CHAPMAN UNIVERSITY | Office of Research

SK Channel Positive Allosteric Modulators

Chapman Case #2021-003

Market Need

Spinocerebellar Ataxia (SCA) is a rare genetic disorder marked by a progressive loss of balance, coordination, and communication skills. Although it is a rare disease, the SCA market was valued at $30.28 million in 2017 and was projected to grow, showing increasing demand for effective treatments. Despite ongoing efforts from pharmaceutical and biotech companies, the available treatment options for SCA are limited. Symptomatic therapies such as neuro-protective agents, nicotine receptor agonists, serotonergic therapy, and GABAergic therapy, have demonstrated modest success in managing symptoms, leaving a substantial unmet need for more effective treatments.

Chapman Solution

Dr. Miao Zhang and Dr. Keykavous Parang of Chapman University, along with researchers at University of Texas Southwestern and Northeastern University, synthesized a new class of SK channel positive allosteric modulators that leveraged modified CyPPA analogue to potentiate $K_{Ca}2.2a$ channels. The proposed modulators, with specific compounds 2o and 2q, have demonstrated to be 10 times more potent than the prototype CyPPA. These compounds exhibited ability to normalize abnormal firing in cerebellar Purkinje cells in a mouse model of SCA Type 2. These modulators are also selective and specific only to the SK2/3 channel subtypes, thus ensuring a targeted approach to addressing the neurological dysfunction associated with SCA.

Applications

- Development of SCA therapeutics
- Precision medicine for $K_{Ca}2.2a$-related disorders
- Structure-aided drug discovery for ion channel modulation
- Research tools for neuroscientists

Key Publication

"Structure-Activity Relationship Study of Subtype-Selective Positive Modulators of KCa2 Channels", Journal of Medicinal Chemistry, December 2021.

Intellectual Property

- US patent application filed

Stage of Development

- In-vivo demonstration of the modulators' ability to normalize abnormal firing in cerebellar Purkinje cells in a mouse model of SCA Type 2
- Available for licensing and further research collaborations

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