

P020 Ultrasensitive Mass Spectrometric Quantification of the PI3K/Akt Signaling Pathway in Absolute Units
Cutillas PR ^{1,2}, **Waterfield MD** ^{2,3}, **Vanhaesebroeck B** ^{1,2}

¹ *Cell Signalling in Cancer, Ludwig Institute for Cancer Research, UCL branch*

² *Department of Biochemistry and Molecular Biology, University College London*

³ *Proteomics Unit, Ludwig Institute for Cancer Research, UCL branch*

Rational cancer therapy aimed at selective inhibition of the PI3K/Akt signaling axis, one of the most frequently deregulated pathways in cancer, will require simple tools to validate and measure the impact of targeted inhibition on primary cancer tissues. We have developed an approach, based on the mass spectrometric measurement of enzymatic activity, for the ultrasensitive quantitation of signaling pathways in absolute units. We used this approach to quantify PI3K pathway activation in solid and liquid tumors. In addition, we also measured PI3K signaling in cancer stem cells, a cell subpopulation in cancers that needs to be eradicated for effective therapy but, because of its low abundance, has thus far been precluded from this type of analysis. This novel application of mass spectrometry may be considered as the closest analytical equivalent in proteomics to the polymerase chain reaction used to amplify nucleic acid sequences, and could contribute to the development and implementation of personalized cancer therapies.