell lines. In the well-differentiated, androgen-sensitive human prostate cancer line LNCaP, a genomic ODC promoter fragment that includes putative androgen response elements was suppressed by androgen. In contrast, the androgen-regulated probasin promoter was induced by androgens. The ODC promoter was also induced by cotransfected androgen receptor in the poorly differentiated, androgen-insensitive human prostate cancer cell line PPC-1. We examined the effects of cotransfected mutant androgen receptors containing the LNCaP mutation or DNA-binding mutations. All cotransfected androgen receptors switched the ODC androgen response from suppression to induction in LNCaP cells. Gel-shift and DNA footprint assays demonstrated androgen receptor binding to an ODC sequence that does not contain a consensus androgen response element. Deletion of the sequence abolished androgen suppression of the ODC promoter. We propose a model of pleiotropic gene regulation by androgen that requires a regulatory balance between androgen receptor and a transcription factor binding to the nonconsensus androgen response element.

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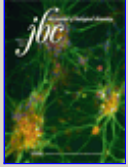
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