**Ion Channels**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Gene Knockout/Overexpression\*** | **Background** | **Operant** | **2BC** | **CIE** | **DID** | **References** |
| Transient receptor potential cation channel, subfamily M member 5 (*Trpm5*)Transient receptor potential cation channel, subfamily V member 1 (*Trpv1*) | B6B6 × 129X1/SvJ |  | ↓↑ |  |  | Blednov et al., 2008 [162]Blednov and Harris, 2009 [183] |
| Galanin-3 receptor (*Galr3*) | B6 | ↑ | ↑ |  |  | Genders et al., 2018 [372] |
| G protein-activated inward rectifier potassium channel 2, GIRK2 (*Kcnj6*) | B6 × 129Sv  |  | — bottle alternation; males/females↑ without bottle alternation; females |  |  | Blednov et al., 2001 [30] |
| G protein-activated inward rectifier potassium channel 3, GIRK3 (*Kcnj9*) | B6 |  | ↑ (2 h)—  |  |  | Herman et al., 2015 [309] |
|  | B6 |  | ↑ (20%)— (3%, 6%, 10%) |  |  | Kozell et al., 2018 [ |
| G protein-coupled receptor GPR88 (*Gpr88*) | C57B1/6 (13/96%), C57B1/6J (60.94%), FVB/N (0.05%), 129/SvPas (25%), SJL/J (0.05%) | ↑ | ↑ (10%)↑ (20% intermittent)) |  |  | Ben Hamida et al., 2018 [371] |
| β-arrestin-1 (*Arrb1*) | B6 |  | — |  |  | Bjork et al., 2008 [168] |
|  | B6 |  |  |  | ↑ females vs. Het females (10%, 4 h)↑ females vs. Het and WT (20%, 4 h) | Robins et al., 2018 |
| β-arrestin-2 (*Arrb2*) | B6 |  | ↓ 9-15% |  |  | Bjork et al., 2008 [168] |
|  | B6 |  | ↑ |  |  | Li et al., 2013 [283] |
|  | B6 |  |  |  | — (10%, 4 h) | Chiang et al., 2016 |
|  | B6 |  |  |  | ↑ (10%, 4 h) | Robins et al., 2018 [373] |
| Voltage-dependent N-type calcium channel subunit α-1B (*Cacna1b*) | B6 × 129SvJae |  | ↓  |  |  | Newton et al., 2004 [94] |
| EF hand domain containing 2 (aka, swiprosin-1; *Efhd2*; calcium-sensing protein) | B6 |  | ↑ |  |  | Mielenz et al., 2018 [374] |
| Calcium-activated potassium channel subunit β-1, BK β1 (*Kcnmb1*)  | B6 |  | —— intermittent | ↑a  | — (2 h) | Kreifeldt et al., 2013 [290] |
| Calcium-activated potassium channel subunit β-4, BK β4 (*Kcnmb4*) | B6 |  | — continuous— intermittent | ↓a  | — (2 h) | Kreifeldt et al., 2013 [290] |
|  | B6 |  |  |  | ↑ (2 h; males/females) | Martin et al., 2008 [179] |
| P2X purinoceptor 4 (*P2rx4*) | B6 |  | ↑ intake   |  | ↑ transient (4 h; 5%, 20%)— (4 h, 10%) | Wyatt et al., 2014 [292] |
|  | B6 |  | ↑ |  |  | Khoja et al., 2018 [364] |
| Glycine receptor subunit α2 (*Glra2*)  | B6 |  | ↓ continuous — intermittent |  | — (2, 4 h, 1B) | Blednov et al., 2015 [324] |
|  | B6 |  |  |  | ↑ (15%, 2 h, 4 h, males, days 1 and 2)— (15%, 2 h, 4 h, males, days 3 and 4)— (15%, 2 h, 4 h, females) | San Martin et al., 2020 [384] |
| Glycine receptor subunit α3 (*Glra3*) | B6 |  | — continuous ↑ intermittent |  | — (2 h, 4 h, 1B) | Blednov et al., 2015 [324] |
| Nicotinic acetylcholine receptor (nAChR) α4 subunit (*Chrna4*) | B6 |  |  |  | ↓ (2 h, 20%)— (2 h, 2%) | Hendrickson et al., 2010 [209] |
| nAChR α5 subunit (*Chrna5*) | B6 |  |  |  | — (4 h) | Santos et al., 2013 [286] |
| nAChR α6 subunit (*Chrna6*) | B6 |  | — males/females |  |  | Kamens et al., 2012 [263] |
|  | C57BL/6J |  |  |  | — males/females (2-20%) | Guildford et al., 2016 [325] |
| nAChR α7 subunit (*Chrna7*) | B6 |  | ↓ females— males |  |  | Kamens et al., 2010 [229] |
| nAChR β2 subunit (*Chrnb2*) | B6 |  | — males/females |  |  | Kamens et al., 2010 [229] |
|  | B6 |  | — intermittent |  |  | Dawson et al., 2013 [276] |
| nAChR β3 subunit (*Chrnb3*) | B6 |  | — males/females |  |  | Kamens et al., 2012 [263] |
| nAChR β4 subunit (*Chrnb4*) | C57BL/6J |  |  |  | — males (2 h, 20%) | Patkar et al., 2016 [332] |
|  | B6 |  | — females (24 h) |  | — males/females (4 h) | Kamens et al., 2017 [355] |
| nAChR α5α3β4\* | B6SJLF1/J |  | ↓ intake |  |  | Gallego et al., 2012 [262] |
| Sodium bicarbonate transporter NBCn1 (*Slc4a7*) | C57BL/6J |  | ↑ males |  |  | Schank et al., 2020 (376) |
| Hyperpolarization-activated cyclic nucleotide-gated channel 1 (*Hcn1*) | B6 × 129s/SvEv |  | ↑ |  |  | Salling and Harrison, 2020 [383] |

–, ↓, ↑: no difference, decreased ethanol intake and/or preference, or increased ethanol intake and/or preference, respectively, in knockout *vs*. wildtype mice. Male mice were tested unless otherwise indicated. Ethanol intake in the two-bottle (2BC) test was measured in 24-h sessions unless otherwise indicated. Drinking session times for the other tests are indicated in parenthesis. CIE, chronic intermittent ethanol; DID, drinking in the dark; 1B, one bottle. a These tests involved weekly limited access (2 h/day) 2BC drinking alternated with weekly CIE vapor (16 h/day) to create alcohol dependence/withdrawal. Deletion of BK β4 attenuated, while deletion of BK β1 accelerated, the escalation of ethanol drinking in dependent mice during withdrawal from CIE. Recommended mouse protein and gene (in italics) names are from Uniprot. B6 refers to C57BL/6J mice.