Supplementary data

A ligand with two modes of interaction with the dopamine D_2 receptor – An induced-fit mechanism of insurmountable antagonism

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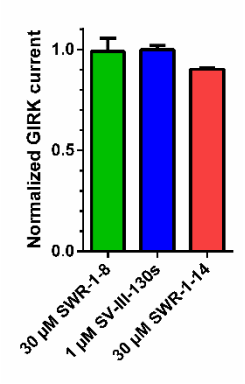

Figure S1. Effect of competing ligands on GIRK currents in the absence of D2R expression. Current amplitudes following application of 30 µM SWR-1-8 (0.99 ± 0.06), 1 µM SV-III-130 (1.00 ± 0.02) and 30 µM SWR-1-14 (0.90 ± 0.01), in oocytes injected with GIRK1 and GIRK4.

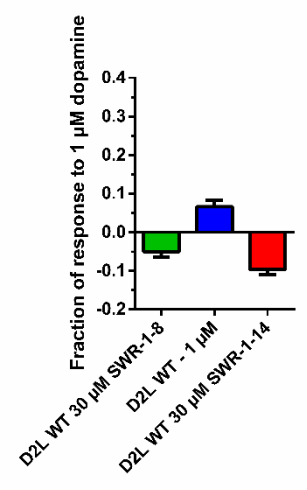

Figure S2. Intrinsic activities of aripiprazole analogues at WT D_2R. Agonist responses of SWR-1-8, SV-III-130 and SWR-1-14 at the D2R, normalized to the response to 1 µM DA.

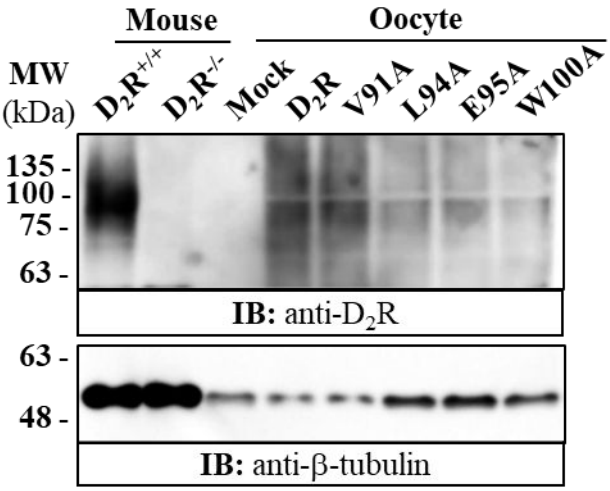

Figure S3. Expression of WT D_2R and receptor mutants in oocytes.

Oocytes were mock manipulated (mock) or injected with WT D_2R, V91A, L94A, E95A, and W100A mutants. Receptor expression was analyzed by immunoblot using total membranes (2 oocytes/lane). Membranes (1 µg/lane) from WT CD-1 mice ($D_2R^{+/+}$) and D_2R knockout ($D_2R^{-/-}$) mice were also immunoblotted and shown as controls. The immunodetection of β-tubulin was used as loading control.

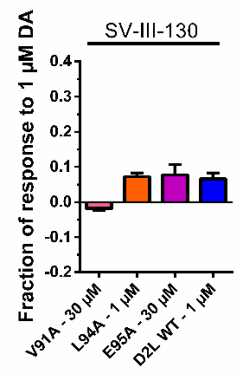

Figure S4. Intrinsic activities of SV-III-130 at D_2R mutants. Agonist responses of SV-III-130 at the V91A, L94A and E95A D2R, normalized to the response to 1 µM DA.