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Estradiol Induction of Post-confluent Focal Cell Proliferation in MCF-7 Human Breast Cancer Cultures: Role of IGF Signaling Pathways

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17-#946; estradiol (E2) and the peptide growth factors insulin-like growth factor I and II (IGF-I and II) are mitogens known to stimulate proliferation of estrogen receptor (ER)-positive breast cancer cells. Synergistic interactions between IGF-I and E2 results in increased preconfluent cell proliferation in the MCF-7 human breast cancer cell line. This behavior is typical of wound healing in normal tissues rather than growth associated with tumor formation and progression however. We have previously established that postconfluent growth of E2-exposed MCF-7 cells results in the formation of multilayered, cellular aggregates called foci which share many common features with the breast cancer phenotype. Addition of physiological levels of IGF-I or IGF-II in conjunction with E2 results in a synergistic increase in foci development over E2 alone, suggesting interaction between the two signaling pathways. Recent Western blot and Real Time RT-PCR data demonstrate that increasing E2 concentration leads to a dose-dependent increase in both IGF-IR protein and mRNA levels as well as IGF-II mRNA. This suggests E2 may sensitize cells to the IGF signaling pathway by increasing its components. One possible mechanism involves increased IGF-II, which is known to be secreted by MCF-7 cells, acting in an autocrine or paracrine manner through IGF-IR with consequent foci formation. Elucidation of the mechanism of this E2-IGF interaction leading to focal development in the MCF-7 breast cancer line will provide fundamental and relevant information pertinent to breast cancer initiation and progression in vivo, as well as provide targets for future cancer therapies.

