This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Autoimmune disease				
Scleroderma	Toll-like receptor 4 (TLR4); fibronectin extra domain A (FnEDA)	<p><i>In vitro</i> and mouse studies suggest inhibiting TLR4 signaling in skin lesions could help treat scleroderma. In samples from skin lesions and sera from patients with scleroderma and in mouse models of cutaneous fibrosis, compared with healthy controls, the TLR4 ligand FnEDA was upregulated. In a mouse model of drug-induced cutaneous fibrosis, knockout of <i>Fneda</i> or subcutaneous treatment with a small molecule TLR4 inhibitor prevented fibrosis and dermal thickening. In mice with established disease, the inhibitor reversed cutaneous fibrosis. Next steps include identifying new TLR4 inhibitors for scleroderma.</p> <p>At least three companies have TLR4 antagonists in Phase II or earlier testing for autoimmune and other indications.</p> <p>In addition, Eisai Co. Ltd.'s Eritoran (E5564), a synthetic lipid A analog that blocks TLR4 activation, failed to meet the primary endpoint of reduced mortality in Phase III testing for sepsis, and development is on hold.</p> <p>SciBX 7(19); doi:10.1038/scibx.2014.550 Published online May 15, 2014</p>	Patent application pending covering the use of new TLR4 inhibitors in scleroderma; BioLineRx Ltd. has an exclusive licensing option	<p>Bhattacharyya, S. <i>et al. Sci. Transl. Med.</i>; published online April 16, 2014; doi:10.1126/scitranslmed.3008264</p> <p>Contact: Swati Bhattacharyya, Northwestern University Feinberg School of Medicine, Chicago, Ill. e-mail: s-bhattacharyya@northwestern.edu</p> <p>Contact: John Varga, same affiliation as above e-mail: j-varga@northwestern.edu</p>