This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cancer				
Pancreatic cancer	Actin α2 smooth aorta muscle (ACTA2; α-SMA); smoothened (SMO); sonic hedgehog homolog (SHH)	Studies in mice and patients suggest depleting tumor stroma and fibrosis could be deleterious as opposed to helpful in treating pancreatic cancer. Past studies suggested tumor stroma and fibrosis impede drug delivery in patients with pancreatic ductal adenocarcinoma (PDAC). Thus, stroma- and fibrosis-depleting compounds such as hedgehog pathway inhibitors were pursued in the indication as potential complements to chemotherapy. In genetic mouse models of PDAC, depletion of α-Sma$^+$ stromal myofibroblasts, knocking out *Shh* or blocking hedgehog signaling with the SMO inhibitor saridegib all decreased tumor stroma and fibrosis but resulted in the development of a more aggressive disease phenotype and decreased survival compared with what was seen in control mice. In a cohort of 53 patients with PDAC, low levels of the myofibroblast marker α-SMA were associated with decreased overall survival (p=0.0053). Next steps include elucidating the role of various stromal cell populations in PDAC and determining whether there are specific scenarios in which stroma- and fibrosis-depleting drugs such as SMO inhibitors could have benefit. Infinity Pharmaceuticals Inc. discontinued saridegib in 2012 after interim data from the Phase II portions of trials in pancreatic cancer, chondrosarcoma and myelofibrosis showed that the compound would not meet its primary endpoint. Roche's Genentech Inc. unit markets the SMO inhibitor Erivedge vismodegib to treat basal cell carcinoma. The drug is being evaluated in multiple investigator-led Phase I and Phase II trials in pancreatic cancer. At least five other companies have SMO inhibitors in Phase III testing or earlier to treat various cancers.	Findings for both studies unpatented; licensing status not applicable	Rhim, A.D. *et al. Cancer Cell*; published online May 22, 2014; doi:10.1016/j.ccr.2014.04.021 **Contact:** Ben Z. Stanger, University of Pennsylvania, Philadelphia, Pa. e-mail: bstanger@exchange.upenn.edu **Contact:** Kenneth P. Olive, Columbia University Medical Center, New York, N.Y. e-mail: kenolive@columbia.edu Özdemir, B.C. *et al. Cancer Cell*; published online May 22, 2014; doi:10.1016/j.ccr.2014.04.005 **Contact:** Raghu Kalluri, The University of Texas MD Anderson Cancer Center, Houston, Texas e-mail: rkalluri@mdanderson.org

SciBX 7(22); doi:10.1038/scibx.2014.642
Published online June 5, 2014