miR-582-5p targets Skp1 and regulates NF-κB signaling-mediated inflammation

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論　文　名　：miR-582-5p targets *Skp1* and regulates NF-κB signaling-mediated inflammation

　　　　　　　（miR-582-5p は *Skp1* を標的とし、NF-κB シグナル伝達を介した炎症を制御する）

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論　文　内　容　の　要　旨

　　A well-tuned inflammatory response is crucial for an effective immune process. Nuclear factor-kappa B (NF-κB) is a key mediator of inflammatory and innate immunity responses, and its dysregulation is closely associated with immune-related diseases. MicroRNAs (miRNAs) are important inflammation modulators. However, miRNA-regulated mechanisms that implicate NF-κB activity are not fully understood. This study aimed to identify a potential miRNA that could modulate the dysregulated NF-κB signaling during inflammation. We identified miR-582-5p that was significantly downregulated in inflamed murine adipose tissues and RAW264.7 cells. S-phase kinase-associated protein 1 (SKP1), a core component of an E3 ubiquitin ligase that regulates the NF-κB pathway, was proposed as a biological target of miR-582-5p by using TargetScan. The binding of miR-582-5p to a 3′-untranslated region site on *Skp1* was confirmed using a dual-luciferase reporter assay; in addition, transfection with a miR-582-5p mimic suppressed SKP1 expression in RAW264.7 cells. Importantly, exogenous miR-582-5p attenuated the production of pro-inflammatory cytokines such as tumor necrosis factor-alpha, interleukin-1 beta, and interleukin-6 through suppressing the degradation of the NF-κB inhibitor alpha, followed by the nuclear translocation of NF-κB. Therefore, exogenously applied miR-582-5p can attenuate the NF-κB signaling pathway *via* targeting *Skp1*; this provides a prospective therapeutic strategy for treating inflammatory and immune diseases.