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Clinico-pathological and transcriptomic determinants of SLFN11 expression in invasive breast carcinoma

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SLFN11 is a putative DNA/RNA helicase we discovered as causally associated with sensitivity to DNA damaging agents, such as platinum salts, topoisomerase I and II inhibitors, and other alkylators in the NCI-60 panel of cancer cell lines [1]. Later, SLFN11 was identified as an early interferon response gene, in association with HIV infection [2]. Here we assessed SLFN11 determinants in a gene expression meta-set of 5,061 breast cancer patients annotated with clinical data and multigene signatures obtained with the package genefu [3]. By correlation analysis, we found 537 transcripts above the 95th percentile of Pearson's coefficients with SLFN11, identifying "immune response", "lymphocyte activation", and "T cell activation" as top Gene Ontology enriched processes [4]. Through multiple correspondence analysis, we discovered a subgroup of patients characterized by high SLFN11 levels, ER negativity, basal phenotype, elevated CD3D, STAT1 signature [5], and young age. Fitting a penalized maximum likelihood lasso regression model [6], we found a strong multivariable association of SLN11 with the stroma 1 and stroma 2 signatures [7,8], associated with basal cancer and response to chemotherapy in ER- tumors. Finally, using Cox proportional hazard regression, ER-, high proliferation, high SLFN11 patients undergoing chemotherapy treatment showed a significantly longer disease-free interval than other patient categories included in our model.

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