CYREX® Laboratories

CLINICAL SPECIFICATIONS

RABAPTIN-5 + PRESENILIN

Function:

Rabaptin is a protein involved in the regeneration of damaged axons. Rabaptin-5 interacts with guanosine triphosphate (GTP). Rab GTPases act as molecular switches cycling between "active" GTP-bound and "inactive" GDP-bound forms.[1] A lack of rabaptin-5 strongly inhibits Rab5-dependent early endosome membrane fusion. Thus, rabaptin-5 is a Rab effector required for membrane docking and fusion necessary for tissue regeneration. Presenilin protein is related to multi-pass transmembrane proteins which constitute the catalytic subunits of the gamma-secretase intramembrane protease complex. Presenilins are postulated to regulate amyloid precursor protein processing. Presenilin is prone to a mutation that enhances the production of toxic amyloid-beta-42, leading to excessive aggregation of this peptide.

Associated With:

Alzheimer's disease[2], reviewed in 3
Mild Cognitive Impairment[4]
Endocytosis[5]
Hepatitis C Virus RNA replication[6]

Known Cross-Reactions:

$A\beta_{42}$ peptide;[7] neurocrescin[8]

Clinical Significance:

Endocytosis is vital to the healthy function of neuronal molecules. Altered endocytosis can have deleterious influence on the nervous system, which can lead to Alzheimer's disease (AD). Rabaptin-5 is a component necessary for endocytosis. Rabaptin-5 immunoreactivity is present in neurons, predominantly located on large endosomes in pre-AD brains.[5] Rabaptin-5's amino acid (AA) sequence displays a high degree of homology with the AA sequence of neurocrescin, a neurite outgrowth factor that contributes to the regeneration of damaged neurons in neurodegenerative disorders, including Alzheimer's disease. Pathogenic mutations of Presenilin correspond to an exacerbation of amyloid beta ($A\beta_{42}$) production,[4] the principal Aβ deposited in the brain.[9] Pathogenic mutation in Presenilin-1 can cause a loss of γ-Secretase enzymatic activity and aggregation of accumulated amyloid-beta-42 in the neurons of AD patients. Rabaptin-5 and Presenilin are considered precursors to the development of AD and thus appear in the early stages of the disease process. In a recent study, Vojdani and Vojdani showed that anti- $A\beta_{42}$ peptide antibody reacted with both Rabaptin-5 and Presenilin.[2] Due to cross-reactivity with peptide,[7] patients with circulating antibodies to Rabaptin-5 + Presenilin may be at greater risk for AD and other neurological disorders when the blood-brain barrier is breached.

References:

1. Korobko et al. Characterization of Rabaptin-5 γ isoform. Biochemistry (Mosc), 2014; 79(9):856-864.
2. Vojdani and Vojdani. Amyloid-beta 1-42 cross-reactive antibody prevalent in human sera may contribute to intraneuronal deposition of A-beta-P-42. Int J Alzheimers Dis, 2018; 2018:1672568.
3. Perez et al. Hippocampal endosomal, lysosomal, and autophagic dysregulation in mild cognitive impairment: correlation with Aβ and tau pathology. J Neuropathol Exp Neurol, 2015; 74(4):345-358.
4. Suh and Checler. Amyloid precursor protein, presenilins, and α-synuclein: molecular pathogenesis and pharmacological applications in Alzheimer's disease. Pharmacol Rev, 2002; 54:469-525.
5. Cataldo et al. Endocytic pathway abnormalities precede amyloid beta deposition in sporadic Alzheimer's disease and Down syndrome: differential effects of APOE genotype and presenilin mutations. Am J Pathol, 2000; 157(1):277-286.
6. Stone et al. Participation of rab5, an early endosome protein, in hepatitis C virus RNA replication machinery. J Virol, 2007; 81(9):4551-4563.
7. Vojdani and Vojdani. Amyloid-beta 1-42 cross-reactive antibody prevalent in human sera may contribute to intraneuronal deposition of A-beta-P-42. Int J Alzheimers Dis, 2018; 2018:1672568.
8. Nishimune et al. Neurocrescin: a novel neurite-outgrowth factor secreted by muscle after denervation. NeuroReport, 1997; 8:3649–3654.
9. Selkoe. Alzheimer's disease: genes, proteins, and therapy. Physiol Rev, 2001; 81(2):741-766.

ALZLINX_SPEC_04032019_REV_A7