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Cancer testis antigen expression in triple negative breast cancer: Candidate targets for cancer immunotherapy

Julie Decock
Qatar Biomedical Research Institute, Qatar

Breast cancer is a major health concern in Qatar with a younger age at diagnosis and projections of 60% increase in new cases. Triple negative breast cancer (TNBC) is associated with advanced disease at diagnosis and poorer outcome and can be sub-classified into 6 gene-expression-based subtypes. These patients do not benefit from endocrine or HER2-targeted therapy and represent 15-20% of cases mandating the need for novel treatments. Although immunotherapy has shown promising results in different cancers, there are 2 clinical trials to-date assessing adoptive cell immunotherapy in TNBC. Cancer Testis Antigens (CTA) could be good candidate targets as their expression is often up-regulated in malignant tissues, while it is restricted in the testis and absent or very low in other somatic tissues. We mined the TCGA and NCBI GEO repositories for genomic data on CTA expression in TNBC and selected a panel of 15 CTAs for further investigation. Gene and protein expression was investigated in a series of 9 human TNBC cell lines, encompassing all subtypes. We found the gene expression of TSAG10, MAGEA5, PLAC1 and DKKL1 to be moderate/highly expressed in our cell lines and in both datasets and are confirming this on protein level. We are establishing a bio-bank of DNA and RNA of Qatari breast cancer patients and will present gene expression data of CTAs in TNBC tumors. Our preliminary findings suggest that TSAG10, MAGEA5, PLAC1 and DKKL1 could be good candidate targets for TNBC immunotherapy and in particular could benefit Qatari breast cancer patients.

jdecock@qf.org.qa

Role of glypican-3 immunocytochemistry in differentiating hepatocellular carcinoma from metastatic carcinoma of the liver utilizing fine needle aspiration cytology

Mohammed Zaakouk
Cairo University, Egypt

Purpose: Evaluation of the sensitivity and specificity of glypican3 (GPC3) in differentiating hepatocellular carcinoma (HCC) from metastatic carcinomas of the liver in cell block material.

Patients & Methods: Sixty cell blocks were prepared from liver FNAs performed in the radio-diagnosis Department, National Cancer Institute, in the period (Aug, 2011 to May, 2012). FNAs were performed in the presence of the cytopathologist for on-site evaluation of the aspirated material and preparation of cell blocks. Cases diagnosed as hepatocellular carcinoma or metastatic carcinoma was included in the study. Cell block sections were stained with anti GPC-3. Sensitivity, specificity and positive and negative predictive values of GPC3 were calculated. The final diagnosis was based on the triple approach of clinical data, radiological findings as well as cytomorphologic features aided by GPC-3 results.

Results: 70% of cases were diagnosed as HCC and 30% as metastatic carcinomas. 95.2% of HCC cases expressed GPC3. Poorly differentiated cases showed the highest GPC3 sensitivity (100%) followed by moderately differentiated cases (96.5%) and while well differentiated cases expressed GPC3 in 90% of cases. 83.3% of metastatic carcinomas were negative for GPC3. In this study, sensitivity of GPC-3 in HCC was 95.2%, specificity was 83.3%, positive and negative predictive values were 93% and 88.2% respectively and total accuracy was 91.7%.

Conclusion: Immunocytochemical staining for GPC3 in cell block material is a highly sensitive and specific method capable of distinguishing HCC from the vast majority of metastatic carcinomas of the liver.

Zaakouk@gmail.com