Neuroimmunology

Targeting key signaling factors as a way to control microglial activation and induction of neuroinflammation

B. Badyra, A. Tejchman, M. Hereta, M. Majka
Department of Transplantation, Medical College Jagiellonian University, Poland

Neuroinflammation is co-occurring phenomenon during pathological processes in the nervous system. Key player in this process is microglia. As moderate activation of microglia is beneficial, excessive one however, leads to more severe degeneration of tissue and inhibition of its endogenous regeneration. One way to prevent this situation is to modulate or inhibit microglia activation. Aim of this study was to use gene silencing technique to influence microglial activation. By targeting key proteins - NF-κB, MyD-88 and TRIF, we intended to decrease inflammatory signaling network. Gene silencing was optimized on stable murine microglia BV-2 cell line. Before stimulation with lipopolysaccharide (LPS), cells were transfected with designed siRNA sequences. Efficacy of transfection was assessed by evaluating expression of NF-κB, MyD-88, TRIF as well as IL-1β, IL-6, TNF-α, TREM1, TREM2 at mRNA and protein level. Optimized sequences of siRNA were then used on primary microglia. Our results showed that siRNA can successfully inhibit activation of microglia *in vitro* after stimulation with LPS. Significant decrease was observed in expression of signaling proteins. However, depending on targeted factor, different decrease patterns were observed for IL-1β, IL-6 and TNF-α. Thus, mixture of siRNA was combined to achieve most successful effect. Our results provide a new method to successfully limit microglia activation with siRNA technique. This approach will be further used in *vivo,* in our models of Parkinson's disease and hypoxia-ischemia encephalopathy, in which severe inflammation is observed. Acknowledgements: The project was supported by the research grant from the Jagiellonian University Medical College: 2015/17/B/NZ5/00294.