中文題目：黃酮素誘導微型核糖核酸 155-5p 以保護敗血症所引致之急性腎損傷

英文題目：Scutellaria baicalensis (Oro-A) induce microRNA 155-5p to protect sepsis induced kidney injury

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Background: Oroxylin A (OroA), an active ingredient of the Chinese herb Scutellariae radix (Huang Qin), exerts greater inhibitory effect on the inflammation induced physiology defect but related modulation axis via microRNA is unclear now.

Methods and Results: Firstly, 24 hrs after LPS (200 ng/ml) application significantly increased iNOS, NF-κBp65, NO expression and were reduced rapidly by OroA treatment. In mice model, OroA (15 mg/kg, iv) administered attenuated circulating WBC degradation and expression of iNOS caused significant attenuation of LPS-induced decreased mean arterial pressure (MAP) and increased heart rate (HR), pulmonary edema formation, and thickened interalveolar septa in lung tissues after LPS challenge. To elucidate the relationship between OroA and microRNAs(miRs), firstly, we identified, using a microRNA array screen and qPCR, that miR-155-5p and NO content both were higher in macrophages with LPS treatment than with OroA or in normal controls. In clinical patients with sepsis also indicated the higher level of miR-155-5p in macrophages compared to normal groups. Using TargetScan, we found that the 3' untranslated region (3'UTR) of anti-inflammatory protein, interferon regulatory factor 2-binding protein 2 (IRF2BP2), is complementary to miR-155-5p and miR-155-5p decreased the fluorescent reporter activity by binding to the 3'UTR of IRF2BP2. In addition, IRF2BP2 and NFAT1 which is IRF2BP2 axis downstream both were increased in macrophages of sepsis patient groups. Furthermore, overexpression of shRNA of miR-155-5p in macrophages significantly attenuated iNOS, NO contents via NFAT1- IRF2BP2 axis. Meanwhile, overexpression of shRNA of miR-155-5p expression in the WT mice dramatically reduced the LPS induced MAP, HR and inflammatory effect via IRF2BP2 pathway.

Conclusions: Our results provided new mechanistic insights for an understanding of the role of OroA induced miR-155-5p- IRF2BP2 in sepsis and revealed shRNA-miR-155-5p may instead of OroA serve as a potential agonist for inhibition sepsis injury.