Protein phosphatase 4 regulates cell survival and responses to PI3K/AKT/mTOR pathway inhibitors in breast cancer cell lines

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Background:
Protein phosphatase 4 (PP4) is a PP2A-related serine/threonine phosphatase which has already been implicated in the control of cell proliferation, cell cycle and tumorigenesis. We have previously identified the catalytic subunit of PP4 (PP4c) as an important gene in the regulation of both apoptosis and cell proliferation in breast cancer cells. The aims of this study were to examine the effects of reducing the expression of PP4c on breast cancer cell survival and their responses mTOR, Akt and PI3K inhibitors.
Material and method:
MCF7 and MDA-MB-231 were transfected with siRNAs to different PP4c sequences, controls received scrambled siRNA. Culture viability, migration, long term survival and apoptosis were assessed post transfection. In some experiments, transfected cells were exposed to chemotherapeutic drugs post-transfection to induce apoptosis, then culture viability and apoptosis were assessed.
Results:
siRNA mediated silencing of PP4 enhanced the proliferation and survival of MCF7 and MDA-MB-231 cells and increased their colony forming and cell migration abilities. In MCF7 cells, reduced PP4c expression decreased their sensitivity to mTOR, Akt and PI3K inhibitors. However, a reduction in PP4c levels in MDA-MB-231 sensitised the cells to mTOR, Akt and PI3K/mTOR inhibitors but had no effects on the response to PI3K inhibitor.
Conclusion
Our results reveal a complex role of PP4 in controlling breast cancer cell survival and highlight the importance of identifying the signalling pathways regulated by PP4c and its role in the development and treatment of breast cancer.

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