

**P002** Components of the mTOR signalling pathway are altered during drug resistance in ovarian cancer

**Helen Foster, Emmanouil Karteris, Amanda Harvey**

*Biosciences, Brunel University*

The major limitation to successful chemotherapy treatments is the acquisition of drug-resistance during treatment. In advanced stage ovarian cancer the mTOR pathway is up-regulated, and inhibition of this pathway increases chemo-sensitivity in ovarian carcinoma cell lines. In this study we investigated the expression of mTOR signalling components in SKOV-3 and PEO-1 ovarian carcinoma cell lines (parent and Taxol resistant).

Using semi-quantitative RT-PCR and Western blotting we have shown that there is no difference in the expression of mTOR mRNA and protein in fully stimulated cells. However, a significant up-regulation of the expression of p90 S6K1 splice variant in PEO-1-TaxR cells at mRNA level was noted, suggesting that effectors downstream of the mTOR might be altered in a drug-resistant state. Moreover, when cells were fully stimulated with 10% FCS, there was no change in the phosphorylation status of mTOR (Ser2448) or the p70 S6K (Ser371, Thr 389) when we compared parent and Taxol resistant cells. These results indicate that the nutrient supply-dependent regulation of the mTOR signalling pathway remains intact in both parent and Taxol resistant ovarian cancer cell lines. We hypothesise that mTOR signalling can play a potential role in mediating the chemo-resistance of ovarian carcinoma cells to therapeutic agents such as Taxol.