DIFFERENTIAL EXPRESSION OF CYP1A1 AND CYP1B1 IN HUMAN MAMMARY EPITHELIAL CELLS FROM PRE-MENOPAUSAL AFRICAN AMERICAN AND CAUCASIAN WOMEN IN RESPONSE TO DIOXIN AND BENZO[a] PYRENE

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Abstract: Although the overall breast cancer incidence rate for African American (AA) women is lower than Caucasian (CA) women, among AA women under the age of 50 the rates are twofold higher. Due to their roles in activation of environmental poly aromatic hydrocarbons (PAH) to ultimate carcinogens, the products of CYP1A1 and CYP1B1 genes are implicated as risk factors for breast cancer. The objective of this study is to examine the hypothesis that higher incidence of breast cancer in pre-menopausal AA women is related to a dysregulated expression of CYP1A1 & CYP1B1 genes. To address this hypothesis our laboratory have isolated and characterized primary cultures of mammary epithelial cells (HMEC) from age-matched pre-menopausal AA and CA women, using normal breast tissues from mammoplasty reduction surgery. These isolated HMEC were used as in vitro model system to examine the response of breast tissues to several PAH including 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and benzo[a]pyrene (B[a]P). In this study, the expression of CYP1A1 & CYP1B1 was measured in HMEC of ten age-matched women donors from each women group ranging in age from 16-47 years. Results from real time RT-PCR analyses showed that CYP1A1 mRNA is expressed at low levels in untreated HMEC samples from both women groups and treatment with either B(a)P or TCDD induced its expression by many folds ranging from 10 to over 400-fold. Western blot analysis of microsomal proteins from these HMEC showed substantial levels of constitutive CYP1B1 protein in HMEC from both AA and CA women, which was further induced by both TCDD and B[a]P. However, HMEC from AA women exhibited higher inducibility of CYP1B1 protein in response to dioxin than HMEC from CA women at each age-match. In contrast, the majority of HMEC from AA women fail to induce CYP1A1 protein in response to dioxin treatment. These findings, although preliminary and require confirmation in larger number of donors, point to the higher risk of these AA women. This is in light of the fact that CYP1B1 more than CYP1A1 is responsible for bioactivation of chemicals, including estrogens into DNA-damaging carcinogens. The study will contribute to a better understanding of differential role of environmental chemicals on the biology of breast cancer in this ethnic minority group.

Keywords: African American, breast cancer, premenopausal, CYP1A1, CYP1B1, HMEC, dioxin, benzopyrene

Acknowledgements: This research is supported by grants from the National Institutes of Health: NCRR and NCI (grants number: RR03032 15, CA91408-01) and from the Department of defense Breast Cancer Program (DAMD17-02-01-0483).