

CLINICAL SPECIFICATIONS

ALPHA-SYNUCLEIN

Function:

Although present in the heart and muscles, the protein, α -synuclein, is predominantly found in the brain, specifically at the presynaptic nerve terminals, which is the tip of the neuron. It plays a role in synaptic transmission and plasticity. α -synuclein interacts with tubulin and is necessary for normal development of cognitive function. Researchers have shown that α -synuclein knockout mice have reduced learning ability in tests requiring both working and spatial memory.¹

Associated With:

Alzheimer's disease²
 Parkinson's disease³
 Huntington's disease⁴
 Dementia²

Known Cross-Reactions: Herpes Simplex Virus-1;⁵ β -synuclein, γ -synuclein;⁶ $A\beta_{42}$ peptide⁷

Clinical Significance:

Synucleinopathies, or α -synucleinopathies, are neurodegenerative diseases characterized by the fibrillary aggregates of α -synuclein protein in the cytoplasm of selective populations of neurons and glia leading to multiple outcomes, including dementia, Parkinson's disease (PD),⁸ Alzheimer's disease (AD) and dementia with Lewy bodies (DLB).² Autoantibodies to α -synuclein, in comparison to controls, are highly elevated in early stage Parkinson's disease (PD) and gradually decrease as PD progresses.⁹ Koehler *et al.* studied IgG α -synuclein reactivity in patients with AD and DLB and found that antibodies increased with disease progression in AD patients, but in DLB patients, titers were higher in the early stages and lowered as the disease progressed.² Tissue transglutaminase-2 has been shown to play a role in Lewy body formation. Transglutaminase can cross-link with α -synuclein, thereby forming α -synuclein aggregates.¹⁰ Transglutaminase-catalyzed cross-links colocalize with α -synuclein was observed in Lewy bodies of PD and DLB patients.¹⁰ Vojdani and Vojdani showed significant immunoreactivity between amyloid beta ($A\beta_{42}$) peptide antibody and α -synuclein.⁷ Due to this cross-reactivity with $A\beta_{42}$ peptide,⁷ patients with circulating antibodies to α -synuclein may be at greater risk for AD and other neurological disorders when the blood-brain barrier is breached.

References:

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