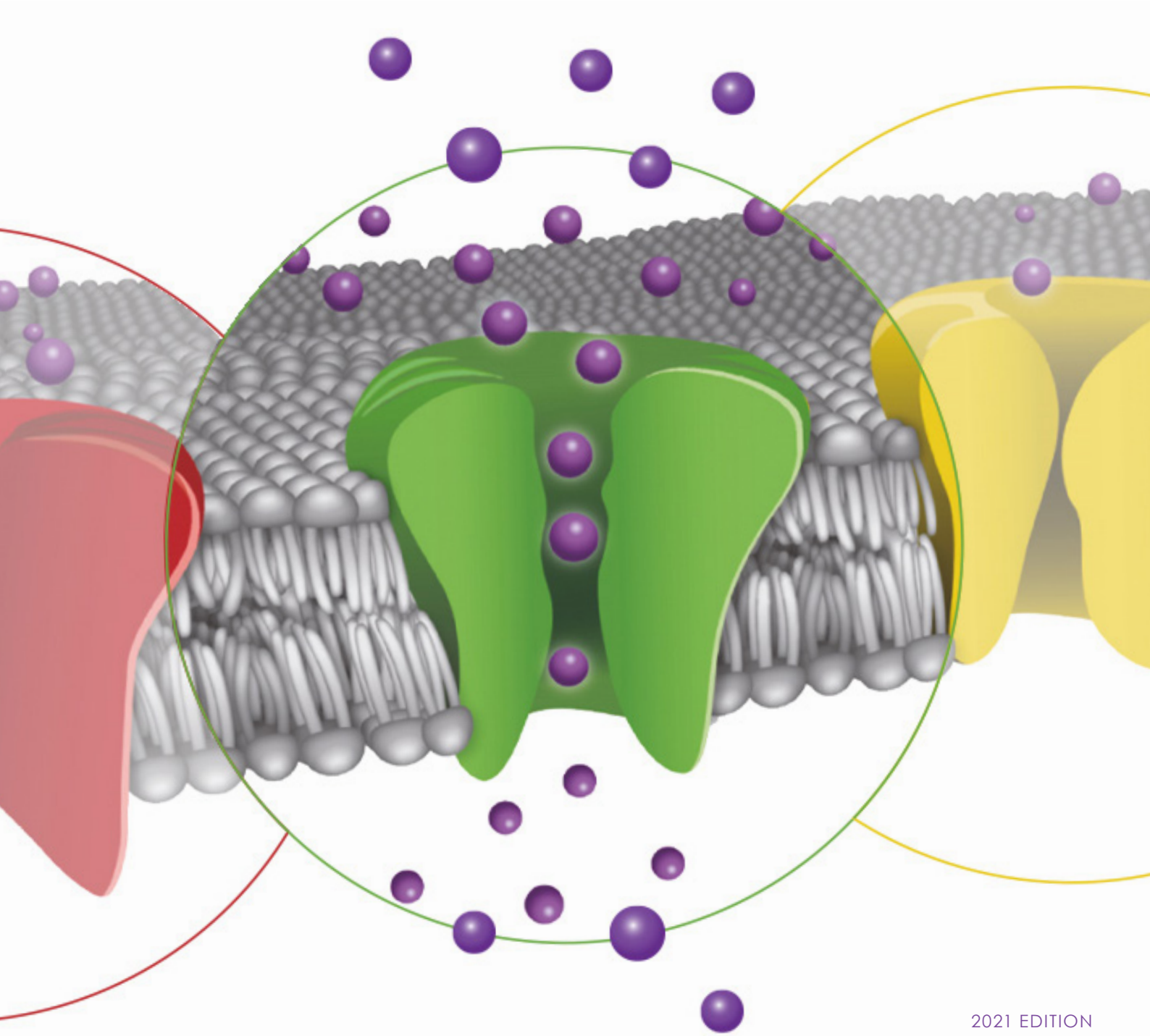
metrion biosciences

METRION BIOSCIENCES

Neuroscience Services Brochure



2021 EDITION

Welcome.

Welcome to Metrion Biosciences, leaders in ion channel drug discovery.

Metrion Biosciences is a preclinical ion channel contract research organisation formed in September 2015.

The Metrion team has substantial experience of providing high quality drug discovery services for ion channel targets to clients on a fee-for-service or collaboration basis.

Metrion is a leading provider of safety pharmacology services including cardiac safety profiling and neurotoxicology testing, as well as offering cardiac and neuronal translational assays using native cells and iPSC models. Our state of the art laboratory facility is located at Granta Park, the largest research park in Cambridge (UK), and the Metrion team takes pride in providing a knowledgeable, collaborative and flexible service to our clients.

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Our Services

Ion channel screening.
Metrion has developed validated screening assays against an extensive panel of ion channel cell lines using a variety of high quality ion channel screening platforms.

Cardiac ion channel screening.
Metrion offers screening services against a premium panel of validated Comprehensive In Vitro Proarrhythmia Assay (CiPA) compliant human cardiac ion channel screening assays.

Neuroscience ion channel screening.
Metrion offers a range of neuroscience related ion channel screening assays and platforms, including native tissue and species selectivity testing.

Translational Assays.
Metrion are developing phenotypic assays to aid the translation of in vitro cardiac safety and neuroscience data to the pre-clinical stage.

Integrated drug discovery.
Our highly experienced interdisciplinary team provides clients with a fully integrated drug discovery service by bringing together experts in ion channel biology, medicinal chemistry, specialist chemistry, translational biology, ADMET & DMPK.

What we do

Metrion staff offer proven ion channel electrophysiology expertise and reliable assays for our clients. Our services include:

- High quality, cost-effective compound screening assays
- Detailed characterisation of lead compounds in human cells and native tissue
- Confirmation of efficacy in stem cell and other phenotypic models
- Rapid reporting and data interpretation by our experienced ion channel team
- A dedicated, flexible service tailored to your requirements

Who we work with

From our Granta Park base in Cambridge, UK, we work with scientists and researchers from biotech and pharmaceutical companies, research institutions, disease charities and start-up companies worldwide to enable them to study this fascinating class of membrane proteins with confidence and insight.

We currently work with clients located in over 20 countries across five continents, many of whom are looking to validate, develop or de-risk ion channel modulators as they progress towards a nomination for clinical development.

METRION BIOSCIENCES – LEADERS IN ION CHANNEL DRUG DISCOVERY

Why choose Metrion?

- **Highly experienced and diligent team with over 100 years combined knowledge of automated patch clamp (APC) and experience within academia, the pharmaceutical industry, contract research organisations and biotech companies.**
- **High quality data, with knowledgeable interpretation, within the defined timeframe.**
- **Fee for service and collaboration project options available.**
- **Client testimonials available.**
- **Flexible support for assay development, primary target screening, hit confirmation, lead optimisation and SAR, mechanistic and phenotypic studies.**

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Neuroscience Services.

Metrion offers a range of peripheral and central nervous system (CNS) neuronal assays utilising native rodent tissue and human iPSC-derived neurons.

Our neuroscience assays are used for two main drug discovery purposes:

- Neurotoxicity screening
- Confirmation of compound effects in native neuronal systems

Phenotypic assays using native neurons offer an important translational step to confirm that client compounds are effective in native tissues that express a wide range of membrane proteins, scaffolding complexes and intracellular signalling cascades. In this way we can confirm that the desired potency and mechanism-of-action are seen in rodent species that are typically used in preclinical animal models. Similarly, the use of human iPSC-derived neurons can help confirm the efficacy of test compounds prior to testing in rare human tissue and give confidence that lead compound candidates may work in human patients as part of clinical trials.

We offer a range of translational CNS and peripheral neuron assays to support our client's drug discovery efforts including neuronal ion channels assays and translational neuroscience assays.

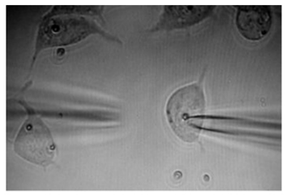
These neuronal assays are not limited to testing ion channel modulators, as they are also suitable for assessing the efficacy of ligands directed against GPCRs, kinases, enzymes, intracellular signalling and homeostatic pathways. Our neuroscience assays are well suited to validating drugs designed to treat pain, epilepsy and a variety of CNS diseases, and we can design custom neuronal assay and cell formats for more specific client needs.

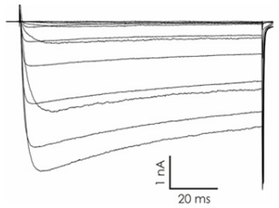
Ion Channel Assays - DRG sensory neuron assays

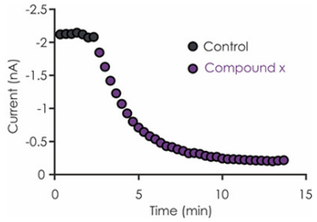
Dorsal root ganglion (DRG) neurons are the most accessible and efficient source of large numbers of peripheral neurons from both rodents and humans.

They are a major target of morphological toxicity deficits and functional manifestation of inflammatory and neuropathic pain.

Peripheral DRG sensory neurons are a workhouse of neuroscience drug discovery and Metrion scientists have proven expertise in creating assays to study voltage- and ligand-gated ion channels using manual patch clamp and multi-electrode array (MEA) biophysical techniques.







Above: a recording of Ca^{2+} currents in single rodent DRG neurons exposed to a test compound. This data is from an 8 year drug discovery collaboration with a global pharma company client that successfully delivered novel chemical matter and an IND candidate.

Neuroblastoma cell lines

Immortalised rodent and human neuroblastoma cell lines provide a useful alternative to native peripheral neurons as they endogenously express many relevant receptors and channels.

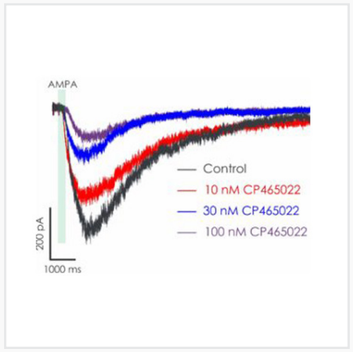
They can be used to address translational challenges by confirming compound efficacy in preclinical species and native human neuronal systems.

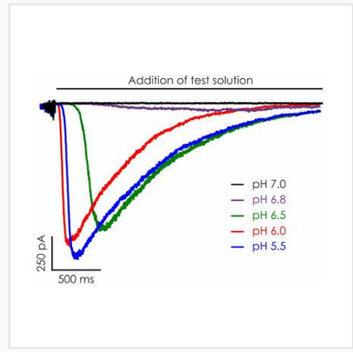
Metrion scientists have extensive experience using neuroblastoma cell lines for electrophysiological study of native and expressed ion channels.

CNS ion channel targets

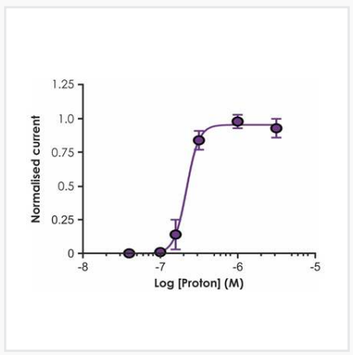
Metrion have to date worked on ligand-gated GluR (such as AMPA **shown below**), nAChR, P2XR and GABA-A receptors, voltage gated Na^+, K^+ and Ca^{2+} channels and two-pore domain (K2P) ion channels. In many cases, work is conducted using heterologous cell lines on manual or automated patch clamp platforms. Metrion also offer manual patch and MEA recordings from native rodent CNS neurons.

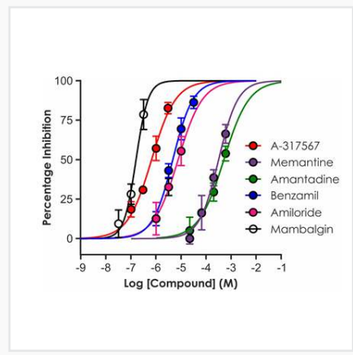
In this example, we show human GluR receptor currents recorded by manual patch (**A, shown below**) and on the automated Qpatch platform from Sophion (**B, shown below**). These assays can establish EC50 and IC_{50} concentrations of agonists and antagonists and investigate the action of negative and positive allosteric modulators.





Metrion's recent application note (ASIC1a-ligand-gated-ion-channel-assay-v1.3, available from the website) illustrates another example of an CNS ion channel assay, describing the optimisation and pharmacological validation of a QPatch automated patch clamp assay for the ASIC1a ligand-gated receptor which is implicated in stroke and ischemia.





Please visit the Translational Assays section overleaf for more information about our neuroscience services.

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About us

Launched in 2015

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