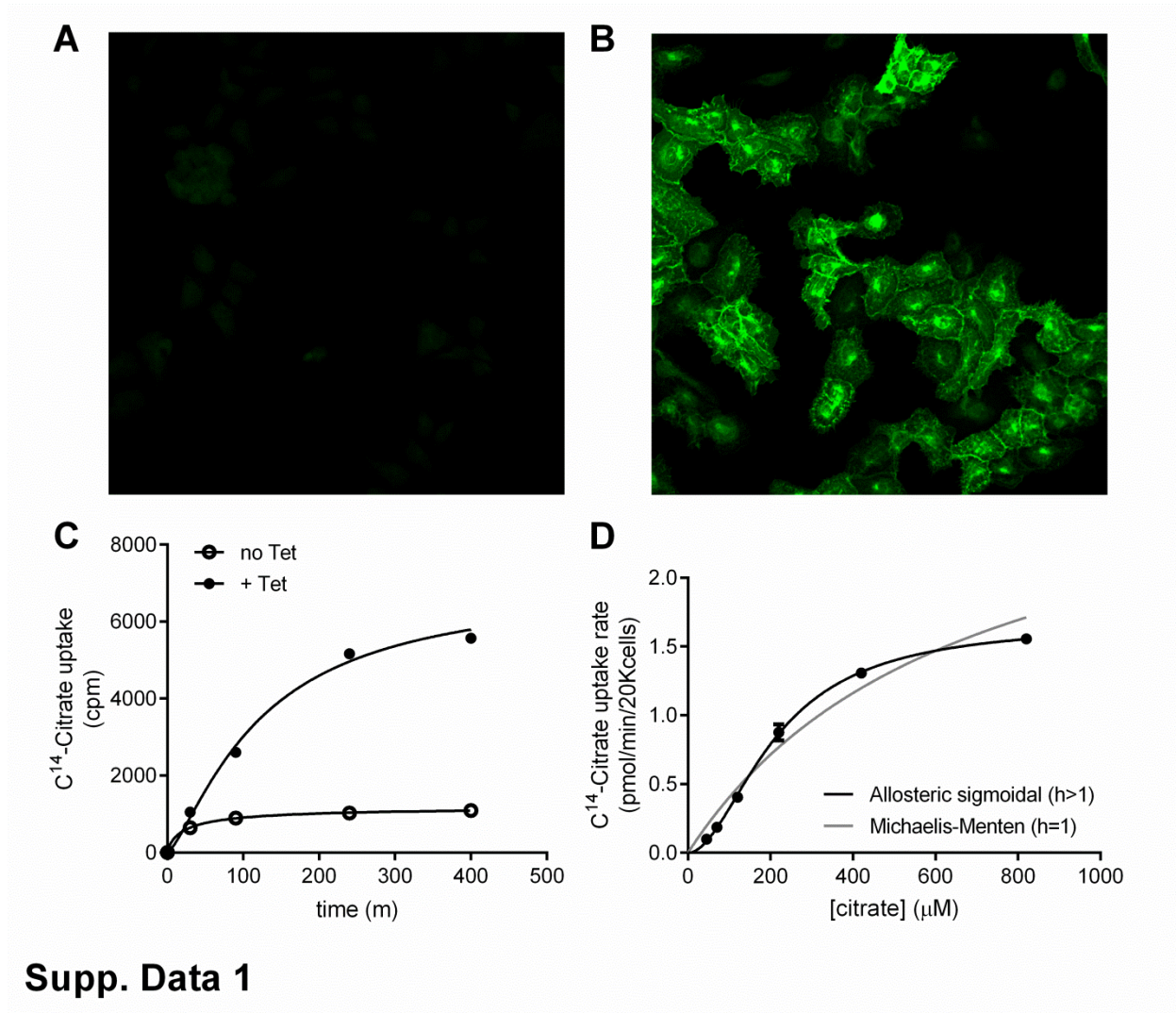


SUPPLEMENTAL INFORMATION

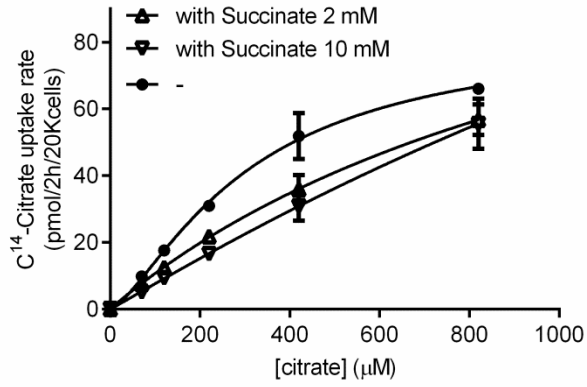
**State-dependent allosteric inhibition of the human SLC13A5 citrate transporter by
hydroxysuccinic acids, PF-06649298 and PF-06761281**

Marie-Laure Rives, Morena Shaw, Bin Zhu, Simon A. Hinke and Alan D. Wickenden

Molecular and Cellular Pharmacology, Discovery Sciences, Janssen R&D, LLC., San Diego, California,
92121 (M-L.R, M.S, A.D.W) and Cardiovascular and Metabolism Discovery, Janssen R&D, LLC.,
Springhouse, Pennsylvania, 19477 (B.Z, S.H)



Supp. data 1: Functional validation of HEK293TRex-TO/hSLC13A5 cells. A. and B. Immunofluorescence validating the expression at the cell surface of hSLC13A5 (HPA044343, Sigma, 1/500) after 1 µg/mL tetracycline induction overnight (B) compared to control (A). C. Kinetics of uptake using 10 µM ^{14}C -Citrate D. Specific citrate uptake in HEK293TRex-hSLC13A5 (K_m 575 ± 85 µM).



Supp. Data 2

Supp. Data 2: Succinate is a competitive inhibitor of citrate uptake at hSLC13A5. C¹⁴-citrate uptake using 20 μM C¹⁴-citrate in presence of increasing concentrations of cold citrate as indicated on graph, in presence or absence of succinate.