PDGF-AA clevage by Furin

Garapati, P V., Heldin, CH., Jassal, B.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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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. ↗

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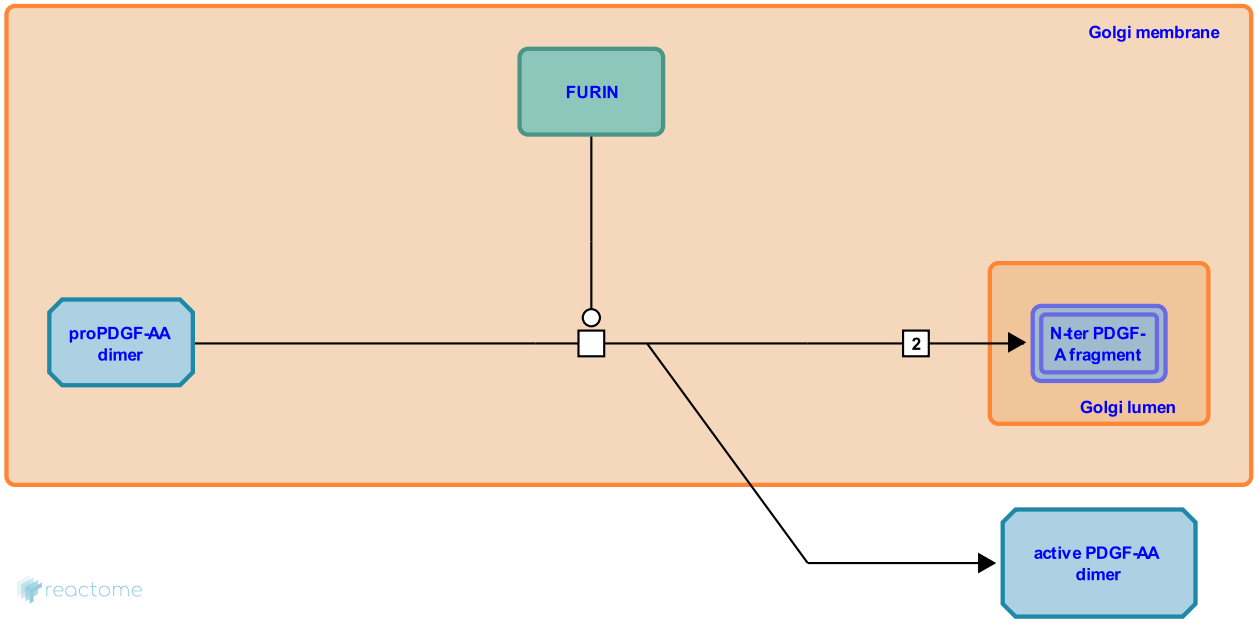
Stable identifier: R-HSA-186785

Type: transition

Compartments: extracellular region, Golgi membrane



After dimerization of the PDGF-A and PDGF-B chains in the ER of producing cells, the dimers are proteolytically cleaved in the trans-Golgi network during protein maturation and secretion. The dibasic-specific proprotein convertase, furin, or related convertases are involved in the conversion of proPDGF forms to active PDGF forms. PDGF-A chains are expressed as two different isoforms, a longer and a shorter form.The longer (241 aa) is less common and differs from the shorter one (196 aa) by a C-terminal extension of 18 aa (Beckmann et al. 1988, Ostman et al. 1992). The PDGF-A chains are cleaved singly at the RRKR sequence at 86 position to yield predominantly, the secreted PDGF-AA forms, while PDGF-BB are reported that at least three forms of PDGF-BB can be formed (Seidah & Prat 2002). This includes an approx 24 kDa form retained intracellularly and degraded in lysosomes, a secreted approx 30 kDa form and an approx 40 kDa cell surface-associated form. PDGF-B is processed at the 'RGRR' sequence at position 81 and a second clevage close to residues 'ARPVT' at position 190 (Siegfried et al. 2005, Ostman et al. 1992, Heldin & Westermark 1999).

Literature references

Westermark, B., Heldin, CH. (1999). Mechanism of action and in vivo role of platelet-derived growth factor. *Physiol Rev, 79*, 1283-316. ↗

Westermark, B., Ostman, A., Heldin, CH., Thyberg, J. (1992). PDGF-AA and PDGF-BB biosynthesis: proprotein processing in the Golgi complex and lysosomal degradation of PDGF-BB retained intracellularly. *J Cell Biol, 118*, 509-19. ↗

Li, H., Eriksson, U., Fredriksson, L. (2004). The PDGF family: four gene products form five dimeric isoforms. *Cytokine Growth Factor Rev, 15*, 197-204. ↗

Editions

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