

3-D prostasphere (PS) culture. Similar to estradiol-17 $\beta$  (E<sub>2</sub>), 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 $\beta$  expression. Together these findings suggest that IGF-1R activation may drive prostate stem cell amplification through suppression of ER $\beta$ . Further studies revealed that E<sub>2</sub> (10 nM) exposure induced IGF-1R phosphorylation while IGF-1R knockdown inhibited the non-genomic E<sub>2</sub>-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 E<sub>2</sub>-induced ER $\alpha$  phosphorylation, suggesting a positive interaction between IGF-1R and ER $\alpha$ . 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**

JD Rinaldi,<sup>1,2</sup> W Hu,<sup>1</sup> S Majundar,<sup>1</sup> D Hu,<sup>1</sup> GS Prins,<sup>1</sup> L Justulin,<sup>2</sup> SL Felisbino<sup>2</sup>. <sup>1</sup>*Urology, UIC, Chicago, Illinois, United States;* <sup>2</sup>*Morfologia, Universidade Estadual Paulista, Botucatu, Sao Paulo, Brazil*

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We previously demonstrated that estrogen regulates human prostate stem/progenitor cell amplification by directly targeting estrogen receptors (ERs); ER $\alpha$  stimulates whereas ER $\beta$  suppresses stem cell self-renewal. In addition to ER $\alpha$  and ER $\beta$ , 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