This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cancer				
Cancer	Integrin $\alpha_v\beta_3$; integrin $\alpha_v\beta_5$; VEGF; VEGF receptor 2 (VEGFR2; KDR/FLK-1)	<p>Studies in cell culture, in <i>ex vivo</i> tissues and in mice suggest that low concentrations of integrin $\alpha_v\beta_3$ and $\alpha_v\beta_5$ inhibitors can promote rather than block tumor angiogenesis. In mouse models of melanoma and Lewis lung carcinoma, two integrin inhibitors, including Merck KGaA's cilengitide, promoted tumor angiogenesis at nanomolar plasma concentrations compared with what was seen at micromolar concentrations. In <i>ex vivo</i> mouse aortas, nanomolar concentrations of the two inhibitors promoted angiogenesis, whereas micromolar concentrations blocked angiogenesis as expected. In mouse endothelial cells, nanomolar concentrations of the inhibitors promoted angiogenesis by increasing VEGFR2 expression and VEGF-stimulated migration of endothelial cells. Ongoing work will determine whether inhibitors with higher affinity for integrin $\alpha_v\beta_3$ can block angiogenesis at nanomolar concentrations.</p> <p>Cilengitide is in Phase III testing to treat glioblastoma. At least four other companies have compounds targeting integrin $\alpha_v\beta_3$, α_v integrins or unspecific integrins in preclinical to early-stage clinical testing to treat cancer.</p> <p>SciBX 2(12); doi:10.1038/scibx.2009.484 Published online March 26, 2009</p>	Unpatented; unlicensed	<p>Reynolds, A. <i>et al. Nat. Med.</i>; published online March 22, 2009; doi:10.1038/nm.1941</p> <p>Contact: Kairbaan Hodivala-Dilke, Institute of Cancer Research, London, U.K. e-mail: Kairbaan.Hodivala-Dilke@cancer.org.uk</p> <p>Contact: Andrew Reynolds, same affiliation as above e-mail: andrew.reynolds@icr.ac.uk</p>