**Elucidating the role of PIM kinase and its therapeutic potential in NSCLC**

**Introduction**

PIM kinases are a family of three serine/threonine kinases: PIM1, PIM2 and PIM3 that have been shown to play a role in tumorigenesis. PIM1 is a downstream effector of oncoproteins ABL and JAK/STAT and regulator of BCL2/BAX and CXCR4. PIM activity is synergistic with the PI3K/Akt/mTOR pro-survival pathway and PIM2 has been shown to phosphorylate translational repressor 4E-BP1 and p70S6 independently of the PI3K pathway. Furthermore a synergism between PIM kinases and c-Myc has been reported. Here we investigate the expression of Pim-1/Pim-2/Pim-3 in NSCLC cell lines and patient matched normal/tissue samples. The effect of a novel combined inhibitor of Pim3/mTOR/PIM kinases (IBL-301) on cell signalling, cell viability is also examined.

**Methods**

- Pim-1/Pim-2/Pim-3 expression were examined by Western blot analysis in NSCLC cell lines.
- Additionally, the frequencies of Pim-1/Pim-2/Pim-3 expression in NSCLC patient tumour and matched normal adjacent samples (n=31) were investigated.
- The effectiveness of the novel inhibitor of Pim3/mTOR/PIM kinase, IBL-301, on cell signalling and cell viability were examined by Western blotting analysis and CellTitre Blue assay respectively.

**Results: Expression of Pim kinase isoforms in lung cancer patients**

![Graph showing expression levels of Pim kinases](image)

**Results: Effect of IBL-301 on NSCLC cell viability**

![Graph showing cell viability](image)

**Results: Alterations to PI3K/mTOR signalling by IBL-301 in NSCLC cell lines**

![Graph showing PI3K/mTOR signalling](image)

**Conclusion**

This is the first study to investigate the expression of all 3 isoforms of Pim kinase in lung cancer specifically. All isoforms were abundantly expressed across cells lines and patient tumour samples. Observed Pim kinase expression in the immune cells of normal adjacent tissue may indicate a role in inflammation. These findings coupled with the promising in vitro data using the novel P3K/mTOR/PIM-targeting inhibitor IBL-301 demonstrate the therapeutic potential of targeting PIM in NSCLC.

**Future Directions**

We are currently investigating the effect of novel compound IBL-301 and the clinically relevant PI3K/mTOR inhibitor BE2235 in an ex vivo lung tumour model. In this model fresh tumour biopsies are cultured for 72 hours with the compounds at a chosen dose. Once we have sufficiently increased the sample study size, the biobanked tissue and tissue conditioned medium (TCM) will be used for down stream studies on alterations to gene and protein expression and the secretome.