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## Multiplicity of acquired cross resistance in paclitaxel resistant cancer cells is associated with feedback control of TUBB3 *via* FOXO3a mediated ABCB1 regulation

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A cquired drug resistance is a primary obstacle for effective cancer therapy. The correlation of point mutations in class III  $\beta$  tubulin (TUBB3) and the prominent overexpression of ATP binding cassette P-glycoprotein (ABCB1), a multidrug resistance gene have been protruding mechanisms of resistance to microtubule disruptors such as paclitaxel (PTX) for many cancers. However, the precise underlying mechanism of the rapid onset of cross resistance to an array of structurally and functionally unrelated drugs in PTX resistant cancers has been poorly understood. We determined that the established PTX resistant cancer cells display ABCB1/ABCC1 associated cross resistance to chemically different drugs such as 5-fluorouracil, docetaxel and cisplatin. We found that feedback activation of TUBB3 can be controlled through the FOXO3a dependent regulation of ABCB1, which resulted in the accentuation of induced PTX resistance and encouraged multiplicity in acquired cross resistance. Regulatory effects of FOXO3a on P-glycoprotein (Pgp) function suggest the involvement of ABCB1 methylation, the ubiquitination of TUBB3, the functional PI3K/Akt pathway and the stimulation of drug induced FOXO3a arginine hyper methylation. In addition, we found that secretome factors from PTX resistant cancer cells with acquired cross resistance support a Pgp association in multidrug resistance (MDR) development, which assisted the FOXO3a mediated control of TUBB3 feedback. The direct silencing of TUBB3 reverses induced multiple cross resistance, reduces drug resistant tumor mass and suppresses the impaired microtubule stability status of PTX resistant cells with transient cross resistance. These findings highlight the control of the TUBB3 response to ABCB1 genetic suppressors as a mechanism to reverse the profuse development of multidrug resistance in cancer.

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## Surgical approaches to cat breast cancer (mammary tumor), their treatment and management at Richmond Crawford

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A study was done during July to August 2015 at Karachi Division; infected cats were carried at Richmond Crawford Veterinary Hospital Karachi (RCVH), Sindh Pakistan. 10 to 12 years old 08 cats with mammary neoplasm, showed signs & symptom; swelling on the breast, change in breast form, liquid coming out from the breast and skin becomes dark pink in color, it was confirmed by breast X-ray & other (blood & urine) test by help of Aga Khan Hospital Karachi. After confirmation a surgical removal of tumor was done with mastectomy procedure, during operation it was noted that tumor could reach on her vascular wall. Further patients treated with antibiotic and anti-inflammatory medicine recommended to owners. Neomycin Cream, Cicatrin Powder, Hydrogen per oxide, Payodine, Tincture Benzoide, Cotton, mepore; to disinfect the area and then finally make the mixture like a paste apply at wound. Results showed, after seven days wound was healed properly, animal movement and other behaviors were normal noted. The main opinion from research is that to reduce infectious perilous disease in our pets, pets directly infected our children and adult family members. When take right actions even aggressive, stiff infectious disease can be defeated easily in pets. At RCVH, Karachi Sindh Pakistan our team performed so many surgeries in different animals; it was first case performed in our country Pakistan and successfully treated Mastectomy (Breast Cancer Surgery) in Cat.

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