

**P008** Upregulation of PI 3-kinase $\gamma$  by Bcr-Abl

**Hickey F and Cotter TG**

*Department of Biochemistry, Biosciences Institute, University  
College Cork, Ireland.*

Chronic myeloid leukaemia is a clonal haematopoietic stem cell disorder characterised by the t(9;22) translocation and resultant production of the constitutively activated bcr-abl kinase. In order to identify genes associated with the expression of BCR-ABL we used microarrays to compare the transcriptome of a normal mouse haematopoietic cell line (32D) with that of a transfected clone expressing high levels of BCR-ABL (C4). Based on a threshold level of a change factor of  $>2.0$  we found that the level of 323 cDNAs were upregulated and conversely 130 cDNAs were downregulated in C4 cells. Among the genes with increased expression in C4 cells was PI 3-kinase gamma. Class IA PI 3-kinases have previously been implicated in the pathogenesis of CML, however, this work represents the first finding of an involvement for the class IB isoform PI3K $\gamma$ . The increase in expression was confirmed by RT-PCR, and real-time PCR shows that this increased mRNA is the result of increased transcription rather than increased stability of the PI3K $\gamma$  mRNA. It was found that the increased mRNA levels in C4 cells are mirrored by an increase in PI3K $\gamma$  protein in these cells. Lipid and protein *in vitro* kinase assays have been used to demonstrate that C4 cells also show increased PI3K $\gamma$  activity.