

**Table S1: EC<sub>50</sub> of OAG and IC<sub>50</sub> of Inhibitor on hTRPC6 constructs**

TRPC6 constructs	OAG		Inhibitor	
	LogEC <sub>50</sub> <sup>a</sup>	EC <sub>50</sub> (nM)	LogIC <sub>50</sub> <sup>a</sup>	IC <sub>50</sub> (nM)
TRPC6 WT	3.43 ± 0.06	2,707	1.01 ± 0.07	10
TRPC6 NGFP	3.28 ± 0.08	1,925	1.20 ± 0.07	16
<b>Mutations in CHS</b>				
<b>binding pocket</b>				
Y392F	3.32 ± 0.09	2,100	1.26 ± 0.11	18
A404C	3.41 ± 0.07	2,589	1.30 ± 0.10	20
F407A	3.25 ± 0.06	1,774	1.13 ± 0.07	13
L408M	3.38 ± 0.09	2,377	1.18 ± 0.07	15
L411F	3.40 ± 0.14	2,494	1.35 ± 0.11	23
A447T	4.02 ± 0.08	10,481	1.07 ± 0.08	12
A447F	3.25 ± 0.05	1,779	1.76 ± 0.13	57
T451F	3.75 ± 0.09	5,684	1.19 ± 0.09	16
T451L	3.29 ± 0.05	1,944	1.35 ± 0.13	22
N617S	3.81 ± 0.10	6,406	0.6 ± 0.08	4
F620L	3.09 ± 0.11	1,227	0.79 ± 0.08	6
<b>Mutations in BTDM</b>				
<b>binding pocket</b>				
W526A	2.93 ± 0.06	850	2.00 ± 0.14	100
S608L	2.51 ± 0.07	326	-	>10,000 <sup>b</sup>
Q624A	3.70 ± 0.07	4,990	3.39 ± 0.16	2,463
I640F	4.07 ± 0.13	11,709	1.62 ± 0.14	42
V644F	2.93 ± 0.03	857	-	>10,000 <sup>b</sup>
T714F	3.17 ± 0.10	1,463	3.93 ± 0.17	8,430
<b>Gain of function mutants</b>				
P112Q	3.32 ± 0.69	2,090	1.15 ± 0.07	14
R895C	3.27 ± 0.09	1,852	1.22 ± 0.09	17
E897K	3.48 ± 0.08	2,993	0.97 ± 0.12	9

<sup>a</sup>Data were expressed as logEC<sub>50</sub> ( or logIC<sub>50</sub>) ± SEM, n=3.

<sup>b</sup>The highest inhibitor concentration (10,000 nM) inhibited the activation of TRPC6 for less than 30%.