Cpc2 the RACK1 orthologous as a potential negative regulator of Gβγ subunit

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Most of the extracellular detection and/or signal transmission within a cell require the involvement of G proteins. G protein-coupled receptors initiate signalling by promoting exchange of GDP for GTP, on the Gα subunit of heterotrimeric G-proteins enabling Gα-GTP to activate downstream effectors. Signalling is terminated when the GTP is hydrolysed to GDP through the intrinsic GTPase activity of the Gα subunit, in a reaction that can be catalysed by the regulator of G protein signalling (RGS) proteins.

Using a systems biology approach, in the pheromone-response pathway in the model organism fission yeast, we have found that RGS protein can play both a positive and negative role for Gα, however our model remains incomplete. Within fission yeast a classical Gβγ-subunit remains to be identified. However from studies in the distantly related budding yeast glucose-sensing pathway has identified a non-canonical Gβγ-like complex (Asc1 – a RACK1 homologue). In fission yeast, based on proteins alignment and similarities to both glucose and pheromone signalling cascades, we have identified Cpc2 as a potentially negative regulator (Gβγ-subunit) for the pheromone cascade.

Therefore using a pheromone-signalling pathway in fission together with mathematical modelling as a system, we will present data demonstrating the role that RACK1 homologues may play within G protein-mediated signalling. Included within our work will be data that suggests a critical role in linking cell cycle progression to G protein signalling.

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