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FGF-2 Incites Biological Activities of Human Pro-state Cancer Cells *via* Hydrogen Peroxide-de-pendent Activation of HARP/Pleiotrophin Gene

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Fibroblast growth factor 2 (FGF-2) has been implicated in prostate cancer pr-gression. We found that exogenous FGF-2 significantly increased human prostate cancer LNCaP cell proliferation and migration. Heparin affin regulatory peptide (HARP) seems to be an important mediator of FGF-2 stimulatory effects, since the latter had no effect on stably transfected LNCaP cells that did not express HARP. FGF-2 significantly induced HARP expression and secretion by LNCaP cells and increased luciferase activity of the 5'-flanking region of the HARP gene introduced in a reporter gene vector. Inhibition of FGFR1-signaling blocked the FGF2-increased HARP gene activation and the consequent protein release, leading to impairment of LNCaP cell proliferation. FGF2-stimulatory effects depended on hydrogen peroxide (HP) generation. Low concentrations of exogenously added HP had similar stimulatory effects. Activator protein-1 (AP-1) seems to be involved in FGF2-stimulated HARP expression and secretion by LNCaP cells, as revealed using AP-1 decoy oligonucleotides and point mutation analyses, as was the case for HP. The effect of FGF-2/HP seems to be due to binding of Fra-1, JunD and phospho-c-Jun to the HARP promoter. These results establish the role and mode of activity of FGF2 in LNCaP cells, extend the notion that HARP is important for prostate cancer cell bio-logy and emphasize on the requirement of HP production in FGF2 downstream effects on LNCaP cells.