Drug efflux activity by transmembrane protein Patched : a preliminary in silico study

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Aberrant activity of the Hedgehog (Hh) signalling pathway has been observed in nearly 25% of cancers. The majority of these cancers contain cells that are resistant to chemotherapy. Ptch1, a transmembrane Hh morphogen receptor protein, is overexpressed in most of these cancers.

Our team has recently shown that Ptch1 has cholesterol and drug efflux activity, and contributes to the chemotherapy resistance of cancer cells [1]. Our team has identified two inhibitors of this drug efflux activity, and shown that these molecules increase the efficacy of different chemotherapeutic agents in vitro and in vivo [2, 3]. However, the drug efflux mechanism of Ptch1 and the mode of action of inhibitors remain to be elucidated.

Since the publication of Cryo-Em structures of Ptch1 in 2018, we have used available in silico tools such as Docking and Molecular Dynamics to understand the transport mechanism of this protein.

Bibliography:

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