

Molecular mechanisms of drug interactions at the level of transport proteins for xenobiotics

» Prof. Dr. Walther Honscha

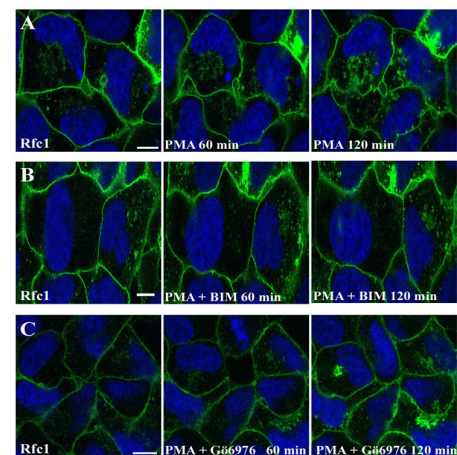
The elucidation of molecular mechanisms of drug interactions between different drugs given simultaneously during therapy is a growing field in clinical pharmacology.

These drug interactions are possible at different levels and can result in serious side effects. Our interests are focussed on the transport proteins for chemotherapeutics (e.g. Methotrexate, Mtx) and their regulation through xenobiotics. While Mtx therapy is often accompanied by co-medication with antikonvulsants, the transport activity for Mtx which is mediated by the reduced folate carrier 1 (Rfc1) was down-regulated in hepatocytes of Phenobarbital (PB) treated rats. Further studies on

a liver cell model showed, that PB induced downregulation of Rfc1 uptake activity is achieved through cPKC-dependent retrieval from the plasma membrane by a mechanism linked to the CAR (constitutive androstane receptor) regulatory pathway. This effect which is induced by all drugs known as P4502B inducers may have consequences for tumour therapy.

Keywords

- Transport of xenobiotics
- Drug interactions
- Chemotherapeutics



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