

P052 The selective pharmacological inhibition of PI3K isoforms and effects on insulin signalling

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Phosphoinositide 3-kinases (PI3Ks) play major roles in controlling cell proliferation, migration, protein synthesis and glucose metabolism. While known to be critical for Insulin mediated signalling, the relative importance of each PI3K isoform has remained elusive until recently. We have employed a panel of inhibitors with distinct isoform selectivity, enabling us to dissect pharmacologically the relative importance of P110 α , β and δ catalytic subunits. In order to elucidate the impact of each isoform on glucose metabolism, downstream markers of the Insulin receptor pathway were monitored upon compound treatment in cells derived from muscle, liver and fat. We have also measured Insulin stimulated glucose uptake in L6-Myocytes and 3T3-L1 adipocytes. Our data indicate that P110 α is the major PI3K isoform controlling insulin signalling, in agreement with recent published findings. With intense interest in targeting P110 α for cancer therapy, these findings highlight the need for glucose monitoring when such therapies enter the clinic.