Title

þÿElevated levels of Secreted-Frizzled-Related-Protein 1 contribute to Alzheimer

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Abstract

þÿThe deposition of aggregated amyloid-² peptides derived from the pro-amyloidog
þÿprecurson protein (APP) into characteristic amyloid plaques (APs) is distinctive
þÿAlternative APP processing via the metalloprotease ADAM10 prevents amyloid-²
downregulation of ADAM10 activity by its secreted endogenous inhibitor secreted-frizzled-related protein 1 (SFRP1) is a common trait of sporadic AD. We demonstrate that SFRP1 is significantly increased in the brain and cerebrospinal
þÿfluid of patients with AD, accumulates in APs and binds to amyloid-², hindering
overexpression in an AD-like mouse model anticipates the appearance of APs and dystrophic neurites, whereas its
þÿgenetic inactivation or the infusion of ±-SFRP1-neutralizing antibodies favors n
Decreased Sfrp1 function lowers AP accumulation, improves AD-related histopathological traits and prevents long-term potentiation loss and cognitive deficits. Our study unveils SFRP1 as a crucial player in AD pathogenesis

and a promising AD therapeutic target.

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