In vitro Toxicology

eCiphr® Neuro: Assessment of Neuronal Activity Using Microelectrode Array

Background Information

- The eCiphr® Neuro assay uses primary cultures of rat cortical neurons.
- Cyprotex's neuronal assay uses high throughput microelectrode array (MEA) technology to monitor electrophysiological activity.
- Neurons grown on microelectrode arrays recapitulate many features of neurons in vivo, including spontaneous activity (spiking and bursting), plasticity, organisation and responsiveness to a wide range of neurotransmitters and pharmacological agonists/antagonists.
- This technology provides a unique in vitro system for preclinical drug discovery, neurotoxicity assessment and disease modelling.

Protocol

**Cell Type**
Primary rat cortical neurons

**Analysis Platform**
Maestro 48-well MEA system (Axion BioSystems)

**Test Article Concentrations**
4 concentrations in triplicate (dependent on customer requirements)

**Quality Controls**
- Negative control: 0.2% DMSO (vehicle)
- Positive controls: picrotoxin and domoic acid (at single concentration)

**Data Delivery**
- Firing rate (spikes/second)
- Burst rate (spikes/second)
- Number of spikes in burst
- Percent of isolated spikes
- Coefficient of variation (CV) of the inter-spike intervals (ISI)
- Burst duration
- Normalised IQR (inter-quartile range) burst duration
- Interburst interval
- Mean ISI-distance (measure of synchrony)
- Normalised Median Absolute Deviation (MAD) burst spike number
- Median ISI/Mean ISI

"The unique capabilities of MEAs to provide functional measurements of network activity, including spontaneous activity, evoked activity, and responses to pharmacological challenges, therefore offers an advantage over other potential screening approaches that rely on biochemical or structural endpoints."

*Robinette BL et al., (2011) Front Neuroeng 4, 1-9"
Neurological effects observed in vivo.

Table 1

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical class</th>
<th>Neurological effect in vivo</th>
<th>eCiphr®Neuro prediction</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2% DMSO</td>
<td>Vehicle</td>
<td>None</td>
<td>No effect</td>
</tr>
<tr>
<td>Gabazine</td>
<td>GABA&lt;sub&gt;A&lt;/sub&gt; antagonist</td>
<td>Seizurogenic&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Seizurogenic</td>
</tr>
<tr>
<td>Bicuculline</td>
<td>GABA&lt;sub&gt;A&lt;/sub&gt; antagonist</td>
<td>Seizurogenic&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Seizurogenic</td>
</tr>
<tr>
<td>Picrotoxin</td>
<td>GABA&lt;sub&gt;A&lt;/sub&gt; antagonist</td>
<td>Seizurogenic&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Seizurogenic</td>
</tr>
<tr>
<td>Pentylenetetrazole (PTZ)</td>
<td>GABA&lt;sub&gt;A&lt;/sub&gt; antagonist</td>
<td>Seizurogenic&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Seizurogenic</td>
</tr>
<tr>
<td>TTX</td>
<td>GABA&lt;sub&gt;A&lt;/sub&gt; antagonist</td>
<td>Seizurogenic&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Seizurogenic</td>
</tr>
<tr>
<td>GABA&lt;sub&gt;A&lt;/sub&gt; agonist</td>
<td>Decreases neural activity&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Decreased activity</td>
<td></td>
</tr>
<tr>
<td>Tetrodotoxin</td>
<td>Sodium channel blocker</td>
<td>Neurotoxic&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Neurotoxic</td>
</tr>
<tr>
<td>Aminopyridine</td>
<td>Potassium channel blocker</td>
<td>Seizurogenic&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Seizurogenic</td>
</tr>
<tr>
<td>Domoic Acid</td>
<td>Glutamate signalling</td>
<td>Neurotoxic&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Neurotoxic</td>
</tr>
<tr>
<td>L-Glutamate</td>
<td>Glutamate agonist</td>
<td>Increase neural activity&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Increased activity</td>
</tr>
<tr>
<td>Strychnine</td>
<td>Glycine receptor antagonist</td>
<td>Seizurogenic&lt;sup&gt;11&lt;/sup&gt;</td>
<td>Seizurogenic</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>NSAID</td>
<td>None</td>
<td>No effect</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>NSAID</td>
<td>None</td>
<td>No effect</td>
</tr>
</tbody>
</table>

References

1. Robinette BL et al, (2011) Front Neuromeng 4; Article 1