This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Neurology				
Alzheimer's disease (AD)	Cholinesterase	A SAR study suggests that molecules combining cholinesterase inhibition with antioxidant activity could help treat AD. *In vitro*, a series of compounds with functional groups derived from the cholinesterase inhibitor tacrine and the aggregation blocker 8-hydroxyquinoline had better cholinesterase inhibition and antioxidant activity than either parent compound. In an *in vitro* model of the blood brain barrier (BBB), the best compounds in the series showed BBB permeation comparable to that of known CNS drugs, as well as good antioxidant activity. Next steps could include lead optimization and testing of candidate compounds in mouse models of AD. Acetylcholinesterase inhibitors marketed to treat AD include Novartis AG's Exelon rivastigmine, Pfizer Inc.'s Aricept donepizil and Shire plc's Reminyl galantamine. Prana Biotechnology Ltd.'s PBT2, an 8-hydroxyquinoline-derived metal protein-attenuating compound, is in Phase II testing for AD. Raptor Pharmaceutical Corp. has bisnorcymserine, a dual inhibitor of butyrylcholinesterase and β-amyloid (Aβ), in preclinical development for AD.	Patent and licensing status undisclosed	Fernández-Bachiller, M.I. *et al. J. Med. Chem.*; published online June 14, 2010; doi:10.1021/jm100329q **Contact:** María Isabel Rodríguez-Franco, Medicinal Chemistry Institute, Spanish National Research Council, Madrid, Spain e-mail: IsabelRguez@iqm.csic.es

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