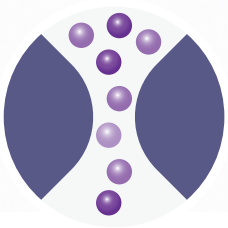
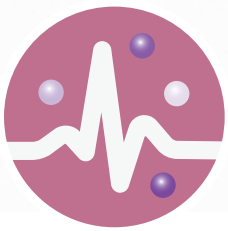
metrion biosciences

Specialist Neuroscience Services

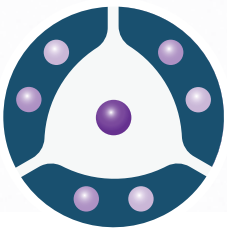
Highly specialised and tailored neuronal assays for pharmacological screening, including disease modelling and neurotoxicity testing



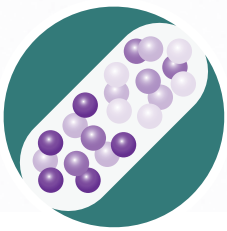
Ion channel screening



Cardiac safety screening



Neuroscience assays



Integrated drug discovery

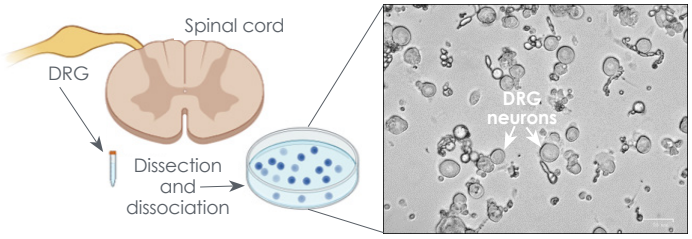
Highly specialised and tailored neuronal assays for pharmacological screening and neurotoxicity testing

Our specialist team of neuroscientists have extensive experience with indications such as pain, neurodegeneration, psychiatry and more.

Panel of models with increasing complexity and translational relevance

- Ion channel expressing cell lines for central and peripheral nervous system targets.
- Primary neuronal cultures, such as dissociated cortical, trigeminal or dorsal root ganglion (DRG) neurons from rodents (Figure 1).
- CNS drug discovery to understand the effects of test compounds on brain slice tissue.
- Human iPSC-derived neurons.

A Preparation of dorsal root ganglion (DRG) neurons for patch-clamp studies.



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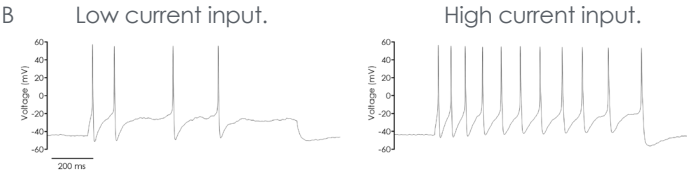

(Images for A created using biorender.com).

Range of assay methodologies

Assay methodologies we provide include:

- Heterologous cell lines and integrative assays.
- Selectivity and safety profiling of lead compounds and IND candidates.
- Translational assays: central and peripheral neuronal firing, and native ion channel screening assays.

These assays will help you:

- Investigate the mechanism of action for pre-clinical compounds.
- Confirm compound effects against specific ion channels in native neuronal backgrounds.
- Address the neurotoxicity of compounds and assess the effects of compounds on a range of excitability parameters.

Figure 1. Visual summary of primary neuronal cells used in electrophysiological recordings. (A) Rodent dorsal root ganglion (DRG) neuron preparation for manual patch-clamp studies and a bright-field image of dissociated cells seeded on a coverslip. (B) DRG action potential responses to 1-second pulses of a low and a high injected current.

Technologies used

- QPatch and Qube automated electrophysiology
- Manual patch clamp electrophysiology
- Plate-based multi-electrode array techniques
- Plate-based and single cell imaging
- PatchScope Pro integrated patch clamp / fluorescence rig

Studying ion channels on the lysosomal membrane

To enable the study of ion channels found on the lysosomal membrane we perform the lysosomal patch-clamp technique.

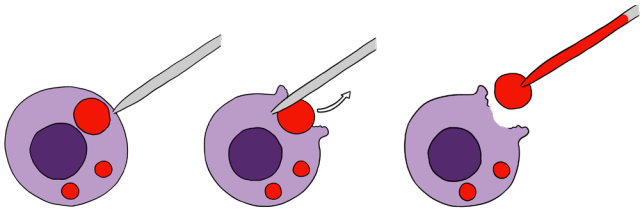

Figure 2. A sharp pipette is used to slice the cell membrane to create a rupture point through which the lysosome can be squeezed. A fresh fire polished pipette is then used to patch the lysosome. It is filled with intracellular solution, placed on the pipette holder, put into the solution chamber, and used to approach the lysosome on the coverslip. When a gigaseal has been formed on the lysosome, a zap or voltage pulse is used to break in and achieve the whole-lysosome configuration.

Watch video demonstrating this in action:
https://www.metrionbiosciences.com/neuroscience

Understand the effects of test compounds on brain slice tissue

Retain the anatomical architecture of brain tissue and the synaptic circuitry within for a more holistic understanding of the effects of pharmacological compounds on the entire tissue, which may directly or indirectly affect neuronal ion channel function and excitatory activity.

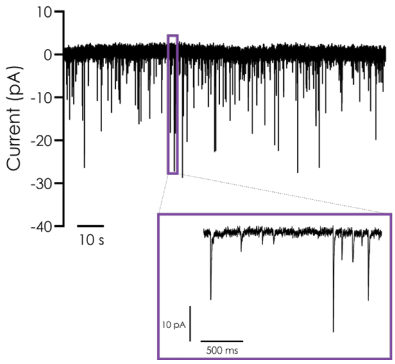

Figure 3. Representative recording of spontaneous post-synaptic currents at -70 mV holding potential. The inset illustrates a zoomed-in area of the recording.

Case Study: Multi-assay high-throughput repurposing screen for rare epilepsy mutation in KCNC1 gene

Eliana is a two-year-old from Canada with a de novo mutation (V434L) in her KCNC1 gene which encodes for the $K_V3.1$ channel in central nervous system neurons such as cerebellar neurons and GABAergic interneurons. The mutation manifests as a variety of neurological disorders which can include myoclonic epilepsy and ataxia, developmental epileptic encephalopathy (DEE), or hypotonia, depending on the specific variant.

Although Eliana does not exhibit typical DEE, she suffers from hypotonia, cortical-visual impairment, vertical nystagmus, and global delays. Eliana's parents founded the KCNC1 Foundation, where 14 different genetic variants from 36 patients have been registered. Of these patients, 25% share the A421V variant, 12.5% share the R320H variant, a few exhibit the V432M variant, and the remaining variants are seen in 1 - 3 patients.

Together with their partners, the Foundation decided to undertake drug repurposing studies to quickly identify safe and cost-effective therapies for Eliana. The KCNC1 Foundation collaborated with Metrion Biosciences, where manual and automated (Qube) patch-clamp techniques and Fluorescent Imaging Plate Reader (FLIPR) high throughput screens (HTS) against the mutant channel were performed to identify hit compounds.

Read the full case study:
www.metrionbiosciences.com/neuroscience/#kcnc1

Specialist Preclinical Drug Discovery CRO

Metrion Biosciences is a sector-leading CRO specialising in preclinical ion channel drug discovery, cardiac safety and neuroscience research services.

We deliver comprehensive drug discovery outsourcing solutions to pharmaceutical and bioscience customers worldwide; all from our state-of-the art research hub.

Priding ourselves on delivering high quality data, our team use their extensive experience to:

- Complete laboratory studies on time and on budget.
- Carefully interpret the experimental findings.
- Communicate the results.
- Provide strategic recommendations.
- Support your decision making to best inform your screening strategy.

1,000+ projects completed across almost 20 countries and 5 continents

Over 51% staff trained to PhD level and over 75% of team trained to Master's degree level and above

250 years combined experience managing ion channel research programmes

130 different customers worked with in the last 4 years

Testimonials describing how customers value working with Metrion

"We recognize this type of study is very difficult and the cells we provided posed technical challenges. We also appreciate the timeliness of the study execution and the detailed report you provided."

Top 10 pharma
Global

"Attention to detail with executing the study and the quality of reports is the best we have ever seen. By far the most accurate and well interpreted data. Explanations clear for a non-expert to understand."

Biotech
USA

"We appreciate the thoroughness, clearness of explanation and results, and the work done above and beyond to troubleshoot."

Biopharma
USA

"Really good data showing exactly what we would expect for this inhibitor; we know how difficult these recordings are to perform."

Large pharma
UK

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