**Cannabinoids and Opioids**

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| **Gene Knockout** | **Background** | **Operant** | **2BC** | **DID** | **References** |
| Cannabinoid receptor 1 (*Cnr1*) | B6 × 129/Ola |  | ↓ (6 h)↓ preference |  | Poncelet et al., 2003 [44]Lallemand and De Witte, 2005 [88] |
|  | B6 |  | ↓ males/females |  | Hungund et al., 2003 [49] |
|  | CD1 |  | ↓ (48 h; males/females) |  | Naassila et al., 2004 [58] |
|  | CD1 |  |  | ↓ (8 h) | Thanos et al., 2005 [99] |
|   | B6 and DBA/2J |  | ↓  |  | Vinod et al., 2008 [165] |
|  | B6 |  | — after 1 week |  | Racz et al., 2003 [57] |
| α-synuclein (*Snca*)  | B6 |  | ↑ |  | Lopez-Jimenez et al., 2013 [273] |
| Cannabinoid receptor 2 (*Cnr2*) | CD1 and B6 | ↑ (1 h) | ↑  |  | Ortega-Alvaro et al., 2015 [313] |
|  | C57/BL/6J |  |  | — (10%, time of test? see vehicle groups at test in Fig 3) | Powers et al., 2015 [331] |
|  | C57/BL/6J |  | ↓ (8%, after 10 weeks) |  | Pradier et al., 2015 [343] |
| Fatty acid amide hydrolase (*Faah*) | B6 × 129/SvJ |  | ↑ males/females |  | Blednov et al., 2007 [156] |
|  | B6 |  | ↑ females— males |  | Basavarajappa et al., 2006 [117] |
|  | B6 |  | ↑ |  | Vinod et al., 2008 [159] |
| μ-opioid receptor(*Oprm1*) | B6 × 129/Sv | ↓ nose-poke↓ lever operant | ↓ post-operant↓ post-operant↓ post-forced ethanol |  | Roberts et al., 2000 [17] |
|  | B6 × 129/Sv |  | ↓ females— males |  | Hall et al., 2001 [32] |
|  | CB6 |  | ↓ after several weeks |  | Becker et al., 2002 [36] |
|  | B6 |  |  | ↓ (2 h)— (2h, ADE) | Contet et al., 2014 [323] |
|  | B6 |  |  | — (4 h) | van Rijn and Whistler, 2009 [193] |
|  | C57BL/6 |  | ↑ males (8%)↓ females (8%) |  | Moriya et al., 2015 [344] |
|  | C57BL/6J × 129SvPas |  | ↓ males (14 day continuous access)↓ males (after 4 days continuous, intermittent Mon/Wed/Fri) |  | Ben Hamida et al., 2017 [381] |
| δ-opioid receptor(*Oprd1*) | B6 |  |  | ↑ (4 h) | van Rijn and Whistler, 2009 [193] |
|  | B6Orl × 129/Sv | ↑  | — ↑ post-operant  |  | Roberts et al., 2001 [27] |
| κ-opioid receptor(*Oprk1*) | B6 |  |  | ↓ (4 h) | van Rijn and Whistler, 2009 [193] |
|  | B6Orl |  | ↓ males/females |  | Kovacs et al., 2005 [95] |
|  | C57BL/6J |  | ↓ females (24 h)↓ females (every other day access to 15% for 3 h)) | — females (4 h) | Van’t Veer et al., 2015 [333] |
| β-endorphin (*Pomc*) | B6  |  | ↑ (48 h, 7%; males/females)— (48 h, 10%; males/females) |  | Grisel et al., 1999 [12] |
|  | B6 |  | — ↑ 2 days, ADE↑ (2 h; days 1-10)↑ day 2, ADE |  | Grahame et al., 2000 [64] |
|  | B6 |  | ↓ females— preference, males |  | Racz et al., 2008 [173] |
|  | B6 |  |  | — females (20%, 2 h) | McGonigle et al., 2016 [335] |
|  | B6 |  |  | ↑ females (20%, 4 h)— males (20%, 4 h) | Nentwig et al., 2018 [380] |
| Prodynorphin (*Pdyn*) | B6 |  | ↑ males/females |  | Racz et al., 2013 [274] |
|  | B6 |  | — |  | Sperling et al., 2010 [208] |
|  | B6 |  | ↑ |  | Femenia and Manzanares, 2011 [256] |
|  | B6 × 129/SvEv-Tac |  | ↓ females— males |  | Blednov et al., 2006 [148] |
| Preproenkephalin (*Penk1*) | B6 |  | — |  | Koenig and Olive, 2002 [33] |
|  | B6 |  | — females↑ 1-3 weeks, males |  | Racz et al., 2008 [173] |
| Nociceptin receptor (*Oprl1*) | B6 |  | ↓ 20%, females |  | Sakoori and Murphy, 2008[161] |
| Sigma 1 receptor (*Oprs1*) | C57BL/6J |  | ↑ (3-20%) |  | Valenza et al., 2016 [340] |

–, ↓, ↑: no significant difference, decreased ethanol intake and/or preference, or increased ethanol intake and/or preference, respectively, in mutant *vs*. wildtype mice. Male mice were tested unless otherwise indicated. Ethanol intake in the operant and two-bottle choice (2BC) test was measured in 30-min and 24-h sessions, respectively, unless otherwise indicated. Wildtype, but not knockout mice, showed a stress-induced increase in ethanol intake/preference (Racz et al., 2003; 2008; 2013; Sperling et al., 2010). DID, drinking in the dark; drinking session times are noted in parenthesis. ADE, alcohol deprivation effect. Recommended mouse protein and gene (in italics) names are from Uniprot. B6 refers to C57BL/6J mice.