This week in techniques

Approach	Summary	Licensing status	Publication and contact information
Chemistry			
Designing therapeutic IgG4 antibodies that do not undergo Fab-arm exchange	<p>Mutations that prevent antibody Fab-arm exchange could guide the development of safer and more efficacious antibody therapies. Fab-arm exchange occurs when the arm fragment of a therapeutic antibody exchanges with the arm fragment of an endogenous plasma antibody. The result is a bispecific antibody that reduces the binding affinity of the therapeutic antibody and potentially leads to side effects such as progressive multifocal leukoencephalopathy (PML). <i>In vitro</i>, an S228P mutation engineered into the hinge region of an IgG4 antibody prevented formation of unwanted bispecific antibodies. In mice, the wild-type IgG4 antibody formed bispecific plasma antibodies whereas the mutated IgG4 antibody did not. Blood samples from multiple sclerosis (MS) patients showed that the therapeutic antibody Tysabri undergoes Fab-arm exchange with human plasma IgG4, which could lead to PML. Next steps could include evaluating non-arm exchanging variants of marketed therapeutic antibodies in animal models.</p> <p>Tysabri natalizumab, a humanized mAb against integrin α_4 from Elan Corp. plc and Biogen Idec Inc., is marketed to treat MS.</p> <p>SciBX 2(30); doi:10.1038/scibx.2009.1195 Published online Aug. 6, 2009</p>	Patent and licensing status unavailable	<p>Labrijn, A.F. <i>et al. Nat. Biotechnol.</i>; published online July 20, 2009; doi:10.1038/nbt.1553</p> <p>Contact: Paul W.H.I. Parren, Genmab, Utrecht, the Netherlands e-mail: p.parren@genmab.com</p>