Kaempferol Alleviates Corneal Transplantation Rejection by Inhibiting NLRP3 Inflammasome Activation and Macrophage M1 Polarization via Promoting Autophagy

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Abstract

Corneal transplantation rejection remains a major threat to the success rate in high-risk patients. Given the many side effects presented by traditional immunosuppressants, there is an urgency to clarify the mechanism of corneal transplantation rejection and to identify new therapeutic targets. Kaempferol is a natural flavonoid that has been proven in various studies to possess anti-inflammatory, antioxidant, anticancer, and neuroprotective properties. However, the relationship between kaempferol and corneal transplantation remains largely unexplored. To address this, both in vivo and in vitro, we established a model of corneal allograft transplantation in Wistar rats and an LPS-induced inflammatory model in THP-1 derived human macrophages. In the transplantation experiments, we observed an enhancement in the NLRP3 / IL-1 β axis and in M1 macrophage polarization post-operation. In groups to which kaempferol intraperitoneal injections were administered, this response was effectively reduced. However, the effect of kaempferol was reversed after the application of autophagy inhibitors. Similarly, in the inflammatory model, we found that different concentrations of kaempferol can reduce the LPS-induced M1 polarization and NLRP3 inflammasome activation. Moreover, we confirmed that kaempferol induced autophagy and that autophagy inhibitors reversed the effect in macrophages. In conclusion, we found that kaempferol can inhibit the activation of the NLRP3 inflammasomes by inducing autophagy, thus inhibiting macrophage polarization, and ultimately alleviating corneal transplantation rejection. Thus, our study suggests that kaempferol could be used as a potential therapeutic agent in the treatment of allograft rejection.

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