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# PGRMC1 Promotes Tumour Progression of Breast Cancer through Upregulation of ER? Expression and EGFR signalling

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The hormone receptor progesterone receptor membrane component-1 (PGRMC1) is upregulated in breast cancer and elevated expression of PGRMC1 is associated with increased tumour growth and poorer outcome, indicating a contribution of PGRMC1 in carcinogenesis of breast cancer. However, the role of PGRMC1 in breast cancer, its activation mechanism and involved signalling pathways are not fully understood yet. Therefore, the aim of the present study was to investigate the role of PGRMC1 in breast cancer progression, the last step of carcinogenesis.

Expression of PGRMC1 in breast cancer subtypes was investigated using TCGA data and correlated with overall- and metastasis free survival. The effect of PGRMC1 overexpression and –knockdown on proliferation was examined in vitro and in a xenograft model. Since the function of PGRMC1 is suggested to be regulated by differential phosphorylation, the PGRMC1 phosphorylation-status and the significance of PGRMC1 phosphorylation on cell proliferation was investigated. With the aim to further elucidate PGRMC1 signalling in breast cancer, we searched for signalling pathways which might be regulated by PGRMC1.

Expression of PGRMC1 was observed in every breast cancer subtype and high expression of PGRMC1 correlated with poorer outcome. Overexpression of PGRMC1 in the hormone-receptor positive cell lines MCF7 and T47D resulted in significant enhanced proliferation. Analysis of PGRMC1-dependent expression and activation of proteins revealed upregulation of ER? and ER?-dependent genes, as well as activation of EGFR signalling cascade. PGRMC1 phosphorylation at S56 and S181 was identified to be essential for enhanced proliferation and upregulation of ER? and ER?-dependent genes.

Our results emphasize an important role of PGRMC1 in breast cancer progression and display a potential embedding of PGRMC1 in important breast cancer signalling pathways. PGRMC1 might therefore be an interesting target for anti-cancer therapy.

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