Signaling by ALK

Inghirami, G., Jassal, B., Orlic-Milacic, M., Rothfels, K.
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


Reactome database release: 79

This document contains 2 pathways and 30 reactions (see Table of Contents)
The anaplastic lymphoma kinase (ALK) is a receptor tyrosine kinase that was discovered as an oncogene in anaplastic large cell lymphomas, but also plays an oncogenic role in other cancer types, such as non-small-cell lung cancer (NSCLC), neuroblastoma and glioblastoma. The activation of anaplastic lymphoma kinase (ALK) requires the binding of the ligand pleiotrophin (PTN) or midkine (MDK), which induces the dimerization of the receptor. ALK dimers undergo trans-autophosphorylation, resulting in a fully activated receptor that triggers downstream signaling cascades such as RAS signaling, PI3K signaling and IRS1 signaling. In cancer, ALK gene frequently undergoes translocation, resulting in formation of fusion ALK proteins, such as NPM-ALK and EML4-ALK. These fusion proteins consist of the C-terminal region of ALK, with the kinase domain and the effector protein binding domain, while the N-terminus contains the dimerization domain of the ALK fusion partner. Fusion proteins of ALK are therefore capable of ligand-independent dimerization, resulting in constitutive ALK signaling. ALK can also undergo ligand-independent activation through RPTPβ/RPTPζ.

ALK gene is mainly expressed in the developing central and peripheral nervous system. PTN and MDK have neuroprotective effect against neurotoxic agents and in neurodegenerative diseases.


**Literature references**


**Editions**

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ALK binds ligand pleiotrophin (PTN)

Location: Signaling by ALK

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