Promising Targets and Strategies to Control Neuroinflammation (Part I)

Neuroinflammation is a condition in which inflammation occurs in the central nervous system (CNS: brain and spinal cord), leading to the activation of microglia and astrocytes. Its role in several central pathologies is nowadays well-known, including neurodegenerative diseases like Alzheimer's disease (AD), Parkinson's disease (PD), multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS) [1]. In fact, neuroinflammation has the role of restoring homeostasis in the CNS when an injury occurs. On the contrary, sustained inflammation is detrimental, and this typically occurs in and characterizes neurodegenerative diseases. The formation of protein aggregates distinctive to neurodegenerative diseases is one of the stimuli that exacerbate neuroinflammation [2]. Thus, searching for targets involved in the control of the neuroinflammatory condition in these still incurable diseases continuously attracts the scientific community's attention. In particular, several enzymes and receptors have been investigated for their role in neuroinflammation and neurodegeneration. In this thematic issue, promising targets and their ligands are discussed with strategies to develop entities able to control neuroinflammation.

In particular, in this first part of the thematic issue, the discussed targets by eminent research groups are protein kinases. The first contribution, "Glycogen Synthase Kinase 3β Involvement in Neuroinflammation and Neurodegenerative Diseases" by Gianferrara *et al.*, describes GSK3β structure and its involvement in both neuroinflammation and neurodegeneration as well as GSK3β inhibitors with a special focus on that used in preclinical or clinical studies [3].

The second contribution, titled "Casein Kinase 1δ Inhibitors as Promising Therapeutic Agents for Neurodegenerative Disorders," by Catarzi *et al.,* highlights the development of CK1δ inhibitors, on their structure-activity relationships comprising computational studies which provide useful insight for the design of novel inhibitors [4].

The third contribution, titled "Role of Fyn Kinase Inhibitors in Switching Neuroinflammatory Pathways" by Marotta *et al.*, reviews efforts to develop small molecules that inhibit Fyn, as an opportunity for therapeutic intervention in neurodegeneration [5].

The fourth and last contribution, titled "Computational Strategies to Identify New Drug Candidates against Neuroinflammation" by Pavan *et al.,* aims to provide a general overview of the most common computational strategies that can be exploited to discover and design small molecules controlling neuroinflammation, reporting several case studies [6].

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REFERENCES

[1] Kwon, H.S.; Kho, S-H. Neuroinflammation in neurodegenerative disorders: the roles of microglia and astrocytes. *Transl. Neurodegener.,* **2020***, 9(1)*, 42.
[2] Currais, A.; Fischer, W.; Maher, P. Schubert, D. Intraneuronal protein aggregation as a trigger for inflammation and neurodegeneration in the aging brain. *FASEB J.*, **2017**, 31(*1*), 5–10.
[3] Gianferrara, T.; Cescon, E.; Grieco, I. Spalluto, G. Federico, S. Glycogen synthase kinase 3β Involvement in neuroinflammation and neurodegenerative diseases. *Curr. Med. Chem.,* **2022**, 29(*27*), 4631-4697.
[4] Catarzi, D.; Varano, F.; Vigiani, E. Lambertucci, C.; Spinaci, A.; Volpini, R. Colotta, V. Casein kinase 1δ inhibitors as promising therapeutic agents for neurodegenerative disorders. *Curr. Med. Chem.,* **2022**, 29(*27*), 4698-4737.
[5] Marotta, G. Basagni, F. Rosini, M.; Minarini, A. Role of fyn kinase inhibitors in switching neuroinflammatory pathways. *Curr. Med. Chem.,* **2022**, 29(*27*), 4738-4755.
[6] Pavan, M.; Bassani, D.; Bolcato, G. Bissaro, M. Sturlese, M. Moro, S. Computational strategies to identify new drug candidates against neuroinflammation. *Curr. Med. Chem.,* **2022**, 29(*27*), 4756-4775.

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