This week in techniques

Approach	Summary	Licensing status	Publication and contact information
Drug platforms			
Crystal structure to guide the design of protease-activated receptor 1 (PAR1) antagonists	The crystal structure of human PAR1 bound to vorapaxar could be used to guide the development of improved PAR1 antagonists. In a Phase III trial, the PAR1 antagonist vorapaxar protected patients from myocardial infarction (MI) but led to increased bleeding, which was attributed to the drug's very tight binding. The vorapaxar-bound human PAR1 crystal structure revealed an unusual mode of drug binding that explained the high-affinity interaction that inhibits PAR1 activation. Next steps include collaborations to identify new PAR1 antagonists based on the PAR1-vorapaxar structure. In 2011, Merck & Co. Inc. discontinued dosing of patients in two Phase III trials of vorapaxar to prevent cardiovascular events because intracranial hemorrhage occurred in a subset of patients. In 2012, the pharma announced plans to file regulatory applications for the compound in the same indication but in a restricted patient population. *SciBX* 5(49); doi:10.1038/scibx.2012.1296 Published online Dec. 20, 2012	Unpatented; licensing status not applicable	Zhang, C. *et al. Nature*; published online Dec. 9, 2012; doi:10.1038/nature11701 **Contact:** Brian K. Kobilka, Stanford University, Stanford, Calif. e-mail: kobilka@stanford.edu