

This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Transplantation				
Renal transplant	High mobility group box-1 (HMGB-1); toll-like receptor 4 (TLR4)	<p>Studies in humans and in cell culture suggest that inhibiting TLR4 may be useful for improving outcomes in kidney transplant patients. In patients receiving donor kidneys with mutated loss-of-function TLR4, the rate of immediate graft function was significantly higher than that for kidneys expressing wild-type TLR4 ($p=0.007$). In human renal epithelial cells, the TLR4 ligand HMGB-1 increased the expression of inflammatory cytokines compared with that seen in untreated controls. Next steps include evaluating TLR4 inhibitors for their ability to prevent ischemia and reperfusion injury following transplantation.</p> <p>Eritoran, a TLR4 antagonist from Eisai Co. Ltd., is in Phase III testing to treat sepsis.</p> <p>TAK-242, a TLR4 signal transduction inhibitor from Takeda Pharmaceutical Co. Ltd., is in Phase III for sepsis.</p> <p>ART-123, a soluble form of recombinant human thrombomodulin from Asahi Kasei Pharma Corp. and Artisan Pharma Inc., inhibits HMGB-1 and thrombin and is approved to treat disseminated intravascular coagulation.</p> <p>At least four other companies have compounds targeting TLR4 or HMGB-1 in Phase I testing for inflammation.</p> <p>SciBX 2(8); doi:10.1038/scibx.2009.335 Published online Feb. 26, 2009</p>	Patent and licensing status unavailable	<p>Krüger, B. <i>et al. Proc. Natl. Acad. Sci. USA</i>; published online Feb. 9, 2009; doi:10.1073/pnas.0810169106 Contact: Bernd Schröppel, Mount Sinai School of Medicine, New York, N.Y. e-mail: bernd.schroepel@mssm.edu</p>