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Exploring the role of hyperforin in modulating the NF-κB/miR-21 axis in sepsis-induced acute kidney injury

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Acute kidney injury, previously called acute renal failure, is a severe and sudden decrease in kidney function [1]. Sepsis is one of the leading causes of acute kidney injury, especially in critically ill patients, as a consequence of inflammatory response and direct nephrotoxic and ischaemic processes [2-4]. The development of acute kidney injury during sepsis significantly increases morbidity and mortality in this group of patients [5]. Despite advances in critical care, effective therapeutic options for sepsis-induced acute kidney injury remain challenging, prompting an ongoing search for novel interventions. The study published in this issue of the Central European Journal of Immunology by Haozhe Fan and collaborators on hyperforin (HYP) offers evidence for its potential role in mitigating inflammation and protecting renal function [6].

Hyperforin, a bioactive compound derived from *Hypericum perforatum* (St. John's Wort), has been previously recognised for its therapeutic potential [7-10]. The study of Haozhe Fan and collaborators extends these findings by exploring the pharmacological effects of HYP on lipopolysaccharide (LPS)-induced inflammation and subsequent acute kidney injury in both *in vitro* and *in vivo* septic models. The researchers administered HYP to LPS-stimulated podocytes and LPS-injected mice, significantly reducing podocyte apoptosis and renal injury.

The study's findings are particularly noteworthy for elucidating the potential mechanism of action of HYP. HYP was observed to inhibit the NF-κB signalling pathway. Specifically, HYP was shown to hinder the LPS-induced transactivation of miR-21 by NF-κB signalling. The excessive activation of the NF-κB/miR-21 axis was found to contribute to the inflammatory cascade, leading to podocyte apoptosis and renal injury. Conversely, HYP reduces podocyte apoptosis and ameliorates LPS-induced renal damage.

This study aligns with previous research published in the *Central European Journal of Immunology* that highlighted the importance of ncRNAs in acute kidney injury, such as the modulation of the lncRNA MALAT1/miR205 axis [11] and the downregulation of lncRNA NEAT1 [12], both of which have been shown to alleviate kidney damage. Mechanisms of regulation and kidney repair in acute kidney injury have been subjects of recent research, especially in critical illness [13].

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