

This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Neurology				
Alzheimer's disease (AD)	Vacuolar protein sorting 35 homolog (VPS35); VPS29; amyloid precursor protein (APP)	<i>In silico</i> and <i>in vitro</i> studies identified a pharmacological retromer chaperone that inhibits pathogenic processing of APP and could help treat AD. <i>In silico</i> docking and screening identified small molecules that bind the retromer complex at the interface of its VPS35 and VPS29 subunits. In <i>in vitro</i> biochemical assays, one compound bound to and stabilized the complex. In cultured murine hippocampal neurons, the compound increased expression of various retromer subunits and decreased accumulation of pathogenic APP derivatives compared with vehicle. Next steps include identifying drug-like retromer chaperones that cross the blood brain barrier and evaluating their safety.	Patent applications filed; licensed to an undisclosed newco; available for partnering	Mecozzi, V.J. <i>et al. Nat. Chem. Biol.</i> ; published online April 20, 2014; doi:10.1038/nchembio.1508 Contact: Scott A. Small, Columbia University College of Physicians and Surgeons, New York, N.Y. e-mail: sas68@columbia.edu Contact: Dagmar Ringe, Brandeis University, Waltham, Mass. e-mail: ringe@brandeis.edu Contact: Gregory A. Petsko, Weill Cornell Medical College, New York, N.Y. e-mail: gpetsko@med.cornell.edu
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