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The possible role of cytochrome P450s in non-small cell lung cancer therapy

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Abstract

Lung cancer is one of the most aggressive forms of cancers resulting in more than one million deaths yearly. From the two types of lung cancer, non-small cell lung cancer (NSCLC) represents about 88% of all lung cancer cases. NSCLC can be further defined by recurrent driver mutations. The most common mutations are KRAS and EGFR. Susceptibility to lung cancer can be influenced by the metabolic capacity of the lung which strongly relies on cytochrome P450 (CYP) enzymes. Therapeutic drug response is influenced by these enzymes also, as they metabolize many of those drugs. In this study the expression of drug metabolizing CYPs were measured with qPCR in primary, normal human lung fibroblasts (NHLF) and primary, small airway epithelial cells (SAEC) and compared to two adenocarcinoma cell lines carrying different mutations: KRAS mutant A549 and EGFR mutant PC9. For their role in drug metabolism CYPs may contribute to drug resistance beside ABC transporters. For this reason adenocarcinoma cell lines were treated with cisplatin, a frequently used chemotherapeutic agent, then the CYP expressions were measured and compared to the non-treated cell lines.

To replicate in vivo environment 3D spheroids (A549: NHLF, PC9: NHLF) were set up and CYP expressions were measured. Besides the obvious differences between 2D and 3D cultures, there were not only differences between the primary cells and adenocarcinoma cell lines, but between the two adenocarcinoma cell lines too. The possible CYP expression changes in cisplatin treatment might influence the outcome of the therapy especially if combination therapy is being used, and the drug is metabolized by a CYP enzyme. Also the difference in the CYP expression in normal and tumor cells should be taken into consideration during therapy. Further studies are planned to measure CYP protein level in the previous samples.

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