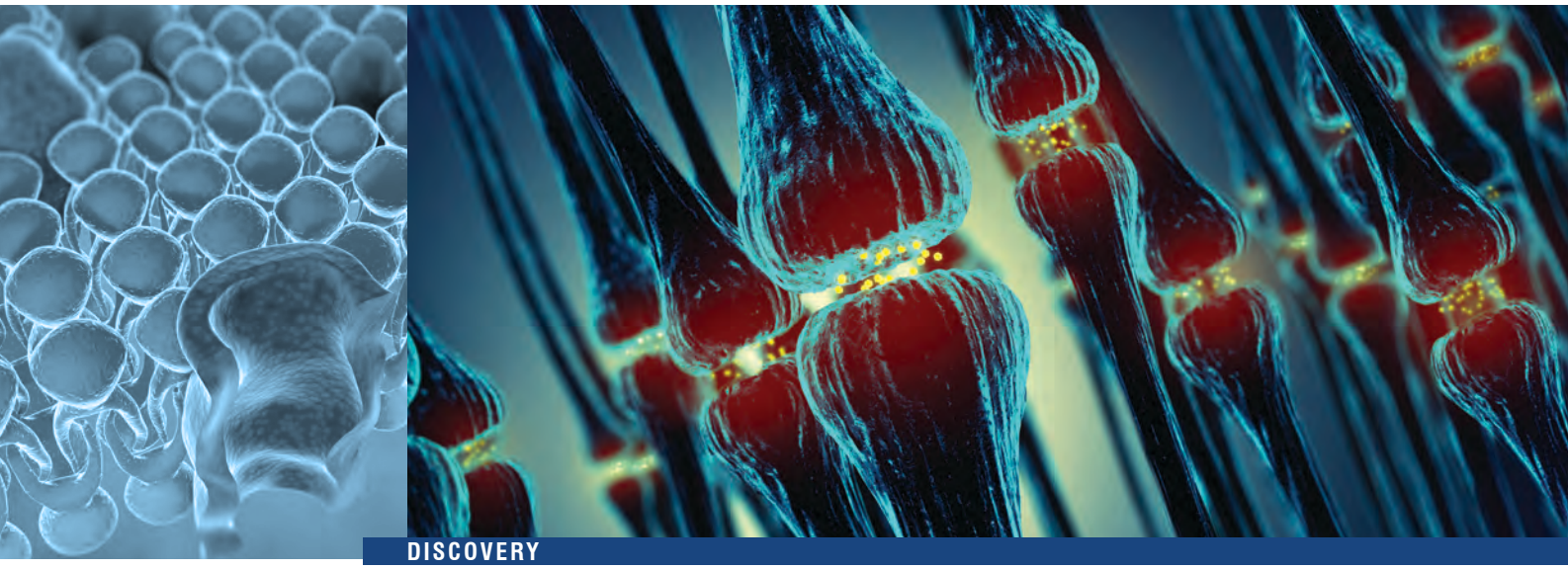
charles river



DISCOVERY

Ion Channel Selectivity Profiling:
Neurodegeneration/Stroke

Ion Channel Families:

- Acid-sensing ion channels (ASIC1a)
- Chloride (CFTR and CLC-2)
- Ligand-gated (NMDA (NR1/NR2A, NRI/NR2B, NR1/NR2C and NR1/NR2D) and nAChR (α_7 and $\alpha_3\beta_4$))
- Potassium, calcium-activated (SK2, SK3 and IK)
- Potassium, inward-rectifier (Kir6.2/SUR1)
- Potassium, voltage-gated (Kv1.1, Kv1.2, Kv1.3, Kv1.5, Kv2.1, Kv3.4 and KCNQ2/3)
- Sodium, voltage-gated (Nav1.1, Nav1.2, Nav1.3 and Nav1.6)
- Transient receptor potential (TRPC4)

The Charles River ion channel portfolio includes over 120 targets which have been organized into Channel Panels® based on current scientific findings, proving a useful tool in guiding early screening and selectivity profiling. Our Neurodegeneration/ Stroke Channel Panel® includes ion channels which have been linked to disorders of the central and peripheral nervous systems.

Selectivity Profiling

Identification of a compound's target specificity and potential for off-target effects is a critical step in the drug discovery process and often includes assessments against specific target class families, critical safety targets or by therapeutic area. In addition to our therapeutic area-specific Channel Panels®, we offer screening on a number of electrophysiology platforms. When required, our scientists can design customized panels to meet a client's needs. As pioneers in the field of ion channels, we are able to provide expert consultation to facilitate interpretation of results.

Ion Channels and Neurodegeneration

Voltage-gated sodium and potassium channels are potential neuroprotective therapeutic targets in ischemic stroke. The metabolism-sparing effects of sodium channel blockade (e.g., Nav1.1, 1.2, 1.3 and 1.6) or potassium channel activation (e.g., KCNQ2/3) may confer neuroprotection. Blockade of acid-induced Ca^{2+} influx via acid-sensing ion channels (ASIC) also may prevent ischemic neuronal damage. Neurodegenerative diseases result in the progressive deterioration of nerve cells. Ion channels in both the central and peripheral nervous systems have been implicated in either the treatment or etiology of neurodegenerative diseases such as multiple sclerosis and Alzheimer's disease. Neurologic symptoms of Alzheimer's disease may be treated by blockade of voltage-gated potassium channels (e.g., Kv3.4) and glutamate receptors (e.g., NMDA), or activation of nicotinic acetylcholine receptors (e.g., nAChRα_7). Ion channels involved in the etiology or treatment of multiple sclerosis include Nav1.6, Kv1.3, and Kv1.5.

EVERY STEP OF THE WAY