charles river

Summary

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.

DISCOVERY

Ion Channel Selectivity Profiling: Pulmonary/Respiratory

Click to learn more

Ion Channel Families:

- Chloride (CFTR)
- Ligand-gated ($GABA_A$ ($\alpha_5\beta_2\gamma_2$))
- Potassium, calcium-activated (BK and IK)
- Potassium, voltage-gated (Kv1.3 and Kv1.5)
- Purinergic receptors (P2X4)
- Sodium, epithelial (ENaC)
- Transient receptor potential (TRPA1, TRPC1, TRPC6, TRPV1 and TRPV4)

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Our Pulmonary/Respiratory Channel Panel® contains several ion channels that regulate airway resistance.

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 Pulmonary/Respiratory Disorders

Increased airway resistance, a symptom of diseases such as asthma and chronic obstructive pulmonary disease (COPD), can be treated by drugs that relax airway smooth muscle (e.g., muscarinic antagonists or adrenergic agonists) by decreasing cytoplasmic Ca^{2+}. TRPV1, which is located in the sensory innervation of the epithelial layer, can be activated by environmental factors (e.g., temperature, pH and irritants) to trigger a local release of neuropeptides that stimulate bronchoconstriction. The respiratory panel also includes airway regulatory channels located in the smooth muscle layer ($GABA_A$ receptors) that conduct chloride current and cause muscle relaxation when activated, and two calcium-dependent potassium channels (BK and IK) that also cause relaxation and bronchodilation when activated.

Increased resistance to flow in the lung blood vessels located in the submucosal layer is a symptom of pulmonary hypertension. The voltage-gated potassium channel (Kv1.5) promotes vasodilation. Transient receptor potential channels (TRPC1 and TRPC6) cause vasoconstriction when activated. These channels are potential therapeutic targets in pulmonary hypertension, and upregulation in chronic hypoxia may contribute to hypoxic pulmonary hypertension.

EVERY STEP OF THE WAY