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A new take on growth factor signaling in tamoxifen resistance

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Differences in growth factor (GF) signaling may cause the poor prognosis in some breast cancer cases. A new study, published in the open access journal *BMC Medical Genomics*, suggests that some estrogen receptor-positive breast cancers respond poorly to tamoxifen because of increased GF signaling.

Sherene Loi, from the Peter MacCallum Cancer Centre, Melbourne, worked with a team of Australian and Belgian researchers to investigate the differences between those estrogen receptor positive (ER+) cancers that respond well to tamoxifen (luminal-A) and those that do not (luminal-B). She said, "This is the first study specifically investigating the biology of the luminal-B, ER+ breast cancer subtype. We propose that activation of GF signaling contributes to this highly proliferative, relatively tamoxifen-insensitive, phenotype and that this exists independently of HER2 overexpression. Targeting this pathway and its upstream mediators could prove to be a useful therapeutic strategy".

The researchers used a new computational method of analysis of gene expression data called gene set enrichment analysis (GSEA) to determine that there is increased growth factor activation from the gene expression profiles of nearly 100 luminal-B breast cancers samples. They then validated this finding by showing that treatment with the growth factor heregulin, which induced growth factor signaling an in-vitro model, could overcome tamoxifen-induced cell cycle arrest.

This research represents a departure from the informative, but

sometimes not terribly useful, process of identifying genes associated with given conditions. Dr Loi said, "Although gene expression data has demonstrated its ability to identify subsets of disease and predict outcomes or drug responses, identifying new therapeutic approaches based on whole genome microarray profiling has, to date, been a significant challenge. By using GSEA, we've been able to use gene expression data to identify that activation of GF signaling pathways as a possible therapeutic target for further exploration in the clinical setting for these particular breast cancer patients".

More information: Gene expression profiling identifies activated growth factor signaling in poor prognosis (Luminal-B) estrogen receptor positive breast cancer, Sherene Loi, Christos Sotiriou, Benjamin Haibe-Kains, Francoise Lallemand, Nelly M Conus, Martine J Piccart, Terence P Speed and Grant A McArthur, *BMC Medical Genomics* (in press), www.biomedcentral.com/bmcmedgenomics/

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