Role of SYK in Microglial NLRP3 Inflammasome Activation by Immune Complexes composed of Virus-like Particles and Their Specific Antibodies

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The inflammasome is a vital component of innate immunity. The best-described inflammasome is NLRP3, which responds to a variety of stimuli. NLRP3 inflammasome activation results in release of inflammatory cytokines, like IL-1β, and inflammatory cell death – pyroptosis. In the context of NLRP3 inflammasome activation, the involvement of non-receptor tyrosine kinase – spleen tyrosine kinase (SYK) has been shown. SYK plays a critical role in signal transduction pathways of immunoreceptors and participates in regulation of NLRP3 inflammasome activation. In our previous research, we showed that viral proteins triggered NLRP3 inflammasome activation depending on their structure. Therefore, the aim of this study was to determine whether immune complexes (IC) of oligomeric proteins could modulate NLRP3 inflammasome activation in macrophages.

Primary murine microglia cell culture was selected as a cell culture model. Cells were treated with spherical virus-like particles (VLPs) of WU human polyomavirus and their IC with different subtypes of murine IgG. NLRP3 inflammasome activation was studied by evaluating cell viability, IL-1β and TNF-α cytokine release and the formation of ASC specks. Specific inhibitor R406 was used to inhibit SYK activity and define its role in inflammasome activation. Western blot was performed to determine SYK activation.

It was found that VLPs and their IC induced cell death, IL-1β secretion and ASC speck formation in microglia indicating NLRP3 inflammasome activation. IC mediated a higher cellular response compared to VLPs alone. IC also activated SYK. In conclusion, our study demonstrates that IC can enhance inflammatory response via SYK-dependent pathway in microglia.

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