

DESCRIPTION

Source Human embryonic kidney cell, HEK293-derived human CACHD1 protein
Glu36-Pro1095, with a C-terminal 6-His tag
Accession # Q5VU97.2

N-terminal Sequence Analysis Glu36

Predicted Molecular Mass 119 kDa

SPECIFICATIONS

SDS-PAGE 113-127 kDa, under reducing conditions

Activity Measured by its binding ability in a functional ELISA.
Recombinant Human CACHD1 His-tag (Catalog # 10750-CA) binds Recombinant Human/Mouse Wnt-5a Biotinylated (Catalog # BT645). The ED₅₀ for this effect is 1.25-10.0 µg/mL.

Endotoxin Level <0.10 EU per 1 µg of the protein by the LAL method.

Purity >95%, by SDS-PAGE visualized with Silver Staining and quantitative densitometry by Coomassie® Blue Staining.

Formulation Lyophilized from a 0.2 µm filtered solution in PBS with Trehalose. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution Reconstitute at 500 µg/mL in PBS.

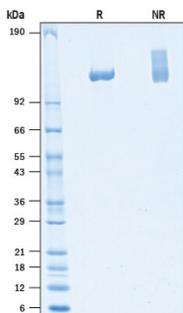
Shipping The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.

Stability & Storage Use a manual defrost freezer and avoid repeated freeze-thaw cycles.

- 12 months from date of receipt, -20 to -70 °C as supplied.
- 1 month, 2 to 8 °C under sterile conditions after reconstitution.
- 3 months, -20 to -70 °C under sterile conditions after reconstitution.

DATA

SDS-PAGE



Recombinant Human CACHD1 His-tag Protein SDS-PAGE. 2 µg/lane of Recombinant Human CACHD1 His-tag (Catalog # 10750-CA) was resolved with SDS-PAGE under reducing (R) and non-reducing (NR) conditions and visualized by Coomassie® Blue staining, showing bands at 113-127 kDa and 110-160 kDa, respectively.

BACKGROUND

CACHD1 (Ca²⁺ channel and chemotaxis receptor Domain Containing 1) is a $\alpha 2\delta$ -Like Protein that modulates CaV3 voltage-gated calcium channel activity (1, 2). Mature Human CACHD1 consists of a 1060 amino acid (aa) extracellular domain (ECD), a 21 aa transmembrane segment, and a 158 aa cytoplasmic domain. The ECD contains a von Willebrand factor A (VWA) domain and two bacterial chemosensory-like cache domains (1). Within the ECD, human CACHD1 shares 97.5% and 97.7% aa sequence identity with mouse and rat CACHD1, respectively. Diseases associated with CACHD1 include Cercarial Dermatitis and Hypertropia. CACHD1 increases the presence of CaV3.1 at the cell surface and causes an increase in channel open probability (2). CACHD1 is a new activity-modifying protein for voltage-gated calcium channels (2). Such physiological actions may have implications in targeting diseases involving aberrant neuronal firing, as CaV3 channels have been proposed as therapeutic targets to combat pain and epilepsy (2). CACHD1 and MDGA1 are novel *in vivo* substrates for beta-site APP cleaving enzyme 1 (BACE1), suggesting that cleavage of both proteins may contribute to the numerous functions of BACE1 in the nervous system (3). BACE1 inhibition is a major therapeutic approach for Alzheimer disease (3). CACHD1 closely interacts with voltage-gated calcium channels of the N-type58 and T-type59 at the cell surface and enhances the densities of their calcium currents (3). BACE1 cleavage is a mechanism to control CACHD1's function in calcium signaling and synaptic transmission (3). Expression of CACHD1 increased both CaV2.2 currents and cell surface trafficking in both cell lines and neurons (4). CACHD1 competed with $\alpha 2\delta$ -1 for binding to CaV2.2 and for its functional effects and can therefore inhibit responses to $\alpha 2\delta$ -1 (4). CACHD1 is widely expressed in many tissues, including the brain, lungs, and small intestine (4). CACHD1 contains a VWA domain that has a disrupted metal ion-dependent adhesion site (MIDAS) motif, a sequence that is conserved in the human, rat, mouse, and zebrafish CACHD1 proteins (4). At the Wnt Signaling Gordon Conference in August 2019, Yvonne Jones (Oxford) presented an unpublished crystal structure of the transmembrane proteins CACHD1 in a complex between LRP6 and Fz5. Their data suggest that CACHD1 is an inhibitor of Wnt signaling.

References:

1. Cottrell, G.S. *et al.* (2018) *J. Neurosci.* **38**:9186.
2. Stephens, G.J. and G.S. Cottrell (2019) *Channels (Austin)* **13**:120.
3. Njavro, J. R. *et al.* (2020) *The FASEB J.* **34**:2465.
4. Dahimene, S. *et al.* (2018) *Cell Reports* **25**:1610.