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ANTI-CANCER DRUG INTERACTION WITH CYTOCHROME P450 CYP1B1

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The major goal of cancer research is the development of therapeutic agents specifically aimed at tumour cells. One mechanism potentially amenable to chemotherapeutic intervention involves cytochrome P450 CYP1B1. Our research has established the concept of over-expression of individual forms of P450 in particular CYP1B1 ina range of solid tumours. Moreover our *invitro* studies have demonstrated the presence of metabolically active CYP1B1 and cytochrome P450 reductase in tumour samples. We have previously identified several anti-cancer drugs (docetaxel, paclitaxel, mitoxantrone and flutamide) as substrates for CYP1B1. Furthermore, our *in vitro* studies have shown that the presence of CYP1B1 reduces the efficacy of docetaxel. In this study we used expressed human CYP1B1 in a competitive microassay involving the deethylation of ethoxyresorufin to resorufin to extended our screen of anti-cancer drugs and identify which ones interact with CYP1B1, by the change in resorufin production over time. Our findings to date indicate that a range of structurally diverse anti-cancer drugs interact with CYP1B1 (melphalan, bleomycin, methotrexate, altretamine, ellipticine, resveratrol, carmustine, dactinomycin, raltitrexed, epirubicin, and mitomycin C). Several of these drugs have been further characterised to determine their mechanism of interaction with CYP1B1. The over-expression of CYP1B1 in tumour cells and interaction of this P450 with anti-cancer drugs highlight CYP1B1 as an important P450 in tumour cells.

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