World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:11, No:06, 2017

Predicting High-Risk Endometrioid Endometrial Carcinomas Using Protein Markers

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Abstract : The lethality of endometrioid endometrial cancer (EEC) is primarily attributable to the high-stage diseases. However, there are no available biomarkers that predict EEC patient staging at the time of diagnosis. We aim to develop a predictive scheme to help in this regards. Using reverse-phase protein array expression profiles for 210 EEC cases from The Cancer Genome Atlas (TCGA), we constructed a Protein Scoring of EEC Staging (PSES) scheme for surgical stage prediction. We validated and evaluated its diagnostic potential in an independent cohort of 184 EEC cases obtained at MD Anderson Cancer Center (MDACC) using receiver operating characteristic curve analyses. Kaplan-Meier survival analysis was used to examine the association of PSES score with patient outcome, and Ingenuity pathway analysis was used to identify relevant signaling pathways. Two-sided statistical tests were used. PSES robustly distinguished high- from low-stage tumors in the TCGA cohort (area under the ROC curve [AUC]=0.74; 95% confidence interval [CI], 0.68 to 0.82) and in the validation cohort (AUC=0.67; 95% CI, 0.58 to 0.76). Even among grade 1 or 2 tumors, PSES was significantly higher in high- than in low-stage tumors in both the TCGA (P = 0.005) and MDACC (P = 0.006) cohorts. Patients with positive PSES score had significantly shorter progression-free survival than those with negative PSES in the TCGA (hazard ratio [HR], 2.033; 95% CI, 1.031 to 3.809; P = 0.04) and validation (HR, 3.306; 95% CI, 1.836 to 9.436; P = 0.0007) cohorts. The ErbB signaling pathway was most significantly enriched in the PSES proteins and downregulated in high-stage tumors. PSES may provide clinically useful prediction of high-risk tumors and offer new insights into tumor biology in EEC.

Keywords : endometrial carcinoma, protein, protein scoring of EEC staging (PSES), stage
Conference Title : ICBCMB 2017 : International Conference on Bioinformatics and Computational Molecular Biology
Conference Location : Toronto, Canada
Conference Dates : June 15-16, 2017