This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Neurology				
Alzheimer's disease (AD)	Anterior pharynx defective 1 homolog B (APH1B)	<p>A study in cell culture and in mice suggests that targeting APH1B could help treat AD. APH1B is a subunit of γ-secretase, an enzyme that cleaves amyloid-β (Aβ) precursor protein (APP) into the AD-associated β-amyloid (Aβ) protein. <i>In vitro</i>, murine cells with deletions of <i>Aph1B</i> and a mouse-specific duplicate gene, <i>Aph1C</i>, had lower levels of toxic Aβ peptides than cells with functional <i>Aph1B</i> and <i>Aph1C</i>. In a mouse model of AD, <i>Aph1B</i> and <i>Aph1C</i> knockout led to lower levels of toxic Aβ peptides and higher cognitive performance than what was seen in AD mice with intact <i>Aph1B</i> and <i>Aph1C</i>. The knockouts also had normal levels of Notch, a γ-secretase substrate required for normal immunity and development. Next steps include screening for small molecule antagonists of APH1B. Eli Lilly and Co.'s LY450139, a nonselective γ-secretase inhibitor, is in Phase III trials for AD. Eisai Co. Ltd. and Wyeth have γ-secretase modulators in Phase I trials for AD. Elan Corp. plc and Cellzome Inc. have preclinical γ-secretase programs.</p> <p>SciBX 2(14); doi:10.1038/scibx.2009.590 Published online April 9, 2009</p>	<p><i>Aph1b</i> knockout mice patented by the Catholic University Leuven; available for licensing Contact: Karine Clauwaert, Flanders Interuniversity Institute for Biotechnology, Leuven, Belgium e-mail: Karine.Clauwaert@vib.be</p>	<p>Serneels, L. <i>et al. Science</i>; published online March 19, 2009; doi:10.1126/science.1171176 Contact: Bart De Strooper, Catholic University Leuven, Leuven, Belgium e-mail: Bart.destrooper@med.kuleuven.be</p>