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A PET-surrogate multigene signature for breast cancer prognosis

Introduction

Breast cancer (BC) is the most frequently diagnosed cancer worldwide, representing approximately 12% of all cancer cases and 7% of cancer-related deaths annually. Several molecular subtypes of BC are recognized and used in the clinic to predict prognosis and guide therapy. Among these, Luminal BCs, characterized by the expression of hormone receptors, account for around 65% of cases and are often associated with favorable outcomes. However, approximately 20% of these patients still experience late metastatic relapse. The identification of these high-risk patients is crucial to improve prediction of tumor recurrence and chemotherapy response.

Unmet Medical Need

Metabolic alterations in cancers can be exploited for diagnostic, prognostic, and therapeutic purposes. This is exemplified by 18-fluorodeoxyglucose (FDG)-positron emission tomography (FDG-PET), an imaging tool that relies on enhanced glucose uptake by tumors enabling imaging of primary tumors and metastasis. However, FDG-PET might exhibit low resolution and low sensitivity, especially in early-stage cancers, often leading to under-detection of aggressive cases. Therefore, an urgent need exists for non-invasive, reliable prognostic molecular tools to capture tumor metabolic profiles that would help improving patient stratification and ameliorating therapeutic decisions.

Solution

PETsign is an innovative multigene signature serving as a FDG-PET surrogate, able to predict tumor metabolic profiles and disease outcome. Derived from BC patients stratified by FDG-PET and validated across independent datasets, PETsign acts as an independent predictor of risk of relapse in Luminal BCs. Furthermore, PETsign has the potential to guide therapy decision by predicting tumor sensitivity to anti-glycolytic drugs. Molecular pathways, such as C-X-C motif chemokine ligand 8 (CXCL8) and epidermal growth factor receptor (EGFR) signaling pathways, are prominent in PETsign and their activation in BC cells causes a shift towards a glycolytic phenotype, supporting the use of PETsign for the design of novel combinatorial therapies, particularly for aggressive BCs lacking targetable alterations.

Advantages

PETsign can be used for:

- Prognostic stratification of breast cancer patients
- Guiding therapeutic decision-making, particularly for response to anti-glycolytic drug therapies
- Supporting the development of novel combinatorial therapies

Opportunity

Istituto Europeo di Oncologia is seeking industrial partners and/or investors interested in advancing PETsign into clinical practice.

Main inventors

Prof. Pier Paolo Di Fiore, MD PhD

Full Professor of General Pathology at the University of Milan
Group Leader and Director of the Novel Diagnostics Program at IEO
Global expert in endocytosis, cancer, and cellular signaling
Pioneer in linking endocytic to tumorigenesis and metastasis
Author of over 250 publications in peer-reviewed journals
Inventor of patent applications on cancer prognostic methods

Prof. Letizia Lanzetti, PhD

Associate Professor of Biochemistry at the University of Torino
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Relevant publications:

Confalonieri et al., Adv Sci 2024 https://doi.org/10.1002/advs.202308255

Priority patent application:

EP24165583.6; co-owned by IEO, University of Milan, University of Turin, and Candiolo Institute - Piedmont Foundation for Oncology – IRCCS

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