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ABC subfamily C member 10 (ABCC10) is a promising novel target in Hodgkin's lymphoma

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Owing to the progress in its treatment, Hodgkin's lymphoma (HL) has become a potentially curable disease. However, there is a subset of HL patients has disease that is either refractory to treatment or relapses early; outcome for these groups is particularly poor. Moreover, patients receiving combined treatment are at higher risk for second malignancies. ABCC10, also known as multidrug-resistant protein 7 (MRP7), is the tenth member of the C subfamily of the ATP-binding cassette (ABC) superfamily. ABCC10 mediates multidrug resistance (MDR) in cancer cells by preventing the intracellular accumulation of certain antitumor drugs. Our study unveiled for the first time the expression pattern and effect of ABCC10 in Hodgkin's lymphoma (HL). Results of our study showed that ABCC10 is over-expressed in most HL derived cell lines and primary HL tumor cells as compared to normal B cells. Our functional studies showed that inhibition of ABCC10 by one of the inhibitor (Tariquidar) had a significant dose-dependent increase in the sensitivity of HL cells to doxorubicin. Importantly, in our study we found that overexpression of TXN was considered to be a negative prognostic factor for HL patients. We showed that there is a significant positive correlation between TXN expression level in tumor cells and tumor stage, that in turn act as a covariant, as it predicted initial response to treatment. These results indicate that ABCC10 plays a role in increasing toxicity of chemotherapy on HL cells, its overexpression affect clinical outcome, and it is a potential target in HL.

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Development and validation of a broadly distributed "Morphometric IHC" based test for optimal treatment planning for stage 1 and 2 IDC breast patients: Beyond ER, PR, Her2 and Ki67

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Assessment of 'risk of cancer recurrence' in ER+ breast cancer patients based on clinical parameters and biomarkers is insufficient leading to over-treatment with chemotherapy. OncotypeDx, Mammaprint are useful in limited sets of node negative (-) patients, but they are largely prognostic with limited chemo-predictivity and are prohibitively expensive in India and SE Asia. A cost-effective 'predictive' test which will: i) accurately estimate the 'risk of recurrence' for ii) a 'broader' (node - and +) set of patients is urgently required. Using a retrospective training cohort of 330 patients, we developed a Morphometric Immunohistochemistry based test comprising 5 biomarkers plus three clinical parameters to arrive at 'CanAssist Score' using a Machine Learning Statistical algorithm. The CanAssist Score stratifies patients into 'low or high' risk for recurrence. Analytical validation experiments performed to assess critical IHC variables confirmed the robustness of the test. Initial 'test validation' on 130 cases was 93% specific. Extended clinical validation on an additional 500 pre and post-menopausal cases shows NPV of 95% and specificity of 80%. Majority patients in 'low risk' group had Stage 2, Grade 2/3 disease over Grade 1. In a head-to-head pilot study with Oncotype Dx test 'CanAssist-Breast' had superior NPV and specificity. Importantly CanAssist-Breast correctly re-stratified many recurred cases as 'high risk' which were stratified as 'low risk' by Oncotype Dx and thus were not treated with chemotherapy. In conclusion, we have developed a highly specific, low-cost test to predict risk of recurrence and prevent overtreatment in patients with early stage breast cancer.

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