Protein kinase inhibitors for Amyotrophic Lateral Sclerosis therapy

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Abstract

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder that causes the progressive loss of motoneurons, and unfortunately, there is no effective treatment to stop the disease. Multiple pathological mechanisms are interconnected in the neuropathology of this disorder, including abnormal aggregation of proteins, neuroinflammation and dysregulation of the ubiquitin proteasome system. Such complex mechanisms, together with the lack of reliable animal models of the disease, have hampered drug discovery in the last decades. Protein kinases, key pharmacological targets in several diseases, have been linked to ALS, as they play a central role in numerous of these pathological mechanisms. Therefore, several inhibitors are currently in their way to achieve a clinical proof of concept in ALS patients. In this review we recapitulate the protein kinase inhibitors currently in development for this disease together with their molecular targets and their involvement in the pathobiology of ALS.

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