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Differential expression of breast cancer signature genes following rapamycin treatment

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Introduction: Breast cancer is classified into intrinsic molecular subtypes, each relating to predictive prognostic and clinical outcomes. Rapamycin inhibits the mammalian target of rapamycin (mTOR) pathway, which is often deregulated in various types of cancer. mTOR inhibitors are associated with antiproliferation and apoptosis. Aim: Investigating the differential expression of breast cancer signature genes following rapamycin treatment in various breast cancer subtypes.

Methods: MDA-MB-436 (ER-PR-HER2-) and MCF7 (ER/PR+ HER2-) cells were exposed to rapamycin concentrations of 0, 10, 25, 35, 50, 65, 75, 100ng/mL. Following 24 hours the cell viability was measured using an MTT assay, or lysed to prepare RNA for transcript quantification using Luminex® beadbased multiplex assay.

Results: MCF7 was sensitive to rapamycin with 10ng/mL. MDA-MB-436 was not sensitive to all rapamycin concentrations. Following mTOR inhibition both cell lines exhibit downregulation of *AURKA*, and as expected a downregulation of *VEGFA*. Upregulation of *TFF3* occurred with rapamycin addition in MCF7. In MCF7, *TFF3* and *PTEN* expression negatively correlates with cell viability.

Conclusion: This study depicts *AURKA*, which has a role in tumour development, being downregulated upon mTOR inhibition with rapamycin. This provides a mechanism for increased sensitivity to mTOR inhibitors in breast cancer with *AURKA* chromosomal amplifications. Although *TFF3* is associated with progression of disease and metastatic breast cancer, upregulation of *TFF3* following rapamycin treatment correlates with decreased viability in MCF7. Identifying the genetic expression changes with different rapamycin concentrations for each subtype, will pave the way towards predicting therapeutic response, and understanding therapeutic effects in different breast cancer cell lines.