

Figure 6

Figure 6A (upper panel)

| ctrl  | 4AP 6h | 4AP 24h | 4AP 48h | 4AP 96h |
|-------|--------|---------|---------|---------|
| 0.911 | 0.855  | 1.165   | 1.273   | 1.212   |
| 0.930 | 1.142  | 1.520   | 1.515   | 0.899   |
| 1.042 | 1.187  | 1.195   | 1.303   | 1.277   |
| 1.116 | 1.349  | 1.513   | 1.184   | 1.425   |
| 0.918 | 1.369  | 1.262   | 1.176   | 1.082   |
| 0.922 | 1.090  | 1.546   | 1.041   | 0.807   |
| 1.006 | 1.328  | 1.472   | 1.167   | 0.871   |
| 1.156 | 1.037  |         |         |         |
|       | 1.364  |         |         |         |
|       | 1.102  |         |         |         |
|       | 1.463  |         |         |         |
|       | 1.254  |         |         |         |
|       | 1.260  |         |         |         |
|       | 1.330  |         |         |         |

Figure 6A (center panel)

| ctrl  | 4AP 6h | 4AP 24h | 4AP 48h | 4AP 96h |
|-------|--------|---------|---------|---------|
| 1.186 | 1.863  | 1.471   | 1.207   | 0.720   |
| 0.982 | 2.129  | 1.309   | 0.912   | 1.143   |
| 0.934 | 1.717  | 1.216   | 0.968   | 1.044   |
| 0.899 | 1.904  | 1.493   | 0.690   | 1.024   |
| 0.986 | 2.587  |         | 0.877   | 0.644   |
| 1.003 | 2.129  |         | 0.744   | 0.642   |
| 1.147 | 1.897  |         | 0.814   | 0.577   |
| 0.863 | 2.193  |         |         |         |
|       | 1.925  |         |         |         |
|       | 2.202  |         |         |         |
|       | 2.306  |         |         |         |
|       | 1.703  |         |         |         |
|       | 1.710  |         |         |         |
|       | 1.518  |         |         |         |

Figure 6A (lower panel)

| ctrl  | 4AP 6h | 4AP 24h | 4AP 48h | 4AP 96h |
|-------|--------|---------|---------|---------|
| 0.913 | 2.288  | 3.094   | 0.712   | 1.170   |
| 1.104 | 3.119  | 1.593   | 1.121   | 1.215   |
| 1.016 | 2.377  | 1.636   | 0.927   | 0.696   |
| 0.941 | 2.765  | 2.054   | 1.375   | 0.764   |
| 0.924 | 2.042  | 1.435   | 1.352   | 0.699   |
| 0.901 | 2.578  | 1.217   | 1.143   | 0.714   |
| 0.867 | 2.336  | 1.719   | 1.027   | 0.773   |
| 1.334 | 3.154  |         |         |         |
|       | 3.770  |         |         |         |
|       | 3.203  |         |         |         |
|       | 3.956  |         |         |         |
|       | 3.138  |         |         |         |
|       | 3.154  |         |         |         |
|       | 3.313  |         |         |         |

Figure 6B (upper panel)

| ctrl  | scrRNA  |         |  | ctrl  | shRNA   |         |  |
|-------|---------|---------|--|-------|---------|---------|--|
|       | 4AP 24h | 4AP 48h |  |       | 4AP 24h | 4AP 48h |  |
| 1.000 | 1.277   | 1.630   |  | 0.663 | 0.821   | 0.683   |  |
| 0.994 | 1.123   | 1.400   |  | 0.678 | 0.748   | 0.790   |  |
| 1.006 | 1.103   | 1.006   |  | 0.603 | 0.871   | 0.753   |  |
| 0.994 | 1.419   | 1.127   |  | 0.609 | 0.867   | 0.756   |  |
| 1.006 | 1.474   | 1.363   |  | 0.408 | 0.778   | 0.623   |  |
| 1.017 | 1.486   | 1.291   |  | 0.475 | 1.020   | 0.711   |  |
| 0.983 | 1.558   | 1.436   |  | 1.291 | 0.437   | 0.798   |  |
| 1.155 | 2.034   | 1.435   |  | 0.432 | 0.817   | 0.872   |  |
| 0.845 | 1.500   |         |  | 1.435 | 0.560   | 0.749   |  |
|       |         |         |  | 0.606 | 0.751   | 0.802   |  |

|              |               |               |               |               |               |
|--------------|---------------|---------------|---------------|---------------|---------------|
| <b>N</b>     | <b>8</b>      | <b>14</b>     | <b>7</b>      | <b>7</b>      | <b>7</b>      |
| <b>Media</b> | <b>1.0000</b> | <b>1.2237</b> | <b>1.3820</b> | <b>1.2369</b> | <b>1.0819</b> |
| <b>SD</b>    | <b>0.0967</b> | <b>0.1641</b> | <b>0.1671</b> | <b>0.1488</b> | <b>0.2333</b> |
| <b>SE</b>    | <b>0.0342</b> | <b>0.0439</b> | <b>0.0632</b> | <b>0.0563</b> | <b>0.0882</b> |

|              |               |               |               |               |               |
|--------------|---------------|---------------|---------------|---------------|---------------|
| <b>N</b>     | <b>8</b>      | <b>14</b>     | <b>4</b>      | <b>7</b>      | <b>7</b>      |
| <b>Media</b> | <b>1.0000</b> | <b>1.9844</b> | <b>1.3723</b> | <b>0.8874</b> | <b>0.8277</b> |
| <b>SD</b>    | <b>0.1134</b> | <b>0.2875</b> | <b>0.1325</b> | <b>0.1703</b> | <b>0.2335</b> |
| <b>SE</b>    | <b>0.0401</b> | <b>0.0768</b> | <b>0.0662</b> | <b>0.0644</b> | <b>0.0883</b> |

|              |               |               |               |               |               |
|--------------|---------------|---------------|---------------|---------------|---------------|
| <b>N</b>     | <b>8</b>      | <b>14</b>     | <b>7</b>      | <b>7</b>      | <b>7</b>      |
| <b>Media</b> | <b>1.0000</b> | <b>2.9424</b> | <b>1.8210</b> | <b>1.0940</b> | <b>0.8615</b> |
| <b>SD</b>    | <b>0.1544</b> | <b>0.5662</b> | <b>0.6171</b> | <b>0.2334</b> | <b>0.2282</b> |
| <b>SE</b>    | <b>0.0546</b> | <b>0.1513</b> | <b>0.2332</b> | <b>0.0882</b> | <b>0.0863</b> |

|              |               |               |               |               |               |               |
|--------------|---------------|---------------|---------------|---------------|---------------|---------------|
| <b>N</b>     | <b>9</b>      | <b>9</b>      | <b>8</b>      | <b>10</b>     | <b>10</b>     | <b>10</b>     |
| <b>Media</b> | <b>1.0000</b> | <b>1.4416</b> | <b>1.3360</b> | <b>0.7200</b> | <b>0.7670</b> | <b>0.7537</b> |
| <b>SD</b>    | <b>0.0781</b> | <b>0.2772</b> | <b>0.1948</b> | <b>0.3530</b> | <b>0.1642</b> | <b>0.0696</b> |
| <b>SE</b>    | <b>0.0260</b> | <b>0.0924</b> | <b>0.0689</b> | <b>0.1116</b> | <b>0.0519</b> | <b>0.0220</b> |

Figure 6B (lower panel)

| ctrl  | scrRNA  |         | shRNA |         |         |
|-------|---------|---------|-------|---------|---------|
|       | 4AP 24h | 4AP 48h | ctrl  | 4AP 24h | 4AP 48h |
| 1.000 | 2.374   | 1.338   | 0.963 | 2.064   | 1.124   |
| 0.796 | 3.519   | 1.263   | 1.037 | 1.924   | 1.033   |
| 1.204 | 2.583   | 1.648   | 0.915 | 3.793   | 2.532   |
| 0.907 | 6.248   | 2.120   | 1.085 | 0.914   | 2.647   |
| 1.093 | 5.132   | 0.779   | 0.439 | 1.958   | 3.038   |
| 0.942 | 5.888   | 0.812   | 1.561 | 2.343   | 2.919   |
| 1.058 | 3.445   | 0.667   | 1.311 | 3.643   | 5.953   |
| 0.875 | 1.863   | 1.087   | 0.689 | 1.688   | 6.424   |
| 1.125 |         | 0.990   | 0.940 | 1.657   | 1.370   |
|       |         |         | 1.060 |         | 1.350   |

Figure 6D (left panel)

| eIPSCs (nA) |          |            |            |
|-------------|----------|------------|------------|
| ctrl/veh    | ctrl/4AP | TrkBfc/veh | TrkBfc/4AP |
| 2.669       | 3.690    | 2.231      | 3.120      |
| 3.169       | 5.600    | 3.442      | 3.507      |
| 2.456       | 5.541    | 3.138      | 2.754      |
| 4.013       | 9.900    | 2.462      | 4.308      |
| 4.472       | 7.400    | 3.558      | 1.976      |
| 2.500       | 4.924    | 1.530      | 2.486      |
| 2.070       | 3.568    | 5.184      | 3.080      |
| 3.448       | 4.722    | 2.560      | 3.700      |
| 3.228       | 4.126    | 3.000      | 1.650      |
| 3.602       | 2.630    | 2.700      | 1.896      |
| 2.418       | 7.646    | 4.300      | 4.812      |
| 4.115       | 7.400    | 3.100      | 3.200      |
| 3.692       | 4.656    | 5.182      | 5.288      |
| 1.702       | 7.000    | 2.130      | 3.556      |
| 2.590       | 9.000    | 2.976      | 0.833      |
| 4.168       | 5.098    | 2.652      | 1.926      |
| 4.238       | 3.596    | 3.278      | 1.966      |
| 1.312       | 5.116    | 5.136      | 1.890      |
| 2.450       | 4.430    | 4.382      | 3.678      |
| 4.008       | 9.500    | 3.896      | 2.620      |
| 4.600       | 3.187    | 2.000      | 3.466      |
| 3.700       | 2.276    | 2.280      | 1.874      |
| 3.868       | 3.696    | 3.108      | 2.610      |
| 4.208       | 6.338    | 4.000      | 1.488      |
| 1.365       | 3.940    | 2.452      | 1.688      |
| 1.524       | 5.076    | 1.386      | 4.446      |
| 4.548       | 3.676    | 2.462      | 3.488      |
| 3.568       | 3.632    | 4.786      | 3.698      |
| 3.440       | 3.902    | 1.876      | 2.684      |
| 3.986       | 2.242    | 2.500      | 3.552      |
| 1.948       | 3.946    | 4.093      | 5.530      |
| 4.028       | 3.650    | 3.134      | 4.082      |
| 4.024       | 3.910    | 4.332      | 6.126      |
| 2.304       | 4.876    | 4.154      | 2.592      |
| 4.250       | 2.526    | 4.384      | 4.942      |
| 3.948       | 2.624    | 4.920      | 2.830      |
| 4.266       | 2.297    | 3.190      | 4.496      |
| 3.430       | 4.074    | 3.228      | 2.372      |
| 4.554       | 2.814    | 3.060      | 3.208      |
| 2.098       |          | 1.654      | 2.678      |
| 4.020       |          | 3.230      | 3.266      |
| 5.008       |          | 1.774      | 4.714      |
| 4.622       |          | 5.380      | 4.172      |
|             |          |            | 3.162      |

Figure 6D (right panel)

| PPR ( $I_2/I_1$ ) |          |            |            |
|-------------------|----------|------------|------------|
| ctrl/veh          | ctrl/4AP | TrkBfc/veh | TrkBfc/4AP |
| 0.272             | 0.188    | 0.248      | 0.259      |
| 0.326             | 0.239    | 0.336      | 0.335      |
| 0.207             | 0.214    | 0.167      | 0.310      |
| 0.224             | 0.150    | 0.346      | 0.238      |
| 0.194             | 0.281    | 0.127      | 0.300      |
| 0.400             | 0.213    | 0.363      | 0.323      |
| 0.247             | 0.185    | 0.272      | 0.260      |
| 0.169             | 0.170    | 0.190      | 0.250      |
| 0.360             | 0.159    | 0.261      | 0.176      |
| 0.367             | 0.148    | 0.182      | 0.273      |
| 0.292             | 0.093    | 0.271      | 0.320      |
| 0.340             | 0.167    | 0.320      | 0.171      |
| 0.214             | 0.161    | 0.214      | 0.350      |
| 0.450             | 0.118    | 0.338      | 0.310      |
| 0.317             | 0.112    | 0.127      | 0.330      |
| 0.209             | 0.131    | 0.158      | 0.286      |
| 0.221             | 0.145    | 0.226      | 0.380      |
| 0.164             | 0.084    | 0.264      | 0.370      |
| 0.108             | 0.206    | 0.347      | 0.213      |
| 0.162             | 0.119    | 0.144      | 0.440      |
| 0.102             | 0.109    | 0.234      | 0.330      |
| 0.116             | 0.158    | 0.299      | 0.144      |
| 0.239             | 0.147    | 0.170      | 0.197      |
| 0.211             | 0.161    | 0.165      | 0.390      |
| 0.301             | 0.134    | 0.147      | 0.340      |
| 0.370             | 0.139    | 0.359      | 0.209      |
| 0.274             | 0.135    | 0.252      | 0.172      |
| 0.133             | 0.139    | 0.185      | 0.173      |
| 0.342             | 0.301    | 0.343      | 0.316      |
| 0.243             | 0.225    | 0.274      | 0.210      |
| 0.267             | 0.172    | 0.167      | 0.162      |
| 0.398             | 0.181    | 0.410      | 0.182      |
| 0.205             | 0.195    | 0.417      | 0.210      |
| 0.286             | 0.209    | 0.394      | 0.181      |
| 0.195             | 0.123    | 0.139      | 0.215      |
| 0.338             | 0.170    | 0.155      | 0.285      |
| 0.165             | 0.257    | 0.431      | 0.240      |
| 0.294             | 0.224    | 0.258      | 0.139      |
| 0.208             | 0.306    | 0.314      | 0.125      |
| 0.244             |          | 0.261      | 0.204      |
| 0.175             |          | 0.211      | 0.348      |
| 0.187             |          | 0.327      | 0.410      |
| 0.213             |          | 0.312      | 0.405      |
|                   |          |            | 0.317      |

9 8 9  
**1.0000 3.8815 1.1893**  
 0.1316 1.6710 0.4661  
**0.0439 0.5908 0.1554**

10 9 10  
**1.0000 2.2204 2.8390**  
 0.3068 0.9355 1.9237  
**0.0970 0.3118 0.6083**

43 39 44 43  
**3.3866 4.7237 3.2587 3.2151**  
 1.0093 1.9850 1.0769 1.1938  
**0.1539 0.3179 0.1623 0.1821**

43 39 44 43  
**0.2500 0.1735 0.2600 0.2670**  
 0.0845 0.0538 0.0866 0.0834  
**0.0129 0.0086 0.0131 0.0127**

**Figure 6**

| <i>Figure 6A (upper panel)</i>          |             |             |                   |
|---|-------------|-------------|-------------------|
| <b>one-way ANOVA/Dunnett's tests</b>    |             |             |                   |
| Dunnett's multiple comparisons test     | Significant | Summary     | P Value           |
| 0 vs. 6                                 | Yes         | *           | 0.0147            |
| 0 vs. 24                                | Yes         | ***         | 0.0003            |
| 0 vs. 48                                | Yes         | *           | 0.03              |
| 0 vs. 96                                | No          | ns          | 0.7404            |
| <i>Figure 6A (center panel)</i>         |             |             |                   |
| <b>one-way ANOVA/Dunnett's tests</b>    |             |             |                   |
| Dunnett's multiple comparisons test     | Significant | Summary     | P Value           |
| 0 vs. 6                                 | Yes         | ****        | <0,0001           |
| 0 vs. 24                                | Yes         | *           | 0.0329            |
| 0 vs. 48                                | No          | ns          | 0.7324            |
| 0 vs. 96                                | No          | ns          | 0.3877            |
| <i>Figure 6A (lower panel)</i>          |             |             |                   |
| <b>one-way ANOVA/Dunnett's tests</b>    |             |             |                   |
| Dunnett's multiple comparisons test     | Significant | Summary     | P Value           |
| 0 vs. 6                                 | Yes         | ****        | <0,0001           |
| 0 vs. 24                                | Yes         | **          | 0.0031            |
| 0 vs. 48                                | No          | ns          | 0.9809            |
| 0 vs. 96                                | No          | ns          | 0.9276            |
| <i>Figure 6B (upper panel)</i>          |             |             |                   |
| <b>two-way ANOVA/Tukey's tests</b>      |             |             |                   |
| Tukey's multiple comparisons test       | Significant | Summary     | P Value           |
| <b>Ctrl :scrRNA vs. 4AP 24h:scrRNA</b>  | <b>Yes</b>  | <b>***</b>  | <b>0.0006</b>     |
| <b>Ctrl :scrRNA vs. 4AP 48h:scrRNA</b>  | <b>Yes</b>  | <b>*</b>    | <b>0.019</b>      |
| Ctrl :scrRNA vs. 4AP 48h:shRNA          | No          | ns          | 0.0954            |
| Ctrl :shRNA vs. 4AP 24h:scrRNA          | Yes         | ****        | <0,0001           |
| Ctrl :shRNA vs. 4AP 24h:shRNA           | No          | ns          | 0.9489            |
| Ctrl :shRNA vs. 4AP 48h:scrRNA          | Yes         | ****        | <0,0001           |
| Ctrl :shRNA vs. 4AP 48h:shRNA           | No          | ns          | 0.9489            |
| <b>4AP 24h:scrRNA vs. 4AP 24h:shRNA</b> | <b>Yes</b>  | <b>****</b> | <b>&lt;0,0001</b> |
| 4AP 24h:scrRNA vs. 4AP 48h:scrRNA       | No          | ns          | 0.786             |
| 4AP 24h:scrRNA vs. 4AP 48h:shRNA        | Yes         | ****        | <0,0001           |
| 4AP 24h:shRNA vs. 4AP 48h:scrRNA        | Yes         | ****        | <0,0001           |
| 4AP 24h:shRNA vs. 4AP 48h:shRNA         | No          | ns          | 0.9489            |
| <b>4AP 48h:scrRNA vs. 4AP 48h:shRNA</b> | <b>Yes</b>  | <b>****</b> | <b>&lt;0,0001</b> |

*Figure 6B (lower panel)*

**two-way ANOVA/Tukey's tests**

| Tukey's multiple comparisons test       | Significant | Summary     | P Value           |
|---|-------------|-------------|-------------------|
| Ctrl:scrRNA vs. Ctrl:shRNA              | No          | ns          | >0,9999           |
| <b>Ctrl:scrRNA vs. 4AP 24h:scrRNA</b>   | <b>Yes</b>  | <b>****</b> | <b>&lt;0,0001</b> |
| Ctrl:scrRNA vs. 4AP 24h:shRNA           | No          | ns          | 0.1702            |
| <b>Ctrl:scrRNA vs. 4AP 48h:scrRNA</b>   | <b>No</b>   | <b>ns</b>   | <b>0.9773</b>     |
| Ctrl:scrRNA vs. 4AP 48h:shRNA           | Yes         | **          | 0.0097            |
| Ctrl:shRNA vs. 4AP 24h:scrRNA           | Yes         | ****        | <0,0001           |
| Ctrl:shRNA vs. 4AP 24h:shRNA            | No          | ns          | 0.1686            |
| Ctrl:shRNA vs. 4AP 48h:scrRNA           | No          | ns          | 0.9773            |
| Ctrl:shRNA vs. 4AP 48h:shRNA            | Yes         | **          | 0.0079            |
| <b>4AP 24h:scrRNA vs. 4AP 24h:shRNA</b> | <b>Yes</b>  | <b>*</b>    | <b>0.035</b>      |
| 4AP 24h:scrRNA vs. 4AP 48h:scrRNA       | Yes         | ***         | 0.0001            |
| 4AP 24h:scrRNA vs. 4AP 48h:shRNA        | No          | ns          | 0.2992            |
| 4AP 24h:shRNA vs. 4AP 48h:scrRNA        | No          | ns          | 0.2992            |
| 4AP 24h:shRNA vs. 4AP 48h:shRNA         | No          | ns          | 0.6651            |
| <b>4AP 48h:scrRNA vs. 4AP 48h:shRNA</b> | <b>Yes</b>  | <b>*</b>    | <b>0.0254</b>     |

*Figure 6D (left panel)*

**two-way ANOVA/Tukey's tests**

| Tukey's multiple comparisons test | Significant | Summary     | P Value           |
|-----------------------------------|-------------|-------------|-------------------|
| <b>NEG:veh vs. NEG:4AP</b>        | <b>Yes</b>  | <b>****</b> | <b>&lt;0,0001</b> |
| NEG:veh vs. ODN:veh               | No          | ns          | 0.9895            |
| NEG:veh vs. ODN:4AP               | No          | ns          | 0.9004            |
| NEG:4AP vs. ODN:veh               | Yes         | ****        | <0,0001           |
| NEG:4AP vs. ODN:4AP               | Yes         | ****        | <0,0001           |
| ODN:veh vs. ODN:4AP               | No          | ns          | 0.9771            |

*Figure 6D (right panel)*

**two-way ANOVA/Tukey's tests**

| Tukey's multiple comparisons test | Significant | Summary | P Value |
|-----------------------------------|-------------|---------|---------|
| NEG:Ctrl vs. NEG:4AP              | Yes         | ****    | <0,0001 |
| NEG:Ctrl vs. ODN:Ctrl             | No          | ns      | 0.8053  |
| NEG:Ctrl vs. ODN:4AP              | No          | ns      | 0.615   |
| NEG:4AP vs. ODN:Ctrl              | Yes         | ****    | <0,0001 |
| NEG:4AP vs. ODN:4AP               | Yes         | ****    | <0,0001 |
| ODN:Ctrl vs. ODN:4AP              | No          | ns      | 0.9816  |