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**Prevention Research 1: Chemoprevention Studies I**
**Abstract #741**

# Chlorophyllin treatment reduces benzo[*a*] pyrene (BP)-induced *CYP1A1* and *CYP1B1* expression and BP-DNA adduct formation in normal human mammary epithelial cells (NHMECs)

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The capacity of cultured NHMECs to activate BP and form BP-DNA adducts has been previously demonstrated. The advantage of these normal breast cells obtained from reduction mammoplasty is that each cell strain reflects the metabolic profile of an individual donor. Recently, we showed wide inter-individual variation in BP-induced *CYP1A1* (≤ 100-fold) and *CYP1B1* (≤ 40-fold) expression in NHMECs. Although levels of *CYP1A1* and *CYP1B1* induction were highly correlated with each other ($r^2 = 0.82$, $p<0.01$) neither appeared to be a good predictor of BP-DNA adduct formation ($r^2 = 0.40$ and 0.50, $p<0.10$ and 0.05, respectively). However, we hypothesized that since the first step in BP activation is dependent on cytochrome p450 (CYP) metabolism, inhibition of CYP induction might result in reduction of BP-DNA adduct formation. In these studies one NHMEC strain was exposed for 24h to 5μM chlorophyllin either before exposure to 4μM BP for 24h, together with BP exposure (4μM for 24h) or both 24h before and during exposure to 4μM BP for 24h. After exposure, *CYP1A1* and *CYP1B1* gene expression was monitored by Affymetrix DNA oligonucleotide microarrays (U133A) and reverse transcription/quantitative real-time polymerase chain reaction (RT-PCR). In addition, DNA was extracted and BP-DNA adducts were measured using an anti-BP-DNA chemiluminescence immunoassay. The data showed that BP-induced *CYP1A1* and *CYP1B1* expression was mitigated by all three chlorophyllin treatment regimens, but that maximal inhibition of enzyme induction was obtained with chlorophyllin exposure before and during BP-exposure. Using RT-PCR, the *CYP1A1* induction was maximally reduced by >85% ($p<0.01$) and *CYP1B1* induction was reduced by >70% ($p<0.01$). BP-induced expression of several other genes (*STAT1*, *1F1TM1* and *G1P3*) was also reduced by chlorophyllin exposure. BP-DNA adduct formation was concomitantly reduced in direct proportion to

the levels of *CYP1A1* and *CYP1B1* reduction ($r^2 = 0.90$, $p<0.01$), and the DNA adduct levels were maximally reduced by >85% ($p<0.01$). These data show that chorophyllin substantially blocks the BP-induction of *CYP1A1* and *CYP1B1* expression and associated BP-DNA adduct formation in NHMECs.

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