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Molecular classifiers of breast cancer patients using multiplex assays

Christian Saliba[1], Shawn Baldacchino[2], Maria Pia Grixti[2], Vanessa Petroni[2], Robert Gauci[2], James DeGaetano[3], Anthony G. Fenech[4], Christian Scerri[5], Godfrey Grech[2]

[1]Centre for Molecular Medicine and Biobanking, University of Malta, [2]Department of Pathology, Faculty of Medicine and Surgery, University of Malta, [3]Department of Pathology, Mater Dei Hospital, Msida, [4]Department of Clinical Pharmacology and Therapeutics, Faculty of Medicine and Surgery, University of Malta, [5]Department of Physiology and Biochemistry, Faculty of Medicine and Surgery, University of Malta

Introduction: Breast cancer patients can be classified using receptor status or based on expression of specific signature genes. Classification of patients provides the basis to select specific targeted therapy and to identify new molecular subytpes with potential therapeutic options. Data from the cBioPortal for cancer genomics demonstrate that PP2A function is likely to be reduced in up to 60% of basal breast tumours. Tumours exhibit either homozygous deletion or underexpression of PP2A, but also overexpression of PP2A inhibitors. In this study we classify molecularly breast cancer cell lines and a cohort of Maltese patients. In addition, we assessed the effect of PP2A activity restoration on the cellular models.

Methods: Twelve human breast cancer cell lines representing different breast tumour subtypes were cultured. Forty breast cancer tumours from various subtypes were collected. A Luminex® beadbased multiplex assay was used to quantify transcript levels of PP2A and its inhibitors, but also other signature genes. Sensitivity to different drugs that target the PP2A complex was determined by MTT assays following treatment with incremental doses. An effective dose was selected and used to assess protein expression and localisation using immunofluorescence.

Results: Our data show that PP2A inhibitors are significantly upregulated in TNBC cell lines and patients. In addition, the TNBC cell lines are more sensitive to low doses of drugs that target the PP2A complex. PP2A inhibitors are downregulated in TNBC cell lines following treatment.

Conclusion: The TNBC subset of patients with suppressed PP2A activity would be eligible for treatment using therapies which target the mTOR pathway.