Neopterin (Neo) is a pteridine metabolite considered a sensitive biomarker of immune system activation which is found at increased levels in cerebrospinal fluid of patients with neurodegenerative diseases; however, the specific role of Neo in the central nervous system is unknown. Inflammatory processes are linked to inflammasome activation, a macromolecular protein complex present in the cytoplasm responsible for the activation of the pro-inflammatory cytokines IL-1β and IL-18, via caspase-1 activation. Taking into consideration that inflammasome activation can be triggered by excessive ROS production and that Neo significantly increases the resistance to oxidative stress in mouse brain, we investigated if neopterin could affect inflammasome activation in vitro. Initially, we investigated the optimal concentration of lipopolysaccharide (LPS) to induce inflammasome activation by exposing rat astroglialoma cell line (C6) to LPS 1 and 5μg/ml for 24 hours. Then, we co-exposed human primary astrocytes to Neo (0-500 nM) and LPS for 24h or 48h, after an additional pre-treatment of Neo for 24 h (0-500 nM). After 24 hours of LPS stimulation, cell RNA was purified to quantify IL-1β and caspase-1 RNA expression by qPCR. Additionally, cell supernatant was collected in order to quantify IL-1β secretion by ELISA, and the cell lysate was used to determine caspase-1 and ASC protein content, after 48h of LPS stimulation. Figure 1 shows that only LPS 5μg/ml induced active caspase-1 release in the supernatant. Figure 2 shows that the pretreatment with neopterin 50nM inhibited both IL-1β gene expression and secretion in human primary astrocytes. In addition, neopterin attenuated caspase-1 gene expression induced by LPS and significantly reduced caspase-1 and ASC content to approximately half of the control group (Figure 3). Therefore, it could be concluded that besides being an inflammatory biomarker, neopterin release during inflammatory events may be a protective response which attenuates neuroinflammation.

Keywords: astrocytes; inflammasome; neopterin.