Episodic Src activation in uveal melanoma revealed by kinase activity profiling

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**Study Design**

The hypothesis was tested that an unidentified tyrosine kinase is responsible for the finding that in metastases of uveal melanoma (UM), in comparison to primary cells, the classical MAPK signaling pathway is deregulated by a reduction in ERK1/2 activity.

UM primary and metastatic cell lines models were investigated in phospho tyrosine kinase assay using the PamGene technology to detect differences in phosphorylation between these two stages in cancer progression.

**Key Findings**

We identified nine peptides derived from eight proteins that were differentially phosphorylated between primary and metastatic cell line lysates (table 1). From these we identified, using literature, the upstream kinases, most often Src (Table 1). To validate the candidacy of Src\textsuperscript{in vitro} inhibition experiments by spiking Src-kinase specific inhibitors PP1 and PP2 into the lysates of primary UM tissue and UM cell line was performed. The inhibitory effect of the Src kinase inhibitors is shown in figure 1. Transfection of the Mel270 cell-line with siRNA constructs that target Src showed a clear decrease in activity of Src in the transfected cell-lines (figure 2). These findings were confirmed with Western, expression RNA and cell-proliferation studies (Maat et al 2009).

**“Author Quote”**

In conclusion, using tyrosine kinase activity profiling we identified Src as a determinant of ERK1/2 activation and showed that Src expression and kinase activity, together with ERK1/2 activation, are reduced in UM metastases cell lines.

**Background**

Uveal melanoma (UM) is a rare neoplasm (6-8 cases per million) that arises from melanocytes in the eyes. Little is known about the molecular pathogenesis of UM. Previous research has shown that although mutations are absent, the RAS/RAF/MEK/ERK pathway is essential for UM growth and suggests that an upstream factor is involved in UM. This hypothesis was tested in this study by use of PamGene’s Tyrosine kinase activity microarray platform.

**Conclusion**

A novel upstream kinase, Src, was identified using PamChip\textsuperscript{®} microarray in primary Uveal Melanoma tissues and cell-lines. This may provide a new treatment modality for Uveal Melanoma by for instance the use of Dasatinib which targets Src.