One of the major causes of death amongst breast cancer patients is due to the development of distal metastases and the acquisition of resistance to chemotherapeutic agents. There is a scientific and clinical need to understand the alterations in cellular signalling pathways that could contribute to chemotherapeutic resistance in breast cancer. One such potential pathway is the serine/threonine kinase mTOR pathway.

We examined the protein and activation levels of mTOR pathway components in a Taxol-sensitive (T-47D) and Taxol-resistant (T-47D TaxR) breast cancer cell line by western blotting. We showed that mTOR signalling was up-regulated in the Taxol-resistant cell line compared to parental Taxol-sensitive cells. This upregulation was also accompanied by increased Brk, a tyrosine kinase that is over expressed in the majority of breast cancers and a potential candidate for mediating chemo-resistance.

Transfection of the Brk-negative breast cancer cell line, MDA-MB-468 with wild-type Brk resulted in an increase in the levels of both mTOR and, to a lesser extent, the downstream signalling component GβL compared to cells transfected with vector only.

These data implicate Brk in upregulating mTOR expression and indicate that Brk may influence mTOR signalling in the development of Taxol resistance.