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Cell Division Cycle 25C (CDC25C) Expression Confers Poor Prognosis in Invasive Breast Cancer

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Background: CDC25C, belonging to the Cdc25 phosphatase family, plays a major role in cell cycle control, impacting on DNA repair and apoptosis. It has been shown that poor prognosis/copy number high Luminal A breast cancers (BCs) are enriched for the Aurora kinase pathway including CDC25C leading to CDK1 activation (Ciriello et al, Breast Cancer Research Treatment, 2013:409). This study examined the associations of CDC25C with clinicopathological and molecular features in BCs including the low grade ER positive cohort.

Methodology: CDC25C mRNA expression was studied in the METABRIC BC cohort (n=1980) and externally validated using online expression datasets [bc-GenExMiner v4.0]. CDC25C protein expression level was assessed immunohistochemically on a large annotated series of BC (n= 1330) and correlations made with clinicopathological parameters and patient outcome.

Results: High CDC25C expression was significantly associated with poor prognostic factors including high grade, large tumour size, medullary like tumours, poorer NPI, ER-/PR- Her2+ status ($p<0.001$) and was differentially expressed in poor prognosis integrative clusters 5 and 10 ($p<0.001$). Cytoplasmic CDC25C (c-CDC25C) protein showed positive association with non-NST and non-medullary tumour subtypes while nuclear CDC25C (n-CDC25C) negatively associated with tumour stage ($p<0.05$). There was no association with ER, PR status, NPI and lymph nodes. However, high c-CDC25C resulted in poor survival at 20 years in the Grade 1 ER+ cohort ($p=0.007$), while high n-CDC25C showed better long term survival ($p<0.001$). Pooled CDC25C expression data in the external validation cohort showed an association with poor outcome ($p<0.0001$, HR = 1.45, 95 % CI 1.28—1.64).

Conclusion: CDC25C appears to be associated with poor prognosis in BC including the Grade 1 ER+ cohort, indicating the importance of further functional analyses.

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