FGF14

FGF14 (Fibroblast Growth Factor 14) is an atypical member of the fibroblast growth factor family. Unlike classical FGFs, it is not secreted and does not act as a ligand for FGF receptors. Instead, it functions intracellularly, primarily within the central nervous system.

Key Features

Gene location: Chromosome 13q33.1 (human)

Expression: Highly expressed in the brain, including the cerebellum, hippocampus, and cerebral cortex

Main function: Modulates voltage-gated sodium channels (Nav), particularly at the axon initial segment. This affects neuronal excitability, action potential initiation, and signal propagation.

Protein interactions: Binds to Nav α-subunits (e.g., Nav1.6), regulating their trafficking, localization, and kinetics.

Clinical Relevance

Mutations in FGF14 are linked to:

Spinocerebellar ataxia type 27 (SCA27):

Autosomal dominant neurodegenerative disorder

Onset often in childhood or adolescence

Characterized by ataxia, tremor, dysarthria, and sometimes cognitive impairment

Epilepsy and neuropsychiatric disorders: Due to its role in ion channel modulation, FGF14 dysfunction has also been implicated in epilepsy, bipolar disorder, and schizophrenia in some studies.

Animal Models

Fgf14 knockout mice show:

Gait ataxia

Motor hyperactivity

Impaired hippocampal-dependent learning These phenotypes resemble aspects of human SCA27 and support FGF14's critical role in neuronal function.