MECHANISMS OF DRUG RESISTANCE IN AN EPITHELIAL BREAST CARCINOMA CELL MODEL

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Description:

Our laboratory is currently investigating the mechanisms by which cells develop resistance to the continued presence of chemotherapeutics. Our hypothesis is that drug accumulation is indirectly controlled by drug efflux pumps rather than what is conventionally accepted as a direct link between drug efflux transporters and drug accumulation. This is supported by the observation that drug resistance is conferred to a multitude of very different substrates and it is conceptually difficult to visualize how certain proteins (e.g., P-glycoprotein) can actively transport over one hundred unrelated compounds.

Preliminary data from our laboratory supports this conclusion. Changes of the intracellular voltage and/or pH were found to alter drug accumulation and efflux. This occurred in a cell line that is essentially devoid of the drug efflux protein (P-glycoprotein).

Objective:

The focus of future research will be to better define the regulation of drug accumulation by the intracellular milieu, in addition to transfection studies with P-glycoprotein to further demonstrate that this protein indirectly affects drug efflux.

Prerequisites:

None