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Inhibition of the Drug Efflux Activity of the Hedgehog Receptor Patch Enhances Chemotherapy Efficiency *In Vitro* and *In Vivo*

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Fighting chemo resistance is a major challenge for cancer therapy. We recently demonstrated that the Hedgehog receptor Patch, which is overexpressed in many recurrent and metastatic cancers, is a multidrug transporter contributing to chemotherapy resistance. Here, we show that a drug-like molecule that inhibits the doxorubicin efflux activity of Patch, enhances the cytotoxic, pro-apoptotic, antiproliferative and anticlonogenic effects of doxorubicin on both adrenocortical carcinoma (ACC) and melanoma cells which endogenously overexpress Patch. Moreover, we report that the addition of this molecule to doxorubicin treatment prevents the development of ACC tumors in xenografts mice much more significantly than doxorubicin alone, suggesting that the use of this molecule in combination with doxorubicin is a promising new therapeutic option for Patch expressing tumors.

Biography:

Isabelle Mus-Veteau is a CNRS Research Director working at the Institute of Pharmacology in Sophia Antipolis (Valbonne) in France. I performed my PhD thesis between France and Mexico and discussed it in 1992. She obtained a CNRS permanent position after a post-doc in the South of France. She is a biochemist and biophysicist specialist of membrane transport proteins. With her collaborators, we discovered the drug efflux activity of the Hedgehog receptor Patch and its role in chemotherapy resistance (Bidet et al 2012). The screening of several chemical libraries allowed us to discover several inhibitors of Patch drug efflux activity which enhance chemotherapy efficiency against several cancers (Fiorini et al. 2015, Hasanovic et al, submitted).