

P013 Characterisation of inter- or intra-molecular interactions in the regulatory subunit of PI3K

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Only the broad outlines of the activation process of PI3K are known currently. The main signal for activation consists of an interaction of the two SH2 domains with phosphotyrosines in target proteins. Additional processes might influence this pathway, e.g. Interactions involving the SH3 and BH domains in the N-terminus of the regulatory subunit. It is also unclear if both SH2 domains have to bind to two phosphotyrosines simultaneously. Recent observations that PI3K becomes oncogenic when the C-terminal SH2 domain from the regulatory subunit is missing might point to a more independent role for the two SH2 domains. In a collaborative effort combining cell biology, NMR spectroscopy and thermodynamics we have characterised the interaction of short peptides from the linker region that connects the coiled-coil domain with the C-terminal SH2 domain. Despite the fact that these peptides do not contain a phosphotyrosine they bind specifically to the phosphotyrosine binding site. Details of the interaction will be described in connection with the thermodynamics of the interaction and put in context to the importance of the C-terminal SH2 domain.