**S6 Table: Significantly enriched transcription regulators and associated harmful effects after morphine exposure.** Each associated harmful effect was given an association score (AS) defined as the sum of the maximum fold changes of the associated DEGs that the corresponding transcription regulator regulated. The DEGs regulated by each factor are also shown in this table. Note that all of the abbreviations used in this table can be found in the legend of Table 1.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Transcription Regulators | Type | Known Regulators (Literature Support) | Associated Harmful Effects (AS) | No. of Regulated DEGs | Regulated DEGs | Phase |
| CTCF (HM) | Epigenetic Reg | Y [1] | Chronic (6.99) | 5 | Cntd1, Nedd9, Rasl11a, Serad4, Rasd1 | Up-IE |
| Dep (2.97) | 2 | Klf2, Kcnk13 |
| Phys harm (2.78) | 2 | Nedd9, Rasl11a |
| SIN3A | Epigenetic Reg | Y [2] | Chronic (6.38) | 5 | Cntd1, Nedd9, Rasl11a, Serad4, Rasd2 | Up-IE |
| Dep (2.9) | 2 | Klf2, Kcnk19 |
| Pleasure (3.77) | 3 | Cntd1, Kcnk13, Scrn3 |
| EZH2 (HM) | Epigenetic Reg |  | Dep (2.9) | 2 | Klf2, Kcnk14 | Up-IE |
| SUZ12 | Epigenetic Reg |  | Dep (1.2) | 1 | Kcnk20 | Up-IE |
| E2F1 | TF |  | Dep (2.9) | 2 | Klf2, Kcnk15 | Up-IE |
| Pleasure (3.77) | 3 | Cntd1, Kcnk13, Scrn3 |
| POLR2A (HM) | RNA Polymerase II | Y [3] | Dep (2.9) | 2 | Klf2, Kcnk16 | Up-IE |
| Phys harm (2.78) | 2 | Nedd9, Rasl11a |
| Pleasure (3.77) | 3 | Cntd1, Kcnk13, Scrn3 |
| TAF1 | TATA box binding protein | Y [4] | Dep (2.9) | 2 | Klf2, Kcnk20 | Up-IE |
| Pleasure (3.77) | 3 | Cntd1, Kcnk13, Scrn3 |
| MEF2C | TF | Y [3] | Dep (1.7) | 1 | Klf2 | Up-IE |
| SIN3A | Epigenetic Reg | Y [2] | Dep (6.46) | 4 | Acer2, Baiap2, Lhx3, Nsun7 | Up-M |
| MEF2A | TF | Y [3] | Phys dep (5.34) | 4 | Btrc, Elac1, Nup133, Tamm41 | Up-M |
| BRF2 | TF |  | Phys dep (1.39) | 1 | Tamm41 | Up-M |
| POL2 | RNA Polymerase II |  | Dep (3.89) | 3 | Col4a6, Numb, Scara3 | Up-L |
| HDAC6 | Epigenetic Reg | Y [3] | Psycho dep (1.21) | 1 | Cyp26a1 | Down-IE |
| E2F6 (HM) | TF |  | Phys dep (17.93) | 13 | Acsl4, Ankrd34a, Anp32b, Glcci1, Grin1, Hist1h3b, Nup50, PPP6c, Purg, Rbm12, Sdf2l1, Sox18, Zscan22 | Down-M |
| SAP30 | Epigenetic Reg | Y [5] | Phys dep (15.49) | 11 | Ankrd34a, Anp32b, Glcci1, Grin1, Hist1h3b, Ppp6c, Purg, Rbm12, Sdf2l1, Sox18, Zscan22 | Down-M |
| ZKSCAN1 | TF |  | Phys dep (6.81) | 5 | Anp32b, Hist1h3b, Ppp6c, Rbm12, Zscan22 | Down-M |
| NR4A1 | NR4a1 | Y [6] | Phys dep (1.57) | 1 | Sdf2l1 | Down-M |
| ZBTB33 | Epigenetic Reg |  | Phys dep (11.41) | 8 | Anp32b, Hist1h3b, Nup50, Ppp6c, Purg, Sdf2l1, Sox18, Zscan22 | Down-M |
| HDAC8 | Epigenetic Reg | Y [3] | Acute (1.78) | 1 | Cldn5 | Down-M |
| Phys dep (6.67) | 4 | Cldn5, Rbm12, Sdf2l1, Sox18 |
| HDAC6 | Epigenetic Reg | Y [3] | Acute (1.78) | 1 | Cldn5 | Down-M |
| Phys dep (4.84) | 3 | Cldn5, Hist1h3b, Sdf2l1 |

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