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Molecular classification of breast cancer using a multiplex assay

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Utilisation of biomarker panels is increasingly being employed to subtype tumours into therapeutic groups. This is exemplified by the oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) molecular classification in breast cancer. Understanding deregulated cellular mechanisms in tumours uncovers new targets for therapy, and defining biomarkers is vital for translation of basic research to the clinical setting. Our study aims to classify breast cancer tumours in accordance with the latest guidelines and to identify tumours eligible for PP2A activation therapy. A set of 40 genes were selected to classify breast cancer patients. These genes can be divided into 4 main categories: 1) Basal vs. luminal classifiers, 2) Epithelial-mesenchymal transition (EMT) markers, 3) PP2A activity regulators, and 4) Breast cancer signature genes. 11 breast cancer cell lines were used for validation of the assay. The 40-gene signatures of archival FFPE tissue were obtained and laser microdissection was used to isolate histological diverse tumour sections along with matched normal tissue. Our results show that PP2A deregulation was predominantly driven by CIP2A overexpression in triple negative (ER, PR and HER2 negative) and in HER2 positive breast tumours whereas SETBP1 was overexpressed predominantly in ER positive and triple positive breast (TNBC) tumours. The 40-gene multiplex assay can be used to classify breast cancer molecular profiles and to identify a new TNBC subtype characterised by PP2A deregulation. These patients, as seen in cell line-based assays, may be eligible for novel PP2A activation therapy.

Biography

Godfrey Grech is Senior Lecturer at the University of Malta and currently responsible for the National Breast Cancer Research Project. He is highly recognised by the clinical sector and runs numerous projects in collaboration with Mater Dei Hospital and International Institutions such as the Molecular Medicine Institute in Leeds. His main research topic aims to identify biomarkers to classify breast cancer patients into a specific therapeutic group that shall benefit from activation of phosphatases as a main therapeutic option. He is part of international scientific committees including the International Scientific Council of the European Group for Molecular Pathology (EMP), Global Leader at the Genomic Medicine within the National Human Genome Research Institute (NHGRI) of the US National Institutes of Health (NIH), member of the Pharmacogenomics Working Group of the Global Genomic Medicine Consortium (G2MC), Leader of the Cancer Position Paper at the European Association for Predictive, Preventive & Personalised Medicine (EPMA), and national contact point for the PharmacoGenetics for Every Nation Initiative (PGENI).

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