

THE DISTILLERY

This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Endocrine/metabolic disease				
Diabetes	Carboxylesterase 1 (CES1; hCE1)	In vitro and mouse studies suggest inhibiting CES1 could help treat type 2 diabetes. In mouse adipocytes, phenotypic screening for compounds that increased lipid storage coupled with activity- based protein profiling to indicate enzymatic targets blocked by the hits identified Ces3, the mouse ortholog of CES1, as the molecular target of bioactive compounds. In mouse models of diabetes, a Ces3 inhibitor protected animals from weight gain, decreased liver lipid accumulation and increased insulin sensitivity compared with vehicle. In adipose tissue from patients with type 2 diabetes, CES1 activity was upregulated compared with that in lean controls. Next steps could include developing inhibitors of the human target.	Patent and licensing status unavailable	Dominguez, E. <i>et al. Nat. Chem. Biol.</i> ; published online Dec. 22, 2013; doi:10.1038/nchembio.1429 Contact: Enrique Saez, The Scripps Research Institute, La Jolla, Calif. e-mail: esaez@scripps.edu Contact: Benjamin F. Cravatt, same affiliation as above e-mail: cravatt@scripps.edu

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