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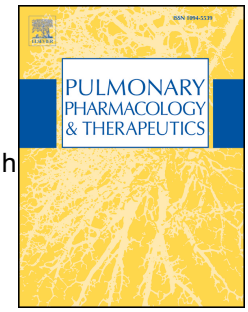

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Blocking Voltage-Gated Sodium Channels as a Strategy to Suppress Pathological Cough

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Abstract

Pathological cough is thought to be secondary to inappropriate activation of vagal sensory nerves. Sensory nerves can be activated by a large number of disparate stimuli. The most relevant stimuli to block for effective anti-tussive therapy likely depend on the specific underlying pathology that is leading to the coughing. Blocking voltage-gated sodium channels (NaV) will prevent action potential initiation and conduction and therefore prevent sensory communication between the airways and brainstem. In so doing, they would be expected to inhibit evoked cough independently of the nature of the stimulus and underlying pathology. There are nine subtypes of NaVs each with distinct pore-forming alpha subunits referred to NaV1.1 – 1.9. Among these channels, based on functional and genetic analysis of cough causing vagal afferent nerve subtypes, we hypothesize that targeting NaV1.7 and NaV1.8 is a rational strategy forward for the effective treatment of pathological cough.

Introduction

In simple terms there are three general types of cough, 1. subconscious reflex involuntary cough; 2. provoked conscious cough; 3. non-provoked voluntary cough. The first two types of cough depend on the activation of peripheral sensory nerves. The vast