

This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Neurology				
Fatigue	Neuronal nitric oxide synthase (nNOS)	<p>Studies in mice suggest that increasing levels of sarcolemma-localized nNOS could be useful for lowering fatigue associated with muscular dystrophy and other musculoskeletal disorders. In two dystrophic mouse models, lower nNOS levels led to more vascular narrowings in skeletal muscle, less capillary perfusion and higher fatigue after mild exercise compared with what was seen in wild-type mice. In one of the models, a phosphodiesterase-5A (PDE-5A) inhibitor improved vascular response and lowered muscle edema compared with what was seen in untreated mice. PDE-5A inhibitors increase intracellular levels of cyclic guanosine monophosphate, a downstream mediator of nNOS signaling. Next steps include identifying derivatives of PDE-5A inhibitors that have greater efficacy in lowering exaggerated fatigue responses to mild exercise. There are at least seven PDE-5 inhibitors in development stages ranging from Phase II to marketed for various cardiovascular and genitourinary indications.</p> <p>SciBX 1(40); doi:10.1038/scibx.2008.979 Published online Nov. 6, 2008</p>	Patent application filed; available for licensing	<p>Kobayashi, Y. <i>et al. Nature</i>; published online Oct. 26, 2008; doi:10.1038/nature07414 Contact: Kevin Campbell, University of Iowa, Iowa City, Iowa e-mail: kevin-campbell@uiowa.edu</p>