About 1 in 3 humans will experience cancer during their lifetime, and about 1 in 6 humans will die of cancer disease. Breast cancer is currently the most diagnosed neoplasm in women, with 2.2 million cases and 685 thousand of deaths worldwide.

Despite significant advances in diagnostics, molecular biology and drug development toward the goal of patient-tailored therapy, the mortality rate stagnates. Patients become unresponsive to treatment due to drug resistance occurs. Generally, cancer can be naturally insensitive to primary treatment (innate resistance) or manifest resistant phenotype after a prolonged period (acquired resistance).

This PhD thesis concerns acquired drug resistance to taxanes in breast cancer cells. We aimed to put light on mechanisms involved in paclitaxel and Stony Brook Taxane 0035 resistance and how we can overcome them.

We found several suspect genes with changed expression at the protein level between taxane-sensitive and taxane-resistant breast cancer cells. Among them, *ABCB1* gene codes for a versatile multidrug transporter P-glycoprotein was pivotal for resistance to paclitaxel and Stony Brook Taxane 0035.

Other genes with altered expression were localized primarily on the q arm of chromosome 7, exemplified by thyroid hormone receptor interactor 6 (*TRIP6*). A combination of active cyclic AMP response element (CRE) motif, hypomethylated *TRIP6* proximal promoter, the lack of *TRIP6*-regulatory miRNA-138-5p and amplification contribute to high TRIP6 expression in taxane-resistant MCF-7 breast cancer cells.

Novel semi-synthetic docetaxel derivatives named second-generation Stony Brook Taxanes, represented by SB-T-1216, efficiently overcome ABCB1-mediated taxane resistance. We hypothesize that C3' and C3'N taxoids poorly interact with residues in the ABCB1 binding pocket in contrast to paclitaxel.

To conclude, ABCB1 transporter has an essential role in taxane resistance *in vitro*. Taxane derivatives, in particular, bearing C3' and C3'N modifications can overcome ABCB1-mediated resistance. Furthermore, when *ABCB1* is amplified, genes proximal to *ABCB1*, exemplified by CRE-stimulated *TRIP6*, can be co-selected.