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


University of Nottingham, Nottingham, United Kingdom

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.