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Neuroinflammation and Microglial Constitutive COX-1 Inhibition

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Neuroinflammation, as the earliest stage of several neurological and neurodegenerative diseases, takes place about 15-20 years before the appearance of specific neurodegenerative clinical symptoms.

Among the known mechanisms involved into the neuroinflammatory complex network, the cyclooxygenase-1 (COX-1) (predominantly localized in microglia) plays a previously unrecognized role in the neuroinflammation as demonstrated by the attenuation of the inflammatory response and neuronal loss due to the genetic ablation or pharmacological inhibition of COX-1 activity.

The lack of drugs to treat diseases involving the central nervous system (CNS) also resides into the shield exerted by the blood brain barrier (BBB) matrix. BBB has a low permeability, and the development of drugs able to penetrate through its network is one of the challenges of all scientists involved in projecting medicines having active principle ingredients targeting the CNS diseases. A commonly used strategy to overcome this drawback consists to incorporate into the pharmacological active molecule a sugar moiety (i.e. glucose or galactose), in turn capable to “carry” the entire molecule into the CNS by the GLUT-1 carrier, which is located on the membrane of the endothelial cells.

In this context, a set of novel compounds endowed with inhibitory activity with cyclooxygenase-1 and GLUT-1 substrate will be presented. Specifically, their design rationale and biological activity will particularly detailed. The work here presented is financially supported by First AIRC Grant-MFAG2015 (Project Id. 17566) “COX inhibitors in conjunction with chemotherapy to target multiple myeloma active disease”.

Biography:

Dr. Maria Grazia Perrone is a researcher of the department of pharmacy – Pharmaceutical Sciences of Bari University, Italy. After a stage at the University of Biochemical Engineering (Stuttgart-Germany), her scientific interests have been devoting to clarify the Cyclooxygenases role in inflammation as the earliest step of both neurodegenerative disorders and oncology. Author of approximately 50 scientific publications on international journals and Principal Investigator of scientific projects, among which the grant supporting my current studies [First AIRC Grant-MFAG2015 (Project Id. 17566)].