High-affinity Inhibitors of Human NAD$^+$-dependent 15-Hydroxyprostaglandin Dehydrogenase: Mechanisms of Inhibition and Structure-activity Relationships

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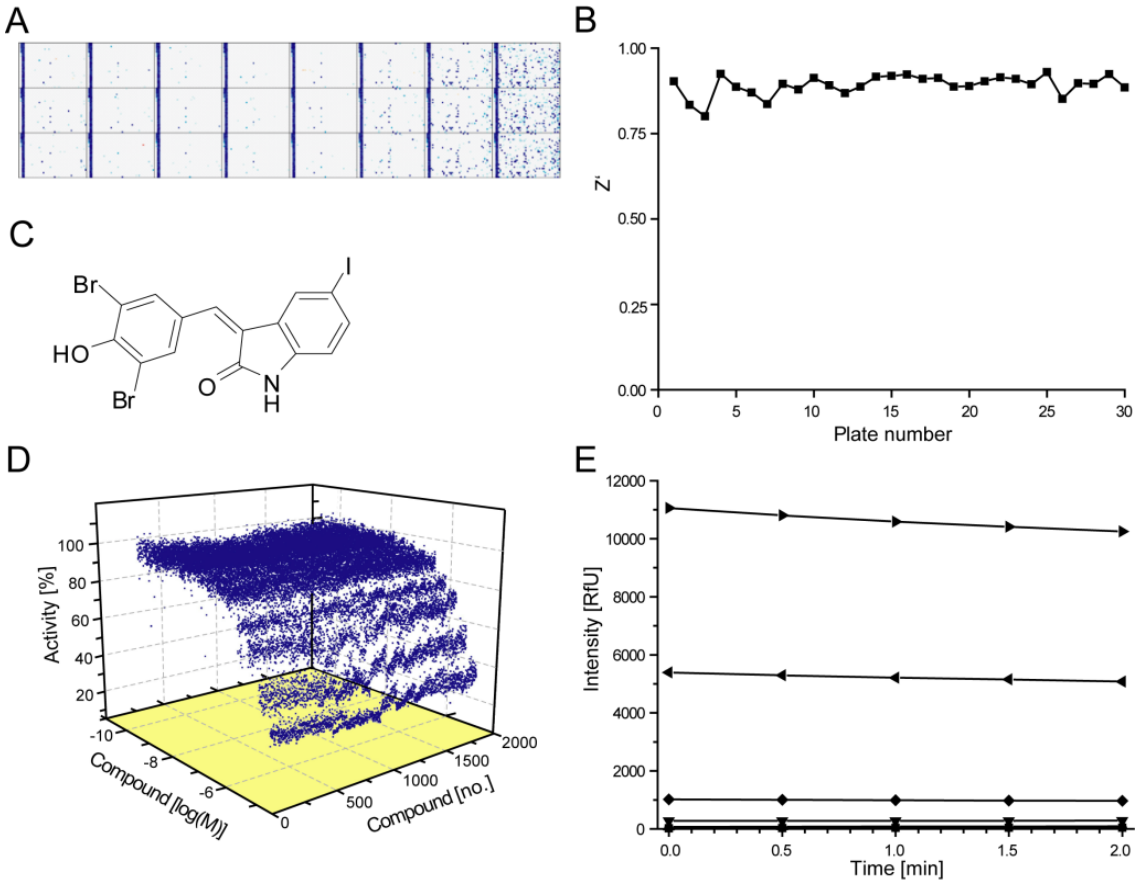
SUPPLEMENTARY INFORMATION FIGURE S1



Miniaturized screening assay for 15-PGDH. *A.* Activity heatmaps showing the assay miniaturization to a 4 µl volume in 1536-well format (increasing concentrations to the right). *B.* Plot of the Z' factor associated with each plate of the pilot concentration-response screen of the LOPAC^{1280} library performed to validate hit reproducibility. *C.* Molecular structure of the control inhibitor GW5074 that was added as a 16-point dilution series in duplicate between 57.5 µM and 1.75 nM into the second column of every assay plate (panel D). The average IC_{50} for the compound was 10.4 µM and the associated minimum significant ratio was approx. 1.5. *E.* Example of a fluorescent inhibitor (applied at between 3.5 nM and 57.5 µM) on the time course of NAD$^+$-reduction upon injection of PGE_2.