Drug resistance induced by ABC-transporter proteins

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Abstract- Three ATP-binding cassette (ABC)-superfamily multidrug efflux pumps are known to be responsible for chemoresistance; P-glycoprotein (ABCB1), MRP1/3 (ABCC1/3) and ABCG2 (BCRP). These transporters play an important role in normal physiology by protecting tissues from toxic xenobiotics and endogenous metabolites. Hydrophobic amphipathic compounds, including many cytotoxic drugs (anthracyclines, vinca-alkaloids, taxanes…), are expelled out of the cell by these pumps. These efflux pumps are expressed in many human tumors, where they likely contribute to resistance to chemotherapy treatment, as it was demonstrated in acute myelogenous leukemia. However, the use of efflux-pump modulators in clinical cancer treatment has proved disappointing. Today we know that the family of ATP-binding cassette transporters (ABC transporters) comprises 48 different proteins. When Heracles fought the ancient Hydra, he had to fight all the heads at once but only one head was vital for the beast. Can we block all the relevant ABC transporters at once? Is there one transporter that is more important than the others?