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Loss of MED23 Leads to Poor Prognosis in Invasive Breast Cancer

TA Aliyeva1 ; C Joseph1 ; E Provenzano2 ; R Russell,3 ; C Caldas4 ; S Sonbul1 ; C Nolan1 ; AR Green1 ; EA Rakha5 ; IO Ellis5 ; P A Mukherjee5

1 Department of Histopathology, School of Medicine, University of Nottingham, Nottingham, UK; 2 Addenbrooke's Hospital, Cambridge University Hospital NHS Foundation Trust, Cambridge, UK; 3 CRUK Cambridge Research Institute, Cambridge, UK; 4 CRUK Cambridge Research Institute, Addenbrooke's Hospital, Cambridge, UK; 5 Department of Histopathology,Nottingham University Hospitals NHS Trust, Nottingham, UK

Purpose of the study: The molecular mechanism of lymphovascular invasion (LVI) which determines the early metastatic phenotype in breast cancer is still not fully

understood. Lead from the METABRIC study revealed that MED23 correlated with negative LVI status (p=0.00005). Hence MED23 expression was studied at the protein level for correlations with LVI and other clinical-pathological parameters.

Methods: The METABRIC BC cohort (n=1980) was evaluated for MED23 mRNA expression and prognostic impact externally validated using the online bc-GenExminer 4.0. Correlation between MED23 protein expression with clinico-pathological parameters, patient outcome and other biomarkers were explored (Nottingham Tenovus series; n=1255) using immunohistochemistry (IHC).

Results: High MED23 mRNA expression was negatively associated with tumour stage and was differentially expressed in good prognosis integrative clusters 7 and 8 ($p<0.001$). MED23 IHC revealed nuclear expression (n-MED23). Although no association was found with LVI, higher n-MED23 expression correlated with low NPI, low grade, older age, ER+ status, low Ki67 index and low N-cadherin expression ($p<0.05$). Positive correlations with PTEN, GATA3, STAT3 and CDC42 ($p<0.001$), indicate possible interacting pathways. In univariate analysis, high n-MED23 expression showed better long-term patient outcome in the whole cohort and ER+ subgroups ($p<0.05$). Pooled MED23 expression in an external validation cohort (ER+LN-) also showed association with better patient outcome ($p<0.02$, HR=0.82, 95% CI 0.69-0.98).

Conclusion: Results of the study suggest that loss of n-MED23 is a marker of poor prognosis in invasive BC, results re-enforced by expression data. The difference in correlation with LVI at gene and protein level highlights the importance of IHC validation and indicates MED23 as a probable bystander in the LVI cascade.

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