The effect of estrogen receptor beta on DNA-damage induced apoptosis

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The role of steroid hormone receptor on DNA-damage induced apoptosis is unknown. We demonstrate herein DNA damage signalling to estrogen receptor β (ERβ) can attenuate the antiapoptotic activity of the ERβ by compromising the Src/Shc/ERK signalling pathway. This DNA-damage proapoptotic action is mediated by activation function-1 (AF-1), and the antiapoptotic, proliferative action is mediated by AF-2/LBD (ligand binding domain). Also, this DNA-damaging induced proapoptotic activity of ERβ can not be dependent on its transcriptional activity. However, ERα can not affect the antiapototic activity induced by ligand signalling, upon DNA damaging. The absence of DNA-damage induced proapoptotic activity in ERα may be due to the failure of DNA damaging signal transduction to the AF-1 domain of ERα. This is consistent with the lower homology between their AF-1 domains. On the other hand, their comparable antiapoptotic ability induced by ligand may come from the high homology between their AF-2/LBD domains. Therefore, they may play the functionally distinct roles, in response to the DNA damage.