

**Supplementary Table 1: Candidate genes associated with at least one drug addiction\***

| Gene symbol   | Gene name                                            | Biological Function                 | Chromosomal location | Drug (phenotype <sup>#</sup> )                           | Evidence from knockout animal model                                                                              |
|---------------|------------------------------------------------------|-------------------------------------|----------------------|----------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|
| <i>ADRA2A</i> | Alpha-2a-adrenergic receptor                         | Signal transduction                 | 10q24-q26            | Nicotine (d); Alcohol (d)                                |                                                                                                                  |
| <i>ANKK1</i>  | Ankyrin repeat and kinase domain containing 1        | Protein amino acid phosphorylation  | 11q23.1              | Alcohol (d); Nicotine (d)                                |                                                                                                                  |
| <i>CD14</i>   | Monocyte differentiation antigen CD14                | Immune response                     | 5q31.1               | Nicotine (d); Alcohol (d)                                | More resistant to endotoxin-induced shock in response to alcohol                                                 |
| <i>CCK</i>    | Cholecystokinin                                      | Signal transduction                 | 11p15.4              | Alcohol (d, c); Nicotine (d)                             | Increased sensitivity and intake to the sedative effect of alcohol                                               |
| <i>COMT</i>   | Catechol-O-methyltransferase                         | Catecholamine metabolic process     | 22q11.21             | Alcohol (d, c); nicotine (i, d, c) heroin (d)            | High alcohol intake in male mice; Cocaine induced hyperlocomotion in mice                                        |
| <i>CHRM2</i>  | Cholinergic receptor, muscarinic 2                   | Neuromuscular synaptic transmission | 7q31-q35             | Alcohol (i, d); Heroin (d); Cocaine (d) ; morphine (d)   |                                                                                                                  |
| <i>CHRNA3</i> | Nicotinic acetylcholine receptor, $\alpha 3$         | Synaptic transmission, cholinergic  | 15q24                | Alcohol (i, d); Nicotine (i, d)                          |                                                                                                                  |
| <i>CHRNA4</i> | Nicotinic acetylcholine receptor, $\alpha 4$         | Synaptic transmission, cholinergic  | 20q13.-q13.3         | Alcohol (i, d); Nicotine (d)                             | Increased extracellular levels of dopamine.                                                                      |
| <i>CHRNA5</i> | Nicotinic acetylcholine receptor, $\alpha 5$         | Synaptic transmission, cholinergic  | 15q24                | Alcohol (i, d); Nicotine (i, d)                          | Resistant to nicotine-induced seizures                                                                           |
| <i>CHRNA6</i> | Cholinergic receptor, neuronal nicotinic, $\alpha 6$ | Synaptic transmission, cholinergic  | 8p11.21              | Alcohol (i, d); Nicotine (i, d)                          |                                                                                                                  |
| <i>CHRNB1</i> | Cholinergic receptor, neuronal nicotinic, $\beta 1$  | Synaptic transmission, cholinergic  | 17p13.1              | Alcohol (d); Nicotine (d)                                |                                                                                                                  |
| <i>CHRNB2</i> | Cholinergic receptor, neuronal nicotinic, $\beta 2$  | Synaptic transmission, cholinergic  | 1q21.3               | Nicotine (d, c); Alcohol (d)                             | Impaired exploratory and social behavior in response to chronic nicotine; Enhances nicotine reinforcing effects  |
| <i>CHRNB3</i> | Cholinergic receptor, neuronal nicotinic, $\beta 3$  | Synaptic transmission, cholinergic  | 8p11.2               | Nicotine (i, d); Alcohol (d)                             |                                                                                                                  |
| <i>CHRNB4</i> | Nicotinic acetylcholine receptor beta 4              | Synaptic transmission, cholinergic  | 15q24                | Alcohol (i, d); Nicotine (i, d)                          | Decreased signs of nicotine withdrawal in mice                                                                   |
| <i>CNR1</i>   | Cannabinoid receptor 1                               | Signal transduction                 | 6q14-q15             | Alcohol (d, c); Cocaine (d); Marijuana (d); Nicotine (d) | Absent alcohol withdrawal symptoms; Reduced alcohol-induced conditioned place preference and self-administration |
| <i>CREB1</i>  | cAMP response element-binding protein 1              | Signal transduction                 | 2q34                 | Alcohol (d); Nicotine (d); morphine (d)                  | Increased alcohol-drinking behaviors; Increased expression of morphine withdrawal                                |

|                |                                                        |                                           |              |                                                                           |                                                                                                                     |
|----------------|--------------------------------------------------------|-------------------------------------------|--------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| <i>CYP17A1</i> | Cytochrome p450, family 17, subfamily a, polypeptide 1 | Oxidation reduction                       | 10q24.3      | Alcohol (i, d); Nicotine (d)                                              |                                                                                                                     |
| <i>CYP2B6</i>  | Cytochrome p450, subfamily IIB, polypeptide 6          | Oxidation reduction                       | 19q13.2      | Alcohol (d, c); Nicotine (d, c)                                           |                                                                                                                     |
| <i>CYP2D6</i>  | Cytochrome P450, family 2, subfamily D, polypeptide 6  | Oxidation reduction                       | 22q13.1      | Alcohol (d); Heroin (d); Cocaine (d); Nicotine (d)                        |                                                                                                                     |
| <i>CYP2E1</i>  | Cytochrome p450, subfamily iiE                         | Oxidation reduction                       | 10q24.3-qter | Alcohol (i, d); Nicotine (d)                                              | Contribute to alcohol-induced fatty liver in mice                                                                   |
| <i>DBH</i>     | Dopamine beta-hydroxylase                              | Synaptic transmission                     | 9q34         | Alcohol (d, c); Cocaine (d); Heroin (d); Nicotine (d, c)                  | Increased alcohol preference; Reduced alcohol preference; Hypersensitivity to cocaine                               |
| <i>DDC</i>     | Dopa decarboxylase                                     | Catecholamine biosynthetic process        | 7p11         | Alcohol (d); Nicotine (d)                                                 |                                                                                                                     |
| <i>DRD1</i>    | Dopamine receptor 1                                    | Synaptic transmission, dopaminergic       | 5q35.1       | Alcohol (d, c); Nicotine (d); Heroin (d);                                 | Alterations in alcohol intake                                                                                       |
| <i>DRD3</i>    | Dopamine receptor 3                                    | Synaptic transmission, dopaminergic       | 3q13.3       | Alcohol (d, c); Cocaine (d); Nicotine (d); Amphetamine (d); Heroin (d)    | Reduced alcohol intake; Severe alcohol withdrawal signs; Enhanced behavioral sensitivity to cocaine and amphetamine |
| <i>DRD4</i>    | Dopamine receptor D4                                   | Synaptic transmission, dopaminergic       | 11p15.5      | Alcohol; Cocaine (d); Nicotine (i, d, c); Methamphetamine (d); Heroin (d) | Reduced alcohol intake; Locomotor supersensitivity to alcohol, cocaine, and methamphetamine                         |
| <i>DRD5</i>    | Dopamine D5 receptor                                   | Synaptic transmission, dopaminergic       | 4p16.1       | Alcohol (d); Nicotine (i); Cocaine (d)                                    | Reduced Alcohol intake; Enhanced locomotor and discriminative-stimulus effects of cocaine                           |
| <i>ESR1</i>    | Estrogen receptor 1                                    | Signal transduction                       | 6q25.1       | Nicotine (d); Alcohol (d)                                                 |                                                                                                                     |
| <i>FAAH</i>    | Fatty acid amynohydroxylase                            | Fatty acid catabolic process              | 1p35-p34     | Alcohol (d, c); Nicotine (d)                                              | Increased alcohol intake; Enhanced the expression of nicotine conditioned place preference                          |
| <i>GABAB2</i>  | GABA receptor A $\beta$ 2                              | Gamma-aminobutyric acid signaling pathway | 5q34         | Alcohol (d); Nicotine (d)                                                 | Lower Alcohol intake                                                                                                |
| <i>GABRA2</i>  | Gamma-aminobutyric acid A receptor 2                   | Gamma-aminobutyric acid signaling pathway | 4p12         | Alcohol (d, c); Nicotine (d); Cocaine (d)                                 | Cocaine-induced hyperactivity; Reduced alcohol intake                                                               |
| <i>GluR1</i>   | Glutamate receptor, ionotropic, AMPA1                  | Signal transduction                       | 5q31.1       | Alcohol (d); Cocaine (c); Amphetamine (d); Opiates (d)                    | Impairs extinction of cocaine-seeking behavior; Alcohol-induced depression of locomotor activity                    |

|               |                                                         |                                      |              |                                                                       |                                                                                 |
|---------------|---------------------------------------------------------|--------------------------------------|--------------|-----------------------------------------------------------------------|---------------------------------------------------------------------------------|
| <i>GluR2</i>  | Glutamate receptor, ionotropic, AMPA2                   | Signal transduction                  | 4q32-q33     | Alcohol (d); Nicotine (d); Amphetamine (d); Opiates (d)               | Impairs extinction of cocaine-seeking behavior                                  |
| <i>GRIK1</i>  | Glutamate receptor, ionotropic, kainate 1               | Glutamate signaling pathway          | 21q22.11     | Alcohol (d, c); Nicotine (d)                                          |                                                                                 |
| <i>GRIN1</i>  | Glutamate receptor, ionotropic, N-methyl D-aspartate 1  | Glutamate signaling pathway          | 9q34.3       | Alcohol (d, c); Nicotine (i, d, c); Cocaine (c); Opiates (d)          |                                                                                 |
| <i>HOMER1</i> | homer homolog 1 (Drosophila)                            | Glutamate signaling pathway          | 5q14.2       | Cocaine (d); Nicotine (d)                                             | Altered behavioral and neurochemical responses to cocaine                       |
| <i>HOMER2</i> | homer homolog 2 (Drosophila)                            | Glutamate signaling pathway          | 15q24.3      | Cocaine (d); Nicotine (d)                                             | Altered behavioral and neurochemical responses to cocaine                       |
| <i>HTR1A</i>  | Serotonin receptor 1A                                   | Signal transduction                  | 5q11.2-q13   | Alcohol (d); Cocaine (d)                                              | Altered behavioral responses to cocaine and alcohol                             |
| <i>HTR1B</i>  | Serotonin receptor 1B                                   | Serotonin receptor signaling pathway | 6q13         | Alcohol (d); Cocaine (d); Heroin (d)                                  | Increased alcohol intake                                                        |
| <i>HTR2A</i>  | Serotonin receptor 2A                                   | Serotonin receptor signaling pathway | 13q14-q21    | Alcohol (d); Cocaine (d); Nicotine (d); Heroin (d)                    |                                                                                 |
| <i>HTR3A</i>  | Serotonin receptor 3A                                   | Serotonin receptor signaling pathway | 11q23.1      | Alcohol (d); Cocaine (d)                                              | Reduction in alcohol self-administration                                        |
| <i>HTR6</i>   | 5-hydroxytryptamine receptor 6                          | Serotonin receptor signaling pathway | 1p36-p35     | Alcohol (d); Nicotine (i)                                             | Increased alcohol intake                                                        |
| <i>MAOA</i>   | Monoamine oxidase A                                     | Immune response                      | Xp11.3       | Alcohol (d); Nicotine (d)                                             | Impaired nicotine preference; Alcohol intake in KO mice same as wild-type       |
| <i>mGluR2</i> | Metabotropic glutamate receptor 2 precursor             | Neurotransmitter catabolic process   | 3p21.1       | Alcohol (d); Cocaine (c); Amphetamine (d); Morphine (d); Nicotine (d) | Enhances cocaine conditioned place-preference                                   |
| <i>mGluR3</i> | Metabotropic glutamate receptor 3 precursor             | Neurotransmitter catabolic process   | 7q21.1-q21.2 | Alcohol (d); Cocaine (c); Amphetamine (d); Morphine (d); Nicotine (d) | Enhances cocaine conditioned place-preference                                   |
| <i>mGluR5</i> | Metabotropic glutamate receptor 5 precursor             | Neurotransmitter catabolic process   | 11p11.12     | Alcohol (d); Cocaine (c); Amphetamine (d)                             | Increased sensitivity to centrally mediated effects of alcohol                  |
| <i>NPY</i>    | Neuropeptide Y                                          | Signal transduction                  | 7p15.1       | Alcohol (d, c); Cocaine (d)                                           | Increased intake of alcohol; Locomotor activation caused by low dose of alcohol |
| <i>NR2a</i>   | Glutamate receptor, ionotropic, N-methyl D-aspartate 2a | Synaptic transmission                | 16p13.2      | Alcohol (d, c) Amphetamine (d) Opiates (d)                            | Impairment in learned reward-related responses to alcohol                       |

|                |                                                                      |                                     |              |                                                                                             |                                                                                                                                                                                                                     |
|----------------|----------------------------------------------------------------------|-------------------------------------|--------------|---------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>NR2b</i>    | Glutamate receptor, ionotropic, N-methyl D-aspartate 2b              | Response to drug                    | 12p12        | Alcohol (d, c)<br>Amphetamine (d)<br>Opiates (d)                                            | Mediates acute sedative effects of alcohol                                                                                                                                                                          |
| <i>NRXN3</i>   | Neurexin 3                                                           | Cell adhesion                       | 14q31        | Alcohol (d); Polysubstances (d);<br>Opioid (d)                                              |                                                                                                                                                                                                                     |
| <i>NTRK2</i>   | Neurotrophic tyrosine receptor kinase 2                              | Cell adhesion                       | 9q22.1       | Alcohol (d);<br>Nicotine (d)                                                                |                                                                                                                                                                                                                     |
| <i>OPRD1</i>   | Opioid receptor, delta 1                                             | Response to DNA damage stimulus     | 1p34.3-p36.1 | Alcohol (d); Heroin/opiates (d); Cocaine (d)<br>Nicotine (c, d)                             | Increased self-administration                                                                                                                                                                                       |
| <i>OPRK1</i>   | Opioid receptor, kappa 1                                             | Signal transduction                 | 8q11.2       | Alcohol (d); Heroin/opiates (d); Cocaine (d)                                                | Reduced self-administration                                                                                                                                                                                         |
| <i>OPRM1</i>   | Opioid receptor, mu 1                                                | Synaptic transmission               | 6q24-q25     | Alcohol (d);<br>Heroin/opiates (d);<br>Cocaine (d);<br>Methamphetamine (d);<br>Nicotine (i) | Reduced alcohol intake; Reduced cocaine conditioned place preference; Enhanced sensitization of cocaine-induced locomotion                                                                                          |
| <i>PDYN</i>    | Preprodynorphin                                                      | Oxidation reduction                 | 20pter-p12   | Alcohol (d); Heroin/opiates (d); Cocaine (d)                                                |                                                                                                                                                                                                                     |
| <i>PENK</i>    | Preproenkephalin                                                     | Synaptic transmission               | 8q23-q24     | Alcohol (d); Heroin/opiates (d); Cocaine (d)                                                | Alcohol intake same as wild type                                                                                                                                                                                    |
| <i>SLC18A2</i> | Solute carrier family 18 (vesicular monoamine transporter), member 2 | Neurotransmitter transport          | 10q25        | Alcohol (d);<br>Nicotine (d);<br>Amphetamine (d);<br>Cocaine (d)                            | Increased dose-dependent alcohol intake in male KO mice; Amphetamine-evoked dopamine release in SLC18A2+/- mice; SLC18A2 heterozygous mice did not develop further sensitization to repeated cocaine administration |
| <i>SLC6A2</i>  | Norepinephrine transporter                                           | Neurotransmitter transport          | 16q12.2      | Alcohol (i, d, c); Heroin/opiates (d); Cocaine (d, c); Methamphetamine (d);<br>Nicotine (d) | Enhanced cocaine reward                                                                                                                                                                                             |
| <i>TAS2R38</i> | Taste receptor, type 2, member 38                                    | Synaptic transmission, dopaminergic | 7q34         | Alcohol (d);<br>Nicotine (d)                                                                |                                                                                                                                                                                                                     |
| <i>TH</i>      | Tyrosine hydroxylase                                                 | Serotonin metabolism                | 11p15.5      | Alcohol (d, c);<br>Nicotine (d)                                                             |                                                                                                                                                                                                                     |
| <i>TPH1</i>    | Tryptophan hydroxylase 1                                             | Serotonin metabolism                | 11p15.3-p14  | Alcohol (d); Heroin (d);<br>Nicotine (i, d)                                                 |                                                                                                                                                                                                                     |
| <i>TPH2</i>    | Tryptophan hydroxylase 2                                             | Signal transduction                 | 12q21.1      | Alcohol (d); Heroin (d);<br>Nicotine (d)                                                    |                                                                                                                                                                                                                     |
| <i>TTC12</i>   | Tetratricopeptide repeat domain 12                                   | Neurotransmitter transport          | 11q23.1      | Nicotine (d);<br>Alcohol (d)                                                                |                                                                                                                                                                                                                     |

Notes: \*: The genes reported here have one or more variants that have been reported to be associated with more than one addiction.  
 #: d – Abuse/Dependence; i - initiation; c - cessation/withdrawal. \* Meta-analyses conducted for genetic associations for at least one of the drug addictions listed in the table. This table may only represent a partial list of genes that have been investigated for association with addictions.