# SIAH1, SIAH2 bind SNCAIP

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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

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

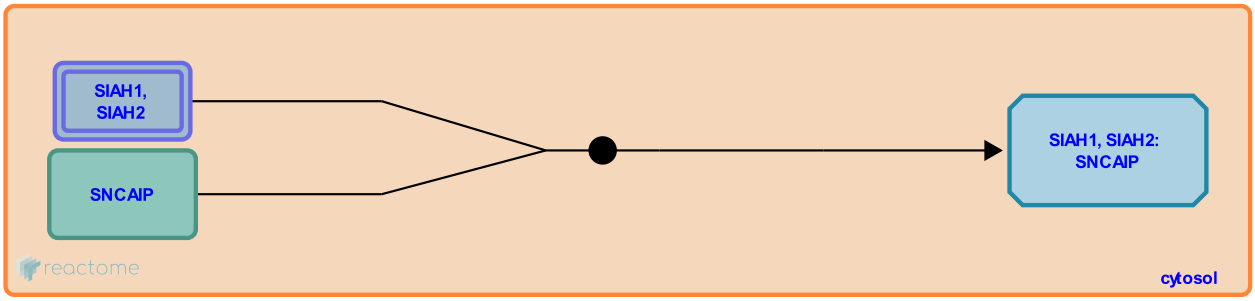
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

## SIAH1, SIAH2 bind SNCAIP ↗

**Stable identifier:** R-HSA-5658092

**Type:** binding

**Compartments:** cytosol




Seven in absentia homolog 1 (SIAH1) and 2 (SIAH2) are E3 ubiquitin-protein ligases that mediate ubiquitination of a number of target proteins including Synphilin-1 (SNCAIP) (Nagano et al. 2003) and alpha-synuclein (Liani et al. 2004). They are inhibited by the 1A isoform of SNCAIP (Szargel et al. 2009). When ubiquitinated by SIAH1, SNCAIP is targetted for proteasomal degradation (Nagano et al. 2003).

Synphilin-1 (SNCAIP) is a presynaptic protein that associates with synaptic vesicles (Ribeiro et al. 2002). It is present in many types of cytoplasmic inclusions, where it colocalizes with alpha-synuclein. It is associated with Parkinson's Disease (PD) because it is an intrinsic component of Lewy bodies (Wakabayashi et al. 2000) and a mutation of the SNCAIP gene has been identified in some PD patients (Marx et al. 2003), suggesting that accumulation of synphilin-1 and its interaction with alpha-synuclein may be relevant for Lewy body formation in PD.

Synphilin-1 (SNCAIP) is ubiquitinated by several other E3 ubiquitin-ligases, including Parkin (Chung et al. 2001) and Dorfin (Ito et al. 2003).

## Literature references

Takahashi, T., Kikuchi, A., Nakamura, T., Yamashita, H., Matsumoto, M., Kishida, S. et al. (2003). Siah-1 facilitates ubiquitination and degradation of synphilin-1. *J. Biol. Chem., 278*, 51504-14. ↗

Riess, O., Shemer, R., Liani, E., Rott, R., Berg, D., Avraham, E. et al. (2004). Ubiquitylation of synphilin-1 and alpha-synuclein by SIAH and its presence in cellular inclusions and Lewy bodies imply a role in Parkinson's disease. *Proc. Natl. Acad. Sci. U.S.A., 101*, 5500-5. ↗

## Editions

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