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Over Expression of Retinoid X Receptor Gamma (RXRG) Predict Good Prognosis in Oestrogen Receptor Positive Breast Cancer

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Background: Breast Cancer (BC) is globally one of the most prevalent malignancies and a leading cause of cancer-related death. Retinoid X Receptor Gamma (RXRG) is a member of the nuclear receptor superfamily, which interacts with other nuclear receptors and plays a role in tumour suppression. This study aims to investigate the prognostic role of RXRG in BC.

Methods: RXRG protein expression was evaluated using a large well-characterised BC cohort (n=923) prepared as tissue microarrays. The association with different clinicopathological parameters and patient outcome were investigated. Prognostic significance of RXRG mRNA expression was also assessed using breast cancer gene miner (bc-GenExMiner v4.2).

Results: High nuclear RXRG expression is associated with good prognostic features including good Nottingham Prognostic Index group ($p<0.05$), lower histological grade ($p=0.04$) and smaller tumour size ($p=0.036$). Strong positive associations were observed with oestrogen receptor (ER) positivity and ER-related biomarkers: GATA3, FOXA1, STAT3 and MED7 ($p<0.00001$), and reduced expression of the proliferation marker Ki67 ($p=0.014$). RXRG overexpression was associated with longer BC-specific survival ($p<0.0001$) and less probability for the development of distant metastasis ($p=0.003$). In ER-positive tumours, high expression of RXRG showed significant survival advantage regardless of adjuvant systemic therapy ($p=0.04$). RXRG expression is an independent prognostic factor associated with improved survival, particularly in ER-positive BC. In the external validation cohorts, RXRG mRNA expression was associated with improved patients' outcome ($p=0.025$). Differential gene expression evaluation identified ER signalling pathway as the principal predicted master regulator of RXRG expression ($p=0.005$).

Conclusion: The findings support the proposed role for RXRG as a prognostic marker in ER-positive BC. Exploring the utility of RXRG as a potential therapeutic marker is warranted.