This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Various				
Various	E3 ubiquitin ligase; SMAD specific E3 ubiquitin protein ligase 2 (SMURF2); NEDD4 family E3 ubiquitin-protein ligase (RSP5)	<i>In vitro</i> studies identified compounds that could help develop inhibitors of E3 ubiquitin ligases to treat various diseases. The activity of SMURF2, NEDD4 and other E3 ubiquitin ligases containing the homologous to E6AP C terminus (HECT) domain have been implicated in cancer, fibrosis and other diseases. <i>In vitro</i> testing of non-cell-penetrating bicycle peptides identified several compounds that targeted the E2 binding site of the HECT domain of SMURF2 and NEDD4 to inhibit the ligases at low micromolar IC ₅₀ values. Screening small molecules against one peptide in a competitive HECT domain-binding assay identified heclin as a low micromolar inhibitor of SMURF2 and NEDD2. However, in a human cell line, heclin exhibited activity against multiple HECT domain-containing ligases. Next steps include identifying ligase-specific, cell-penetrating inhibitors.	Findings unpatented; licensing status not applicable	Mund, T. <i>et al. Proc. Natl. Acad. Sci. USA</i> ; published online Nov. 10, 2014; doi:10.1073/pnas.1412152111 Contact: Hugh R. Pelham, Medical Research Council Laboratory of Molecular Biology, Cambridge, U.K. e-mail: hp@mrc-lmb.cam.ac.uk
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