THE PROSPECT FOR SODIUM VOLTAGE-GATED CHANNEL INHIBITORS TO RELIEVE THE PATHOLOGICAL COUGH

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Pathological excessive cough is a serious clinical problem in many patients. It is no doubt that an increased activation of airway vagal nociceptors in disease conditions results from dysregulation of the neural pathway that control cough. Because current antitussives have limited efficacy and unwanted side effects there is a continual demand for a development of a novel more effective antitussive. Because voltage-gated sodium channels (NaVs) are absolutely required for action potentials initiation and conduction irrespective of the stimulus, NaVs become a promising and an attractive neural target. Current studies establish that NaV1.7 and NaV1.8 subtypes contribute to the action potential initiation in the nerve terminals of C-fibres.

We recently demonstrated that the inhaled NaV1.8 inhibitor A-803467(3mM) blocked capsaicin-induced cough by about 50% that did not alter respiratory rate. NaV1.7 inhibitor PF05089771(100μM) also suppressed capsaicin-induced cough by about 50-60%. A similar inhibitory response about 60-70% was observe in a study where combined mixture aerosol of NaV1.8 inhibitor A-803467(1mM) and NaV1.7 inhibitor PF05089771(10μM) was used.

We can conclude that NaV1.7 and NaV1.8 may present a promising therapeutic target for antitussive therapy.

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