P009 Analysis of P-REX1 a Novel PtdIns(3,4,5)P_3 and Gβγ-Regulated RAC Exchange Factor

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P-Rex1 is a novel PtdIns(3,4,5)P_3 and Gβγ-regulated Rac exchange factor expressed in myeloid-derived cells and brain. Rac is a member of the Rho family of monomeric GTPases and is an integrator of intracellular signalling in a variety of cellular processes, from universally important responses such as transcriptional activation, definition of cell shape and cell motility to neutrophil specific responses such as the formation of superoxide by the NADPH oxidase. P-Rex1 has been shown to provide a major link between Phosphoinositide-3-Kinase, G-proteins and Rac in neutrophils.
P-Rex1 is an 185kDa protein containing a typical Rho-GEF domain and tandem PH domain, two DEP and two PDZ domains and significant similarity over its C-terminal half to Inositol Polyphosphate-4-Phosphatase. A panel of P-Rex1 deletion and point mutants have been created to gain an insight into P-Rex1 activation and regulation. Results will be presented here addressing the role of the PH and DEP domains in P-Rex1 activation by PtdIns(3,4,5)P_3 and Gβγ. This will help in understanding the relative contributions of Phosphoinositides and Gβγ to P-Rex1 activation and the eventual identification of the domains to which they bind.