This week in techniques

Approach	Summary	Licensing status	Publication and contact information
Drug delivery			
Induction of immune tolerance to improve delivery and efficacy of enzyme replacement therapies to treat lysosomal storage disorders (LSDs)	Studies in dogs suggest that coadministration of immunosuppressive agents with enzyme replacement therapy could improve the efficacy of drugs marketed to treat LSDs. In a canine model of mucopolysaccharidosis I (MPS-I, Hurler's syndrome), tolerization with the immunosuppressive compounds cyclosporin A and azathioprine coadministered with a low dose of Aldurazyme laronidase increased the efficacy of subsequent Aldurazyme treatment compared with that in untolerized controls. Tolerized animals showed 260% higher Aldurazyme activity in lung, heart, kidney and synovial tissue and lower tissue pathology in the same tissues compared with untolerized dogs receiving the same Aldurazyme dose. Aldurazyme levels in macrophage-rich tissues such as the liver, spleen and lymph nodes were lower in tolerized dogs than in untolerized controls, suggesting that tolerization protects from antibody-mediated clearance of Aldurazyme. A clinical trial using the same tolerance regimen will start soon, according to BioMarin Pharmaceuticals Inc. BioMarin markets Aldurazyme laronidase, a recombinant α-L-iduronidase, as an enzyme replacement therapy to treat MPS-I.	Patent applications filed in the U.S., European Union and Japan related to the methods of use, composition and other aspects of antigen-specific tolerance; licensed by BioMarin Pharmaceuticals Inc.; available for licensing in certain indications	Dickson, P. *et al. J. Clin. Invest.*; published online July 24, 2008; doi:10.1172/JCI34676 **Contact:** Emil D. Kakkis, BioMarin Pharmaceutical Inc., Novato, Calif. e-mail: ekakkis@bmrn.com