

Progress Report

“The Role of an Environmental Chemical Receptor, the Aryl Hydrocarbon Receptor, in Breast Cancer Cell Growth and Invasion”

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A substantial and growing body of data indicate that exposure to certain environmental chemicals contributes to the development of breast cancer. For several years our laboratory has focused on the role of common air pollutants and food contaminants in the development of breast cancer. Using laboratory animal models, we have shown that hydrocarbons commonly found in ambient air as a consequence of the burning of fossil fuels or several industrial processes, preferentially induce breast cancers. The ability of these environmental hydrocarbons to turn normal breast cells into tumors is dependent on the interaction of the environmental chemicals with a specific receptor called the aryl hydrocarbon receptor (AhR). In previous studies supported by Art BeCAUSE, we demonstrated that activation of this receptor tends to increase cell growth, a characteristic of cancer cells. In our most recent studies, we tested the hypothesis that activation of the AhR also increases invasiveness and possibly metastasis of breast cancer cells. These possibilities are of particular concern since tumor metastasis to and then invasion into distant organs is the ultimate cause of death in breast cancer patients.

To test this hypothesis, we first used molecular biology techniques to artificially decrease the level of the AhR (pollutant receptor) in human breast cancer cell lines and then to measure their invasive potential in tissue culture. Results obtained to date strongly support the hypothesis that the AhR is involved in tissue invasion. That is, when the AhR was down-regulated, invasive cells behave more like normal mammary cells.

From these results, we predicted that chemical inhibitors of the AhR would similarly block tumor invasion in our model system. While we are still in the process of screening hundreds of potential AhR inhibitors (in collaboration with the Boston University Chemistry Department), we have been able to demonstrate that at least one candidate not only suppresses the activation of the AhR by environmental pollutants but also inhibits the AhR-dependent invasion of human breast cancer cells in tissue culture (see figure). These exciting studies suggest the possibility of preventing breast cancer formation or of reversing its aggressive behavior with AhR inhibitors. Since there are a number of natural sources of such inhibitors (e.g., resveratrol in red wine and galangin in honey), it seems possible that these studies may lead to relatively simple, diet-based approaches to breast cancer prevention and treatment.

