Kv1.3 Ion Channel Blockers as Novel, Oral Therapies for Multiple Sclerosis
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**Background**

Kv1.3: A drug target for the treatment of multiple sclerosis and other autoimmune diseases

Multiple Sclerosis (MS) is an autoimmune disease characterized by axonal demyelination in the central nervous system (CNS) which results in a myriad of debilitating neurological symptoms. The initial stages of MS are associated with episodes of CNS inflammation followed by periods of remission where recovery due to remyelination is often partial or complete. Eventually, the disease enters a secondary progressive phase associated with permanent loss. The majority of the MS drug market is dominated by the B-cell treatments (Azathioprine, Cyclophosphamide) which show the onset of clinically defined MS and reduce the severity and rate of disability. All treatments are currently administered either by injection or infusion. A non-invasive opportunity exists therefore for a orally administered drug with fewer side effects.

Blockade of Kv1.3, a voltage gated potassium channel, is a potential anti-inflammatory target for MS and other autoimmune diseases (1). It is expressed in a wide variety of immune cells such as T cells, NK cells, monocytes, macrophages and antigen-presenting cells, and has been shown to be present in human brain extracts (2). However, it is the expression in Th17 cells, a T cell subset involved in damage to the CNS, that is of most interest. 

**Methods**

1. BNC245 is a novel potent blocker of the Kv1.3 ion channel that inhibits the proliferation of encephalitogenic T cells and displays good oral efficacy in animal inflammatory disease models with no side effects.

2. The effectiveness of BNC245 in EAE demonstrates the potential of Kv1.3 blockers for further development as an oral MS treatment.

3. An ongoing medchem program has recently produced more metabolically stable analogs that display greater potency for Kv1.3 and selectivity over other Kv channels.

**Conclusions**

BNC245 is a novel drug target for the treatment of multiple sclerosis and other autoimmune diseases. It shows promise as an orally administered drug with fewer side effects and holds the potential to be developed into an effective treatment for MS.

**References**