

STable 4. 101 activity-depednt *dPum* regulators

| 101 genes | Flybase_ID  | VDRC          | gene name                                          | human orthologs                           | FF/Ren ratio | Relative recovery time |
|-----------|-------------|---------------|----------------------------------------------------|-------------------------------------------|--------------|------------------------|
|           |             |               | <i>para<sup>bss</sup></i> Control                  |                                           |              | 1.00                   |
| CG2259    | FBgn0040319 | 33512         | Glutamate-cysteine ligase catalytic subunit        | GCLC                                      | 0.48         | 0.16                   |
| CG7574    | FBgn0026263 | 26106         | bip1                                               | -                                         | 0.67         | 0.27                   |
| CG4561    | FBgn0027080 | 105615        | Tyrosyl-tRNA synthetase                            | YARS, AIMP1                               | 0.57         | 0.28                   |
| CG8922    | FBgn0002590 | 101472        | Ribosomal protein S5a                              | MRPS7, RPS5                               | 0.69         | 0.34                   |
| CG13630   | FBgn0039219 | 107078        | unknown gene (CG13630)                             | METAP1D, METAP1                           | 0.65         | 0.36                   |
| CG5543    | FBgn0034908 | 27454         | unknown gene (CG5543)                              | WDR70                                     | 0.36         | 0.37                   |
| CG12749   | FBgn0004237 | 51759         | Heterogeneous nuclear ribonucleoprotein at 87F     | MSI1, HNRNPA1L2, DAZAP1, SRSF10, BOLL,    | 0.20         | 0.38                   |
| CG33202   | FBgn0053202 | 4797          | defective proboscis extension response 11          | KIRREL, KIRREL3, IGSF9B, KIRREL2, USH2A   | 0.62         | 0.39                   |
| CG9750    | FBgn0040075 | 19021         | reptin                                             | RUVBL2, RUVBL1, SCCPDH                    | 0.32         | 0.39                   |
| CG4022    | FBgn0035986 | 26359         | unknown gene (CG4022)                              | PIH1D2                                    | 0.59         | 0.40                   |
| CG7393    | FBgn0024846 | 108099        | p38b MAP kinase                                    | MAPK7, MAPK12, MAPK1, MAPK14, MAPK11      | 0.57         | 0.42                   |
| CG5650    | FBgn0004103 | 35025         | Protein phosphatase 1 at 87B                       | PPP1CC, PPP1CA, PPP1CB                    | 0.60         | 0.43                   |
| CG31671   | FBgn0031390 | 25793         | tho2                                               | THOC2, ZC3H13                             | 0.62         | 0.43                   |
| CG17800   | FBgn0033159 | 25623         | Down syndrome cell adhesion molecule 1             | PTPRU, MYLK4, PTPRM, DSCAML1, IL12RB2     | 0.56         | 0.44                   |
| CG6824    | FBgn0003028 | 41584         | ovo                                                | OVOL3, ZNF770, OVOL2, ZNF131, REST, OVN   | 0.62         | 0.44                   |
| CG7808    | FBgn0039713 | 35277         | Ribosomal protein S8                               | RPS8                                      | 0.61         | 0.45                   |
| CG15899   | FBgn0264386 | 31961         | Ca <sup>2+</sup> -channel protein alpha1 subunit T | CACNA1G, CATSPER1, CACNA1I, CACNA1H       | 0.58         | 0.47                   |
| CG11981   | FBgn0026380 | 31608         | Proteasome beta3 subunit                           | PSMB3                                     | 0.45         | 0.48                   |
| CG9900    | FBgn0004643 | 24171         | Zeste-white 10                                     | ZW10                                      | 0.64         | 0.48                   |
| CG5151    | FBgn0036576 | 27363         | unknown gene (CG5151)                              | LDLRAD4                                   | 0.50         | 0.48                   |
| CG15319   | FBgn0261617 | 102885        | nejire                                             | CREBBP, EP300                             | 0.54         | 0.49                   |
| CG5371    | FBgn0011703 | 15683         | Ribonucleoside diphosphate reductase large su      | RRM1                                      | 0.56         | 0.50                   |
| CG42314   | FBgn0259214 | 30203         | plasma membrane calcium ATPase                     | ATP2B1, ATP2B3, ATP2B2, ATP2B4            | 0.69         | 0.53                   |
| CG10361   | FBgn0036208 | 16034         | unknown gene (CG10361)                             | GCAT, ALAS1, NCLN, ALAS2                  | 0.58         | 0.53                   |
| CG18495   | FBgn0263121 | 49681         | Proteasome alpha1 subunit                          | PSMA6                                     | 0.49         | 0.55                   |
| CG9983    | FBgn0001215 | 29523         | Heterogeneous nuclear ribonucleoprotein at 98B     | DAZAP1, SLIRP, HNRNPD, HNRNPA1L2, DA      | 0.13         | 0.55                   |
| CG15218   | FBgn0025674 | 36215         | Cyclin K                                           | CCNT1, FAM58A, CCNK, CCNT2                | 0.21         | 0.56                   |
| CG8392    | FBgn0010590 | 35923         | Proteasome beta1 subunit                           | PSMB9, PSMB6                              | 0.45         | 0.56                   |
| CG2852    | FBgn0034753 | 15069         | unknown gene (CG2852)                              | NKTR, PPIB, RGPD4, RGPD5, PPIAL4A, PPIA   | 0.66         | 0.57                   |
| CG10938   | FBgn0016697 | 16105         | Proteasome alpha5 subunit                          | PSMA8, PSMA5, PSMA2, PSMA7                | 0.41         | 0.58                   |
| CG11840   | FBgn0031260 | 7247          | Signal peptide peptidase                           | SPPL2C, SPPL3, HM13                       | 0.65         | 0.58                   |
| CG10809   | FBgn0036052 | 38407         | unknown gene (CG10809)                             | ANKRD46, ANKRD61, ANKRD54                 | 0.59         | 0.58                   |
| CG7671    | FBgn0038609 | 108595        | Nucleoporin 43kD                                   | NUP43                                     | 0.63         | 0.58                   |
| CG4252    | FBgn0004367 | 11251         | meiotic 41                                         | ATR                                       | 0.59         | 0.59                   |
| CG42276   | FBgn0259171 | 106959        | Phosphodiesterase 9                                | PDE4D, PDE10A, PDE2A, PDE8B, PDE4C, P     | 0.54         | 0.60                   |
| CG1163    | FBgn0003275 | 105937        | RNA polymerase II 18kD subunit                     | POLR2F                                    | 0.41         | 0.62                   |
| CG5363    | FBgn0004106 | 106130        | Cyclin-dependent kinase 1                          | CDK5, CDK1, CDK18, CDK14, CDK3, CDK15,    | 0.65         | 0.62                   |
| CG4157    | FBgn0028693 | 21799         | Regulatory particle non-ATPase 12                  | PSMD8                                     | 0.53         | 0.63                   |
| CG14788   | FBgn0266284 | 18379         | Nucleostemin ortholog (H. sapiens) 3               | GNL1, LSG1                                | 0.53         | 0.63                   |
| CG2128    | FBgn0025825 | 20814         | Histone deacetylase 3                              | HDAC3, HDAC1, HDAC2, HDAC8                | 0.63         | 0.64                   |
| CG10320   | FBgn0034645 | 8837          | NADH dehydrogenase (ubiquinone) B12 subunit        | NDUFB3                                    | 0.57         | 0.64                   |
| CG10682   | FBgn0264848 | 27306         | vihar                                              | UBE2U, UBE2C                              | 0.46         | 0.64                   |
| CG4173    | FBgn0014029 | 26413         | Septin 2                                           | SEPT9, SEPT12, SEPT5, SEPT4, SEPT10, SE   | 0.50         | 0.65                   |
| CG10601   | FBgn0014343 | 50133         | mirror                                             | TGIF2-C20orf24, MKX, MEIS2, TGIF2LX, IRX5 | 0.34         | 0.65                   |
| CG32082   | FBgn0052082 | 50019         | Insulin receptor substrate 53 kDa                  | ALG10, PACSIN3, ALG10B, BAIAP2L2, BAIAP   | 0.56         | 0.66                   |
| CG12113   | FBgn0026679 | 18743         | Integrator 4                                       | INTS4                                     | 0.56         | 0.67                   |
| CG33129   | FBgn0053129 | 27554         | unknown gene (CG33129)                             | TMEM214                                   | 0.59         | 0.68                   |
| CG8190    | FBgn0034029 | 43917         | elf2B-gamma                                        | EIF2B3                                    | 0.59         | 0.68                   |
| CG8787    | FBgn0261823 | 107274        | Additional sex combs                               | ASXL1, ASXL3, ASXL2                       | 0.63         | 0.68                   |
| CG7340    | FBgn0040493 | 3175          | granny smith                                       | LAP3, NPEPL1                              | 0.21         | 0.69                   |
| CG12249   | FBgn0021776 | 51484         | miranda                                            | SLMAP                                     | 0.13         | 0.69                   |
| CG3068    | FBgn0000147 | 108446        | aurora A                                           | AURKC, AURKB, AURKA                       | 0.67         | 0.69                   |
| CG5986    | FBgn0043455 | 101446        | unknown gene (CG5986)                              | SDE2                                      | 0.58         | 0.69                   |
| CG42342   | FBgn0259244 | 24934         | unknown gene (CG42342)                             | COL5A1, COL17A1, COL6A3, COL14A1, COL4    | 0.59         | 0.69                   |
| CG11115   | FBgn0037202 | 49941         | Suppressor of Stem-Loop mutation ortholog (S.      | GTF2H2C_2, GTF2H2C, GTF2H2                | 0.40         | 0.71                   |
| CG8975    | FBgn0011704 | 7965          | Ribonucleoside diphosphate reductase small su      | RRM2, RRM2B                               | 0.69         | 0.73                   |
| CG6593    | FBgn0003134 | 105525        | Protein phosphatase 1alpha at 96A                  | PPP1CB, PPP1CA, PPP1CC                    | 0.48         | 0.78                   |
| CG14821   | FBgn0035719 | not available | target of wingless                                 | C1orf21                                   | 0.53         | -                      |
| CG30382   | FBgn0050382 | not available | unknown gene (CG30382)                             | PSMA6                                     | 0.44         | -                      |
| CG31666   | FBgn0086758 | not available | Chronologically inappropriate morphogenesis        | ZBTB12, ZBTB49, ZBTB9, ZBTB10, BACH2, Z   | 0.66         | -                      |
| CG5520    | FBgn0039562 | not available | Glycoprotein 93                                    | HSP90AB1, HSP90AA1, HSP90B1               | 0.22         | -                      |
| CG14791   | FBgn0025382 | not available | Rab27                                              | RAB27B, RAB27A                            | 0.67         | -                      |
| CG18616   | FBgn0260444 | not available | unknown gene (CG18616)                             | CNOT10                                    | 0.68         | -                      |
| CG34186   | FBgn0262954 | not available | Rpb12                                              | POLR2K                                    | 0.40         | -                      |

|         |             |        |                                                 |                                             |      |         |
|---------|-------------|--------|-------------------------------------------------|---------------------------------------------|------|---------|
| CG1057  | FBgn0037262 | 101488 | Mediator complex subunit 31                     | MED31                                       | 0.55 | ns      |
| CG12000 | FBgn0250746 | 16381  | Proteasome beta7 subunit                        | PSMB4                                       | 0.66 | ns      |
| CG13316 | FBgn0023215 | 101991 | Mnt                                             | MNT, MXI1, MXD3                             | 0.47 | ns      |
| CG13628 | FBgn0039218 | 29253  | Rpb10                                           | POLR2L                                      | 0.35 | ns      |
| CG15862 | FBgn0022382 | 101763 | cAMP-dependent protein kinase R2                | PRKAR2B, CNBD2, PRKAR1B, PRKAR2A, PR        | 0.54 | ns      |
| CG18009 | FBgn0261793 | 101318 | TATA box binding protein-related factor 2       | TBPL1, TBPL2, TBP                           | 0.63 | ns      |
| CG2252  | FBgn0004656 | 108662 | female sterile (1) homeotic                     | BRDT, BAZ1A, BAZ2B, CECR2, BRD4, CCDC       | 0.70 | ns      |
| CG3127  | FBgn0250906 | 110081 | Phosphoglycerate kinase                         | PGK2, PGK1                                  | 0.65 | ns      |
| CG3180  | FBgn0262955 | 45960  | RNA polymerase II 140kD subunit                 | POLR3B, POLR2B                              | 0.67 | ns      |
| CG42330 | FBgn0263219 | 23488  | Down syndrome cell adhesion molecule 4          | NRCAM, MYLK4, SPEG, NFASC, DSCAML1, H       | 0.70 | ns      |
| CG4746  | FBgn0029003 | 100700 | mab-21                                          | MAB21L1, MAB21L3, MB21D1, C2orf54, TMEN     | 0.32 | ns      |
| CG5669  | FBgn0039169 | 30734  | Sp1-like factor for pairing sensitive-silencing | SP9, SP4, SP2, SP5, SP8, KLF10, SP3, SP7, S | 0.61 | ns      |
| CG6050  | FBgn0024556 | 48981  | Elongation factor Tu mitochondrial              | TUFM                                        | 0.53 | ns      |
| CG7564  | FBgn0036734 | 100562 | unknown gene (CG7564)                           | LUC7L2, LUC7L3, LUC7L                       | 0.49 | ns      |
| CG7764  | FBgn0261109 | 12596  | marionette                                      | GTF2H4                                      | 0.57 | ns      |
| CG7977  | FBgn0026372 | 101337 | Ribosomal protein L23A                          | RPL23A                                      | 0.56 | ns      |
| CG8151  | FBgn0033929 | 12580  | TFB1 ortholog (S. cerevisiae)                   | GTF2H1                                      | 0.44 | ns      |
| CG8542  | FBgn0001220 | 106236 | Heat shock protein cognate 5                    | HSPA9                                       | 0.54 | ns      |
| CG10281 | FBgn0010282 | 110225 | Transcription factor II <sup>F</sup> alpha      | GTF2F1                                      | 0.26 | ns      |
| CG10377 | FBgn0004838 | 101555 | Heterogeneous nuclear ribonucleoprotein at 270  | HNRNPA3, HNRNPA0, HNRNPA2B1, HNRNP          | 0.50 | ns      |
| CG11103 | FBgn0030522 | 110763 | unknown gene (CG11103)                          | TM2D2                                       | 0.69 | ns      |
| CG14981 | FBgn0035473 | 109502 | maggie                                          | TOMM22                                      | 0.49 | ns      |
| CG32743 | FBgn0263968 | 41988  | no-on-and-no-off transient C                    | BOLA2-SMG1P6, BOLA2B, BOLA2, PRKDC, N       | 0.44 | ns      |
| CG33106 | FBgn0043884 | 103411 | multiple ankyrin repeats single KH domain       | ANKRD17, ANKRD22, ANKHD1-EIF4EBP3, AN       | 0.19 | ns      |
| CG3710  | FBgn0010422 | 22979  | RNA polymerase II elongation factor             | MED26, TCEANC2, TCEA3, TCEA2, TCEANC        | 0.47 | ns      |
| CG3756  | FBgn0031657 | 15675  | unknown gene (CG3756)                           | POLR1C                                      | 0.70 | ns      |
| CG3931  | FBgn0034879 | 102375 | Rrp4                                            | EXOSC2                                      | 0.68 | ns      |
| CG4097  | FBgn0002284 | 105673 | Proteasome beta6 subunit                        | PSMB1                                       | 0.57 | ns      |
| CG42273 | FBgn0259168 | 107066 | minibrain                                       | DYRK4, DYRK3, DYRK2, DYRK1A, HIPK1, HII     | 0.58 | ns      |
| CG4319  | FBgn0011706 | 12045  | reaper                                          | TSC1, RIN1                                  | 0.68 | ns      |
| CG6323  | FBgn0039465 | 109600 | Tetraspanin 97E                                 | TSPAN13, TSPAN31                            | 0.64 | ns      |
| CG7903  | FBgn0039730 | 106475 | unknown gene (CG7903)                           | RBM4, ADK, RBM14                            | 0.56 | ns      |
| CG9412  | FBgn0015778 | 109911 | rasputin                                        | G3BP2, G3BP1                                | 0.65 | ns      |
| CG9819  | FBgn0267912 | 109858 | CanA-14F                                        | PPP3CA, PPP3CB, PPP3CC                      | 0.62 | ns      |
| CG1528  | FBgn0028968 | 25101  | Coat Protein (coatomer) gamma                   | COPG2, COPG1                                | 0.67 | sterile |
| CG2009  | FBgn0026262 | 48036  | bip2                                            | ING4, TAF8, ING2, ING3, ING1, ING5, TAF3    | 0.68 | sterile |
| CG5949  | FBgn0263600 | 41027  | DNA-polymerase-delta                            | POLD1, REV3L                                | 0.51 | sterile |

94 lines tested

60.6% 57 lines reduced seizure duration of para<sup>bss</sup>

44.7% 42 lines exhibited similar or greater rescue effect compared to phenytoin treatment (64%)

3 lines are sterile