11th International Conference on

Parkinsons and Movement Disorders

December 09, 2022 | Webinar

Received date: 25-07-2022 | Accepted date: 29-07-2022 | Published date: 28-12-2022

Inhibition Of Mark4 by Serotonin is an Attractive Therapeutic Approach to Combat Alzheimer's Disease and Neuroinflammation

Anas Shamsi
Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, India

The Mitogen-Activated Protein Kinases (MAPKs) govern various cellular programs and crucial intermediate pathways in signaling. Microtubule Affinity-Regulating Kinase 4 (MARK4) is a part of the kinase family recognized for actively phosphorylating neural Microtubule-Associated Proteins (MAP) like MAP2, MAP4 and most importantly, tau. The Ser/Thr kinase MARK4 overexpression is associated with various life-threatening conditions such as neurodegenerative disorders, diabetic neuropathy, and cancer. Functionally, MARK4 is correlated with many important signaling cascades and transcription factors contributing to neurodegeneration and cancer onset and progression. Serotonin is a key molecule associated with regulating mood, stress, and various behavioral aspects. Low serotonin levels promote the progression of neurological and psychotic disorders, which is also a consequence of tau accumulation. MARK4 being a major contributor to phosphorylating tau, leading to its accumulation, and contributing to tauopathy, is targeted for inhibition by serotonin. The study deals with the inhibition of MARK4 by serotonin using combined computational and experimental studies. The results presented in this paper provide strong evidence for the direct physical binding of serotonin to recombinant MARK4 and subsequent inhibition of its kinase activity. In addition, we have performed molecular docking, followed by 100 ns MD simulations of MARK4 in the presence of serotonin to estimate the stability of the protein-ligand complex. Since MARK4 is a potential drug target and can be exploited for drug design and discovery for cancer and neurodegenerative disorders; therefore, the results presented here are of interest and may be further exploited for Alzheimer's and other neurodegenerative diseases.

Recent Publications

1. Shamsi A, Mohammad T, Anwar S, Alajmi MF, Hussain A, Hassan MI, Ahmad F, Islam A. Probing the interaction of Rivastigmine Tartrate, an important Alzheimer's drug, with serum albumin: Attempting treatment of Alzheimer's disease. Int J Biol Macromol. 2020 Apr 1;148:533-542. doi: 10.1016/j.ijbiomac.2020.01.134. Epub 2020 Jan 16. PMID: 31954794.

2. Anwar S, Shamsi A, Mohammad T, Islam A, Hassan MI. Targeting pyruvate dehydrogenase kinase signaling in the development of effective cancer therapy. Biochim Biophys Acta Rev Cancer. 2021 Aug;1876(1):188568. doi: 10.1016/j.bbcan.2021.188568. Epub 2021 May 21. PMID: 34023419.

3. Anwar S, Shamsi A, Kar RK, Queen A, Islam A, Ahmad F, Hassan MI. Structural and biochemical investigation of MARK4 inhibitory potential of cholic acid: Towards therapeutic implications in neurodegenerative diseases. Int J Biol Macromol. 2020 Oct 15;161:596-604. doi: 10.1016/j.ijbiomac.2020.06.078. Epub 2020 Jun 11. PMID: 32535203.

Biography

Anas Shamsi is working in the field of cancer and neurodegenerative diseases. His current research focuses on therapeutic strategies targeting cancer and neurodegenerative disorders in protein biochemistry and drug discovery. Cancer therapeutics research is primarily focused on identifying novel small molecules that can serve as potential leads in drug discovery. The group focuses on finding potent and selective new therapeutic agents through the generation, integration, and translation of scientific knowledge. To date, he has more than 75 publications in internationally reputed journals and serves as an editor in many reputed journals.

e: mshamsi1@jmi.ac.in