

# PKA phosphorylates RET:GDNF:GFRA di- mer

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## Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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## Literature references

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Reactome database release: 88

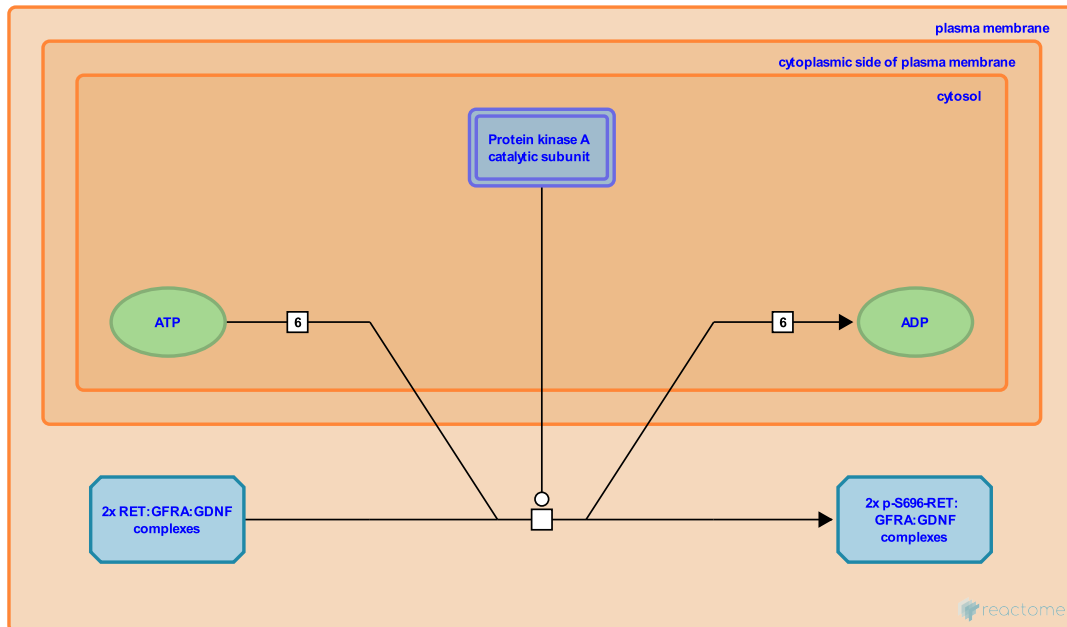
This document contains 1 reaction ([see Table of Contents](#))

## PKA phosphorylates RET:GDNF:GFRA dimer [↗](#)

**Stable identifier:** R-HSA-8854908

**Type:** transition

**Compartments:** extracellular region, plasma membrane, cytosol



Serine (S) 696 in RET is phosphorylated by protein kinase A. Mutation of this serine almost completely inhibits the ability of RET to activate the small GTPase Rac1 and stimulate formation of cell lamellipodia (Fukuda et al. 2002). Homozygous knock-in mice carrying this mutation lacked enteric neurons in the distal colon, resulting from a migration defect of enteric neural crest cells (Asai et al. 2006). The effects of the S696 RET mutant could be alleviated by simultaneous mutation of Tyrosine-687 (Fukuda et al. 2002). Activation of PKA by forskolin was found to impair the recruitment of SHP2 to RET and negatively affect ligand-mediated neurite outgrowth (Perrinjaquet et al. 2010). Mutation of S696 enhanced SHP2 binding and eliminated the effect of forskolin on ligand-induced neurite outgrowth.

### Literature references

Fukuda, T., Takahashi, M., Kiuchi, K. (2002). Novel mechanism of regulation of Rac activity and lamellipodia formation by RET tyrosine kinase. *J. Biol. Chem.*, 277, 19114-21. [↗](#)

### Editions

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