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Antibody based detection of biomarkers predicting response to taxanes in breast cancer patients

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Taxanes are an important class of agents for the treatment of a broad range of malignancies including breast cancer. They improve survival in patients with early stage breast cancer and metastatic breast cancer, however, drug resistance usually hinders successful cancer treatment. We investigated the expression of biomarkers associated with improved response and resistance to this class of cytotoxic drugs in various subtypes of breast cancer. We assessed protein expression of multidrug resistance protein 1 (MRP1), P-glycoprotein (Pgp), Secreted protein acidic and rich in cystein (SPARC) and Transducin-like enhancer of split 3 (TLE3) using immunohistochemistry (IHC) in 978 breast cancer samples. TLE3 have been previously implicated in response to taxane therapy and the biomarker SPARC has been shown to be associated with response to albumin bound paclitaxel. On the other hand, Pgp and MRP1 being part of the multidrug resistance proteins are associated with resistance to taxanes. Tumor subtypes included 36% hormone receptor positive, 15% HER2 positive and 49% triple receptor negative. MRP1 was positive in majority of the samples (95%), Pgp was negative in 93% of samples. Hormone receptor positive subtype had the highest number of TLE3 positivity (82%), followed by HER2 positive subtype (73%) and triple negative subset (61%). SPARC expression was not different between the different subtypes of breast cancer and the expression frequency ranged from 83-88%. Even though the frequency of TLE3 and SPARC was fairly high in the patients tested, there were very few patients who did not express any drug resistant proteins. Since both paclitaxel and docetaxel are substrates for Pgp and MRP1 mediated efflux, and their efficacy is compromised in cells that overexpress it, the evaluation of these predictive biomarkers may prove to be a valuable aid in the identification of individuals who may not benefit from taxanes.

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