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Decreased expression of *CIP2A* and *SETBP1* following drug-induced activation of the PP2A complex in triple negative breast cancer cell lines

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Introduction: Triple negative breast cancer (TNBC) patients derive little benefit from target-specific therapies due to lack of the favourable prognostic targets. 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 namely CIP2A, SET and/or SETBP1. In this study we assess the effect of FTY720, an activator of PP2A, on breast cancer cell lines.

Methods: Twelve human breast cancer cell lines representing different breast tumour subtypes and a non-tumorigenic epithelial breast cell line were cultured. Luminex® bead-based multiplex assay was used to quantify transcript levels of PP2A and its inhibitors. FTY720 sensitivity was determined by MTT assays following treatment with incremental drug doses.

Results: *In silico* analysis of datasets show that CIP2A is significantly upregulated in the HER2+ and the TNBC patients. To support this, our data show higher expression of CIP2A in TNBC cell lines. In addition, the TNBC cell lines are more sensitive to low doses of FTY720. CIP2A and also SETPB1 are downregulated in TNBC cell lines following treatment.

Conclusion: The PP2A complex is perturbed in the majority of TNBC cell lines. Moreover, this subset of breast cancer cell lines with overexpression of PP2A inhibitors CIP2A and SETBP1 are sensitive to the PP2A activator, FTY720. This suggests a possible class of breast tumours that may be eligible to the novel PP2A activating targeted therapy.