OR23-4 Oral session

Adenosine A3 receptor, as a novel therapeutic target to reduce secondary events and improve neurocognitive functions following traumatic brain injury

Salvatore Cuzzocrea[1], Michela Campolo[1], Emanuela Esposito[1], Giovanna Casili[1], Timothy Doyle[2], Daniela Salvemini[2]

[1]*Department of Chemical, Biological, Pharmaceutical and Environmental Sciences, University of Messina, Italy,*
[2]*Department of Pharmacology and Physiology Saint Louis University, MO, USA*

Background: Traumatic brain injury (TBI) is a common pathological condition that presently lacks of a specific pharmacological treatment. Evidence from different models suggests that neuroprotective effects may be mediated by the A3 adenosine receptor (A3AR), a G protein-coupled receptor. Therefore, development of A3AR selective agonists as drug candidates has been a major aim to treat central nervous system (CNS) diseases. The aim of this study was to evaluate the role of A3AR in the pathophysiology of brain trauma and recognize in A3 agonists such as MRS5980, a new therapeutic strategy to reduce secondary events in an in vivo model of TBI in mice.

Methods: We used the well-characterized model of TBI caused by controlled cortical impact. Mice were injected intraperitoneally with MRS5980 (1mg/Kg) at 1h and 4h after trauma.

Results: Our results demonstrated that this specific A3AR agonist exerted significant beneficial effects on TBI pre-clinical scores in term of anti- inflammatory effects in particular on modulation of NF-kB and inflammosome pathways. Moreover this compound was able to decrease T-cell activation visible by reduction of CD4+, to reduce the lesioned area (measured by TTC staining), to preserve tissue architecture and improved neurological function.

Conclusion: Altogether, our results clearly demonstrate the effectiveness of A3AR agonist in a TBI animal model; therefore, the adenosine-to-A3 receptor pathway represents an important endogenous system that can be targeted to ameliorate secondary events in CNS injuries.