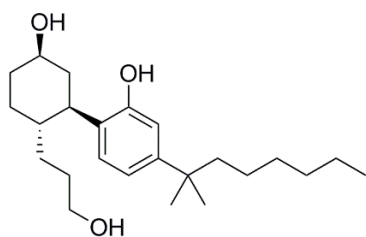
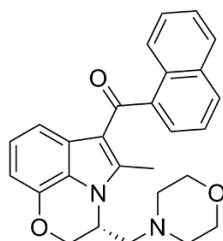


Supplementary Figure 1

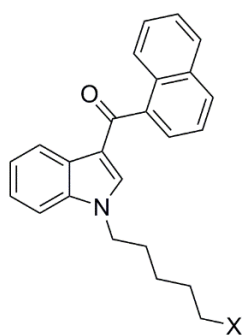
Structure of selected SCRA



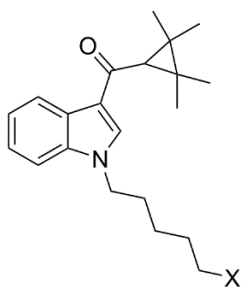
CP55940



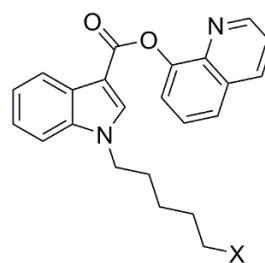
WIN55212-2



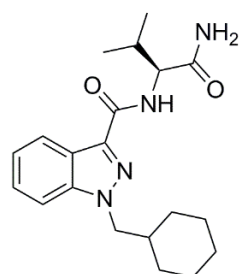
JWH-018 (X = H)
AM-2201 (X = F)



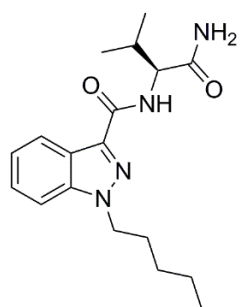
UR-144 (X = H)
XLR-11 (X = F)



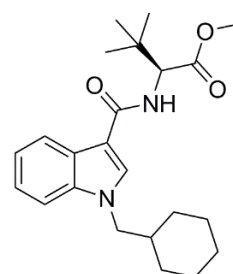
PB-22 (X = H)
5F-PB-22 (X = F)



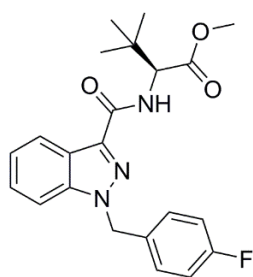
AB-CHMINACA



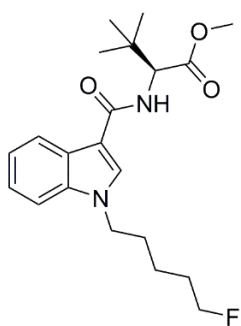
AB-PINACA



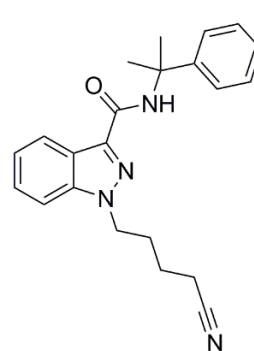
MDMB-CHMICA



MDMB-FUBINACA

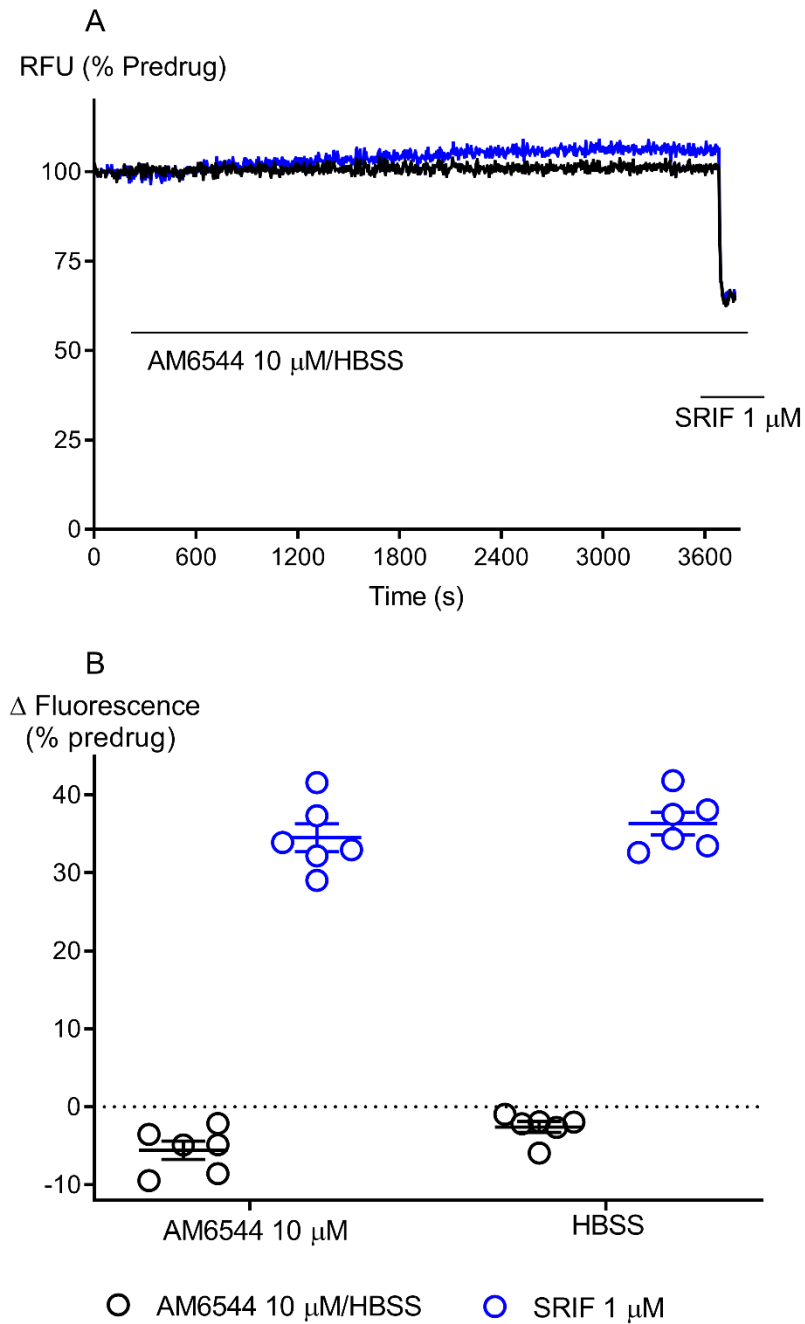


5F-MDMB-PICA



CUMYL-4CN-BINACA

Supplementary Figure 2



AM6544 does not activate GIRK channels in AtT20 cells. (A) Raw trace showing minimal changes in hyperpolarisation induced by maximally effective concentration (10 μ M) of AM6544 or vehicle on At-T20-CB1 cells (B) Scatter dot plot showing the percentage change in fluorescence of SRIF (1 μ M) on AtT20-CB1 cells in the presence of HBSS or AM6544 (10

μM) for 60 mins. Data represents the mean \pm SEM of 6 independent determinants performed in duplicate.

Supplementary Table 1

Functional activity of CP55940, Δ^9 -THC, and other SCRAs. Values were calculated using the four-parameter nonlinear regression to fit the concentration response curves.

Compound	pEC ₅₀ ± SEM (EC ₅₀ , nM)
CP55940	7.62 ± 0.07 (23)
WIN55212-2	6.7 ± 0.05 (200)
Δ^9 -THC	6.81 ± 0.12 (156)
2-AG	6.47 ± 0.07 (338)
AEA	5.91 ± 0.07 (1229)
JWH-018	7.37 ± 0.08 (43)
AM-2201	8.02 ± 0.1 (9.6)
UR-144	6.3 ± 0.08 (503)
XLR-11	7.14 ± 0.08 (72)
PB-22	8.36 ± 0.05 (4.4)
5F-PB-22	9.02 ± 0.08 (0.95)
AB-CHMINACA	7.67 ± 0.14 (21)
AB-PINACA	8.68 ± 0.08 (2.1)
MDMB-CHMICA	8.33 ± 0.09 (4.7)
MDMB-FUBINACA	9.1 ± 0.13 (0.8)
5F-MDMB-PICA	9.15 ± 0.08 (0.7)
CUMYL-4CN-BINACA	9.16 ± 0.08 (0.68)