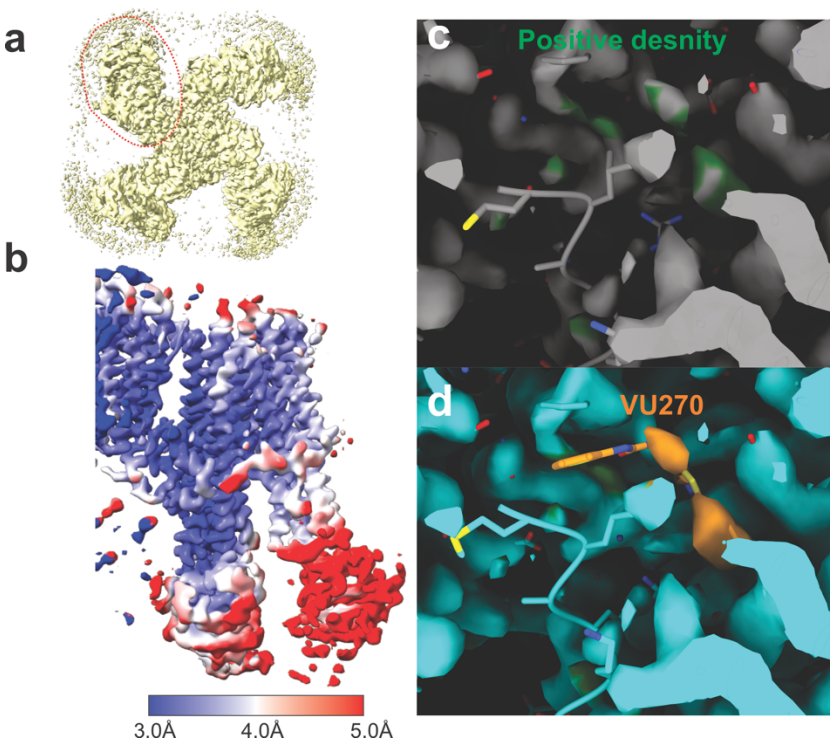

Figure 1. Structure determination of vKATP in complex with VU270. a. The 3D electron density map is symmetry expanded and focused on one SUR2B subunit, marked by a dotted line. b. Local resolution of the focused SUR2B subunit is shown. c. Positive density in green is observed at the glibenclamide binding site, with the Kir6.1 N-terminus and SUR2B proteins being modeled, but without VU270. d. The putative VU270 pose, determined by docking simulations, occupies the positive density observed in c.

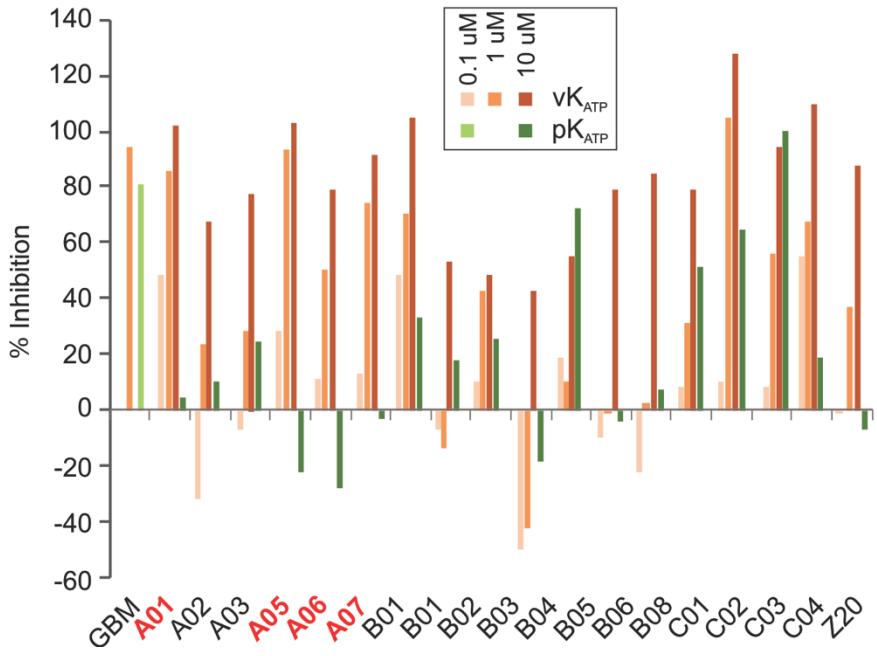

Figure 2. Drug screening to identify vKATP specific inhibitors. Nineteen different drugs structurally similar to VU270 were tested for their inhibitory effect using a cell-based Tl^+ influx assay. Overexpressed vKATP channels were activated by the K channel openers (KO) pinacidil (100 uM), and the drugs were treated at three different concentrations (0.1, 1, and 10 uM) to determine dose-dependent inhibition. For pKATP channels, diazoxide (300 uM) was used for activation, and the drugs were treated at 10 uM to assess any inhibitory effect. Glibenclamide was used as a positive control. The promising candidates that showed specific inhibition are marked in red.