

## Poster #26

### Cross-Talk Between PI3K-AKT and the Estrogen Receptor

Bich Duong, Matthew Burow, Daniel Frigo, Steven Elliott, Christopher Weldon, Bridgette Collins-Burow, Jawed Alam, Barbera Beckman, and John McLachlan

Molecular and Cellular Biology Program and Environmental Endocrinology Project at the Tulane-Xavier Center for Bioenvironmental Research, New Orleans, LA 70112

e-mail: [bduong@tulane.edu](mailto:bduong@tulane.edu) Phone (504) 988-6623; Fax (504) 988-6215

The hormone 17 $\beta$ -estradiol (E2) functions through binding to the estrogen receptor, thereby initiating transactivation of genes involved in the regulation of cell proliferation and survival. In addition to E2, synthetic or natural compounds have been shown to bind and to activate the ERs. Given the previously described cross-talk between ER and peptide hormone signaling, we wish to determine the role of intracellular signaling pathways on the regulation of ER function by E2, DES, and the phytoestrogen genistein. Activation of the phosphatidylinositol-3 kinase (PI3K) and its downstream target AKT has been implicated in cell proliferation and survival. Despite the involvement of PI3K/AKT in cell proliferation and survival by the peptide hormones IGF and EGF, this pathway has not been examined in relation to cross-talk with the ER. Our initial experiments show that IGF and EGF potentiate estrogen signaling through a PI3K-dependent pathway in both breast and endometrial carcinoma cells. Use of constitutive active PI3K or AKT in estrogen receptor negative 293 cells demonstrate the ability of this pathway to potentiate ER activity preferentially to ER $\alpha$  versus ER $\beta$ . In addition, constitutive active AKT enhances DES and genistein potentiation of ER activity to a higher level than does E2. Furthermore, while both PI3K/AKT and the ER have been previously shown to regulate cell survival independently, we demonstrate a necessity for an intact ER in AKT-mediated suppression of TNF-induced cell death. Our experiments show a novel link between peptide hormones, PI3K/AKT and the ER and thus provide a possible mechanism for ER function.