

# Toxicology and Clinical Pharmacology

## & Generic Drugs and Biosimilars

December 14-16, 2017 Rome, Italy



### *Manuela Marcoli*

*University of Genova, Italy*

#### **Astrocytes and glutamate in striatum: A2A-D2 receptor-receptor interaction controls glutamate release from striatal astrocytic processes**

In the 1980s, a new model of chemical signal recognition/decoding was proposed, according to which integrative information handling already occurs at membrane level, via receptor-receptor interactions. Specifically, evidence for striatal A2A and D2 receptor-receptor interaction in A2A-D2 heterodimers in striatal neurons, opened new perspectives on the Parkinson's disease pathophysiology, and provided new targets for anti-parkinsonian drugs. Roles for astrocytes, the most numerous cells in the nervous system, and relevance of the neuron-astrocyte network function in disease vulnerability are increasingly recognized. In particular, astrocyte dysfunction at tripartite synapses and altered glutamatergic transmission are emerging in neuropsychiatric disorders including the Parkinson's disease. Despite the change from a neurocentric to an astrocentric view of neuropsychiatric disorders, and major attention to striatal A2A and D2 receptors, striatal glial A2A and D2 receptors have so far received scarce attention. Our findings suggest - combining confocal microscopy and functional neurochemical approaches on purified preparations of astrocyte processes from adult rat striatum and indicate a crucial integrative role of A2A-D2 circuits at the plasma membrane of striatal astrocyte processes in the control of glutamatergic transmission. Indeed, we obtained evidence that: D2 and A2A receptors are expressed in striatal astrocyte processes; D2 receptors inhibit the release of glutamate from astrocyte processes; astrocytic A2A and D2 receptors can form A2A-D2 heterodimers; homocysteine can reduce D2-mediated control of astrocytic glutamate release. It is to note that hyperhomocysteinemia has been hypothesized to play roles in tardive L-dopa side-effects in Parkinson's patients. Notably, expansion of presynaptic astrocyte processes, and altered neuron-astrocyte interactions at striatal glutamatergic synapses, have been found in Parkinson's disease. Thus, reduced D2-mediated control at striatal presynaptic astrocyte processes might result in an increase in synaptic glutamate level and in turn helps understand how astrocytes (and remodeling of astrocyte processes) contribute to the pathophysiology of Parkinson's disease.

#### **Biography**

Manuela Marcoli has completed her MD degree from Pavia University, Italy (PhD. Degree in Clinical Pharmacology from Pavia University, Italy). She is Professor of Pharmacology at the University of Genova, Italy. She has over 85 publications that have been cited over 1300 times, and her publication H-index is 22 and has been serving as a Reviewer of reputed Journals.

marcoli@pharmatox.unige.it

#### **Notes:**