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## **Interaction of Estradiol and Insulin-like Growth Factor I on Foci Formation in MCF-7 Human Breast Cancer Cells**

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The Insulin-like Growth Factor (IGF) system is a key growth regulatory pathway in human breast cancer as demonstrated through in vitro studies and inhibition of tumor xenograph growth using anti-IGF methods. IGF-I and IGF-II, as well as insulin, stimulate the proliferation of cells and are potent mitogens for breast cancer cells in culture. Synergism between estrogen and the IGF system has been shown in a number of model systems including normal and malignant breast and uterine tissue. The interaction between estrogen (E2), the estrogen receptor (ER), and the IGF system is extremely complex. In MCF-7 breast cancer cells, IGF-IR and ER are co-expressed, and it has been found that the two signaling systems are involved in cross-talk resulting in a synergistic stimulation of proliferation. Our lab has developed a three-dimensional model of estrogen-dependent cell proliferation utilizing the MCF-7 cell line that we propose represents in vivo cell proliferation similar to estrogen-dependent breast cancer. This model exhibits postconfluent, multilayered tumor-like focal growths (foci) in response to estradiol (10 nM) or Insulin-like Growth Factor I (100 ng/ml). Exposure of cultures to the nonsteroidal antiestrogen ICI 182, 780 reduces foci number to control levels, suggesting a common pathway involving the estrogen receptor. Further characterization of the MCF-7 focus system will be used to establish the MCF-7 focus system as an invaluable tool for the future study of growth factor/E2 interactions and cancer progression.