

3-D prostasphere (PS) culture. Similar to estradiol-17 β (E₂), 5 nM IGF-1 treatment increased the number of PS as well as long-term BrdU-retaining prostate stem cells. Conversely, knockdown of IGF-1R by siRNA decreased both parameters and consistently increased PS ER β expression. Together these findings suggest that IGF-1R activation may drive prostate stem cell amplification through suppression of ER β . Further studies revealed that E₂ (10 nM) exposure induced IGF-1R phosphorylation while IGF-1R knockdown inhibited the non-genomic E₂-induced pAkt and pERK confirming the cross-talk between these two signaling pathways. IGF-1R knockdown decreased PHLDA1, a known IGF-1 target gene, inhibited E₂-induced ER α phosphorylation, suggesting a positive interaction between IGF-1R and ER α . In summary, the present results document robust crosstalk between estrogen and IGF-1 signaling which together regulate their downstream signal molecules including pAKT/pERK and PHLDA1. We propose that these pathways coordinately modulate prostate stem and progenitor cell numbers to effectively maintain glandular homeostasis. Supported by NIH/NCI award R01 CA172220; scholarship by FAPESP grant#2014/10965-6.

ID: 85 **CROSS-TALK BETWEEN ESTROGEN RECEPTORS AND INSULIN-LIKE GROWTH FACTOR TYPE-1 RECEPTOR MODULATES HUMAN PROSTATE STEM/PROGENITOR CELL AMPLIFICATION**

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10.1136/jim-2016-000120.38

We previously demonstrated that estrogen regulates human prostate stem/progenitor cell amplification by directly targeting estrogen receptors (ERs); ER α stimulates whereas ER β suppresses stem cell self-renewal. In addition to ER α and ER β , we find that human prostate stem/progenitor cells express robust level of IGF-1R. Since ER actions can be modified by IGF-1R through ligand-independent ER phosphorylation, we herein sought to characterize potential cross-talk between estrogen and IGF-1 signaling pathways in regulating human prostate stem/progenitor cell amplification. Human prostate stem/progenitor cells were isolated from normal primary prostate epithelial cells (PrEC) using