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Prolactin pro-differentiation pathway in triple negative breast cancer: Impact on prognosis and potential therapy

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Triple negative breast cancer (TNBC) is a heterogeneous disease associated with poor clinical outcome and lack of targeted therapy. TNBC tumor cells are characterized by the loss of epithelial differentiation phenotype and the acquisition of stem cell-like mesenchymal features with high tumor-initiating capacity. The hormone prolactin (PRL) is a well-established differentiation factor for mammary epithelial cells. Here we examined the role of prolactin-mediated differentiation pathway in prognosis, sub-classification and potential therapeutic option in TNBC. Our findings showed that PRL and its signaling pathway serve as a sub-classifier and predictor of pro-differentiation therapy in TNBC. Using immunohistochemistry and various gene expressions in silica analyses, we observed that prolactin receptor (*PRLR*) protein and mRNA levels are down regulated in TNBC cases. In addition, examining correlation of *PRLR* gene expression with metagenes of TNBC subtypes (580 cases), we found that *PRLR* gene expression sub-classifies TNBC patients into a new subgroup (TNBC-*PRLR*) characterized by epithelial-luminal differentiation. Importantly, gene expression of PRL signaling pathway components individually (PRL, *PRLR*, Jak2 and Stat5a), or as a gene signature, is able to predict TNBC patients with significantly better survival outcomes. As PRL hormone is a druggable target, we determined the biological role of PRL in TNBC biology. Significantly, restoration/activation of PRL pathway in TNBC cells representative of mesenchymal or TNBC-*PRLR* subgroups led to induction of epithelial phenotype and suppression of tumorigenesis. Altogether, these results offer potential new modalities for TNBC stratification and development of personalized therapy based on PRL pathway activation.

Biography

Vanessa M Lopez Ozuna has completed her Medical degree at the National Autonomous University of Mexico, School of Medicine. She has experience as a Medical Doctor and as a Professor in the Faculty of Medicine. She is now a PhD candidate in the Experimental Medicine Program at McGill University. She has participated in several publications and chapters of books as a first author.

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