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Novel molecular classifiers of basal-type subset in breast cancer patients

Shawn Baldacchino[1], Christian Saliba[2], Jean Paul Ebejer[2], James DeGaetano[3], Christian Scerri[4], Godfrey Grech[1]

[1]Department of Pathology, Faculty of Medicine and Surgery, University of Malta, [2]Centre for Molecular Medicine and Biobanking, University of Malta, [3]Histopathology, Department of Pathology, Mater Dei Hospital, [4]Department of Physiology and Biochemistry, Faculty of Medicine and Surgery, University of Malta

Introduction: The basal breast cancer subtype persists as a heterogeneous group that shows worse prognosis due to lack of targeted therapy. Understanding the deregulated cellular mechanisms uncovers new therapeutic targets which require biomarkers to select eligible patients. Analysis of datasets (cBioPortal) show that 59.6% of basal cancer exhibit deregulation of the PP2A cellular feedback mechanism. Our study aims to define biomarkers for PP2A deregulation in the basal subtype.

Methods: Genes commonly deregulated in basal cancer associated with PP2A regulation were selected as potential basalPP2A biomarkers. A 40-gene expression panel was compiled, consisting of basal/luminal classifiers; epithelial-mesenchymal transition markers; PP2A subunit expression; basal PP2A biomarkers and housekeeping genes. The Luminex® beadbased expression assay was validated and used to analyse 44 Laser microdissected Maltese formalin fixed paraffin embedded (FFPE) breast tumours. Data was converted to a z-score, analysed using the RapidMiner Studio software (version 6.3.0.0) and illustrated using Principal Component Analysis (PCA). This analysis could be applied to breast cancer RNASeq data from TCGA (N=520).

Results: breast cancer datasets were accurately defined into luminal, HER2enriched and basal molecular subtypes using 10 classifier genes with 98.2% concordance to the PAM50. When using the 5 basal PP2A biomarkers to drive classification, the basal subgroup is segregated into 2 groups which are predicted to have distinct PP2A activity.

Conclusion: The novel biomarkers divide the basal breast cancer patients into subtypes, one of which is potentially eligible to PP2A activating therapy. Further analysis shall correlate PP2A activity with PP2A inhibitory subunit expression using immunohistochemistry.

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