

Inflammatory Cytokine Elaboration Following Long-term Secondhand Smoke Exposure is Mediated in Part by RAGE Signaling

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Background

The receptor for advanced glycation end products (RAGE) is a key contributor to the immune and inflammatory response in a myriad of diseases. Previous studies demonstrate a role for RAGE in inflammation following acute exposure to secondhand smoke (SHS). Chronic inflammatory mechanisms associated with RAGE have yet to be fully elucidated. In this study, we address the impact of long-term SHS exposure on RAGE signaling.

Methods

RAGE knockout (RKO) and wild type (WT) mice were exposed to SHS five times weekly via a nose-only delivery system (Scireq Scientific, Montreal, Canada) for six months. SHS animals were compared to mice exposed to room air only. Immunoblot and colorimetric high throughput FACE assays (Active Motif) were used to assess phospho-AKT and NFκB, respectively. A mouse cytokine antibody array (Abcam) was used to screen secreted cytokines in bronchoalveolar lavage fluid (BALF).

Results

Phospho-AKT was decreased and NFκB was elevated in both groups of SHS exposed mice, with RKO+SHS mice demonstrating tempered outcomes for both intermediates compared to WT+SHS exposed mice. BALF contained increased levels of pro-inflammatory cytokines including IFNγ, IL-13, MIP-1γ and Eotaxin1 in exposed groups and diminished secretion was observed in exposed RKO mice.

Discussion

These results validate a role for RAGE in the mediation of chronic pulmonary inflammatory responses and suggest AKT signaling as a viable pathway of RAGE dependent inflammatory responses. Additional characterization of RAGE-mediated pulmonary responses to prolonged exposure will provide valuable insight into cellular mechanisms of lung diseases such as chronic obstructive pulmonary disease.

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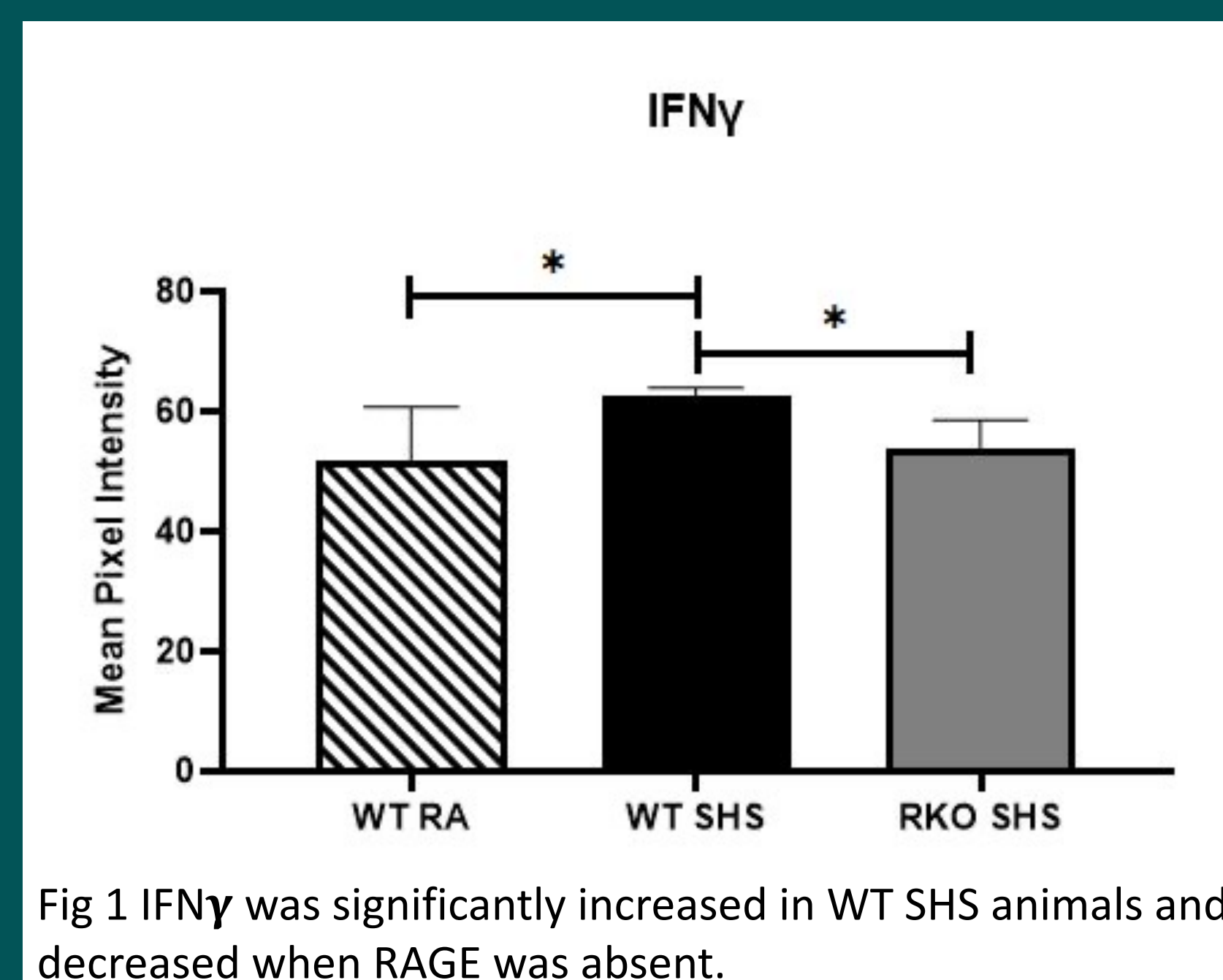


Fig 1 IFN γ was significantly increased in WT SHS animals and decreased when RAGE was absent.

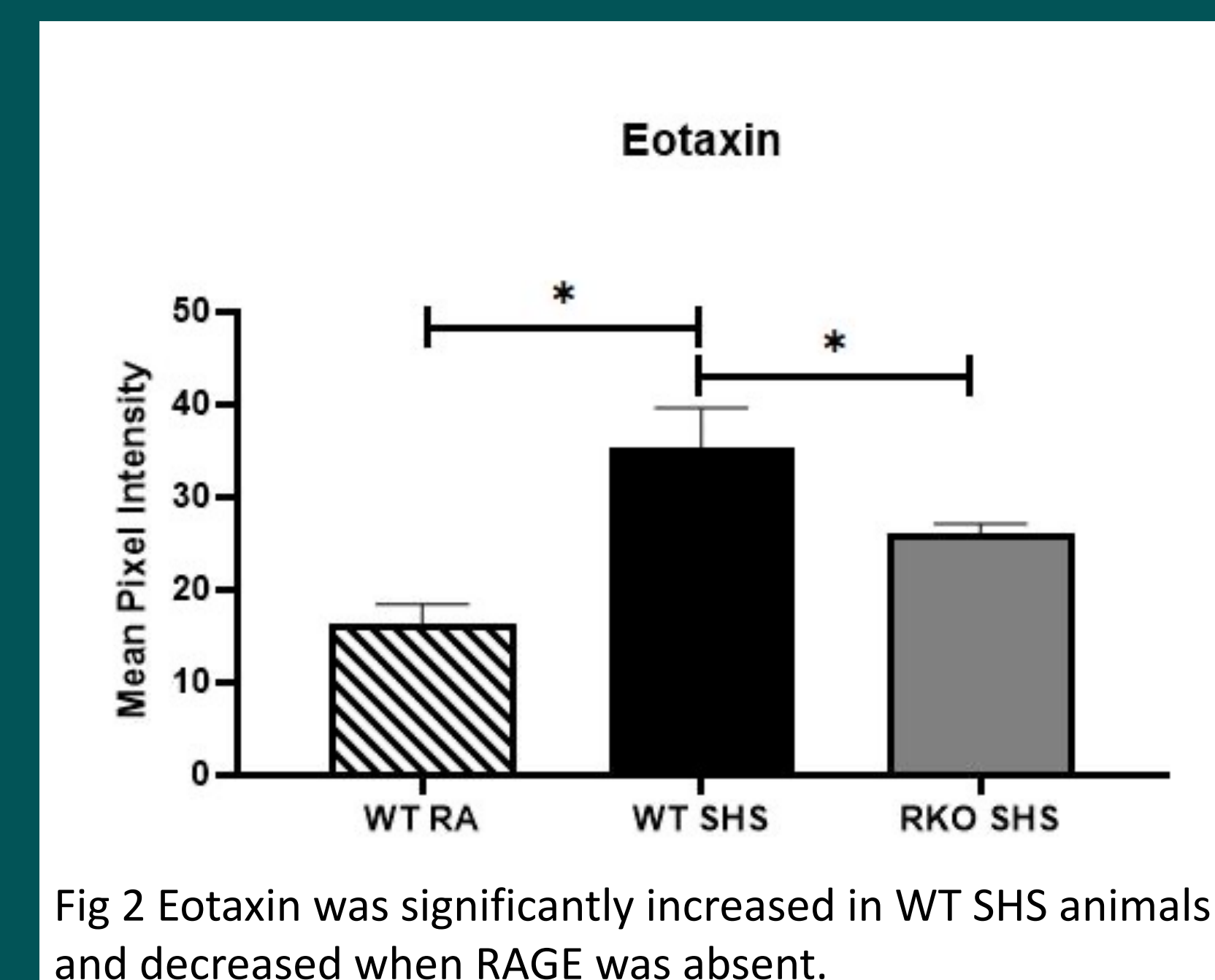


Fig 2 Eotaxin was significantly increased in WT SHS animals and decreased when RAGE was absent.

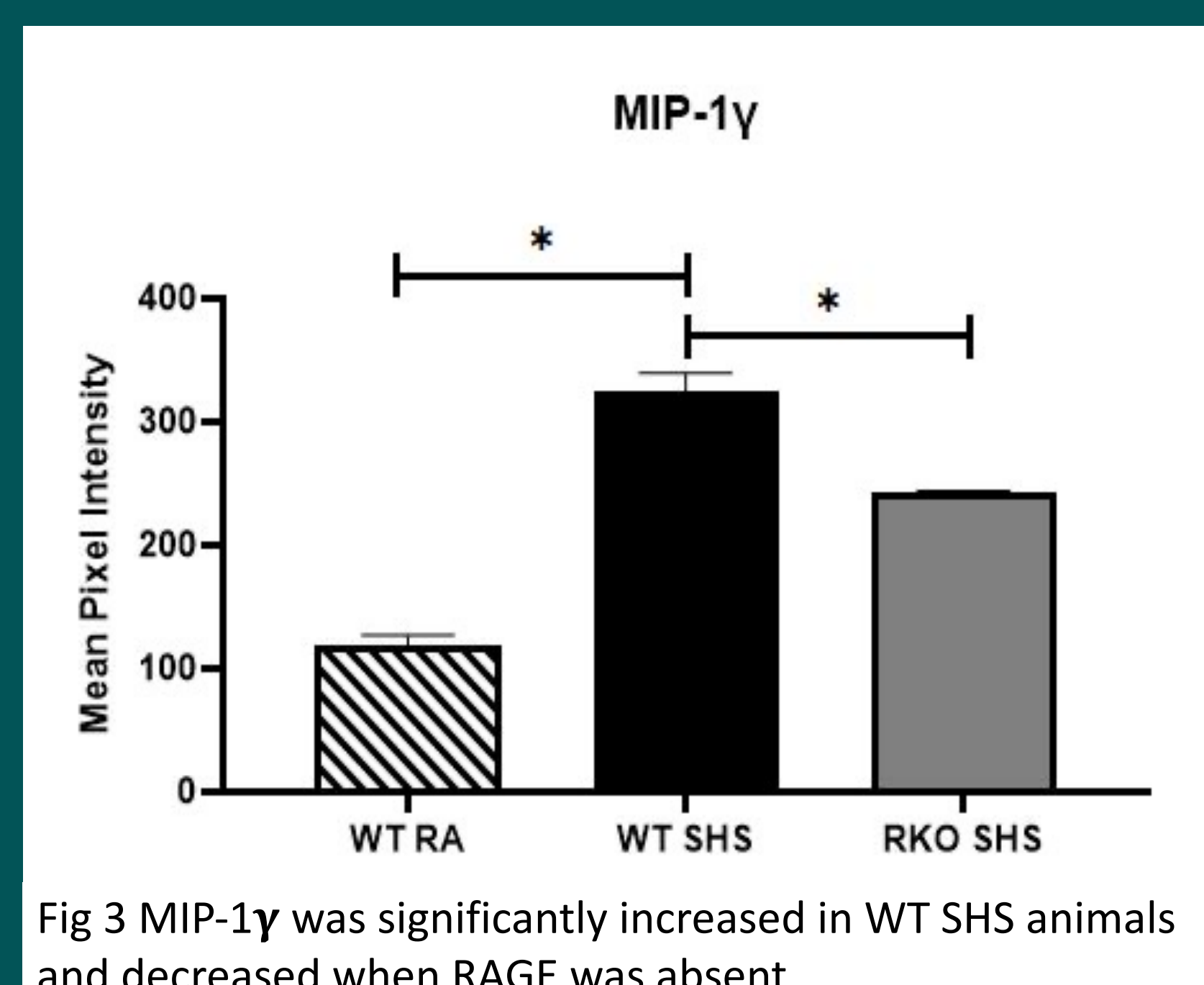


Fig 3 MIP-1 γ was significantly increased in WT SHS animals and decreased when RAGE was absent.

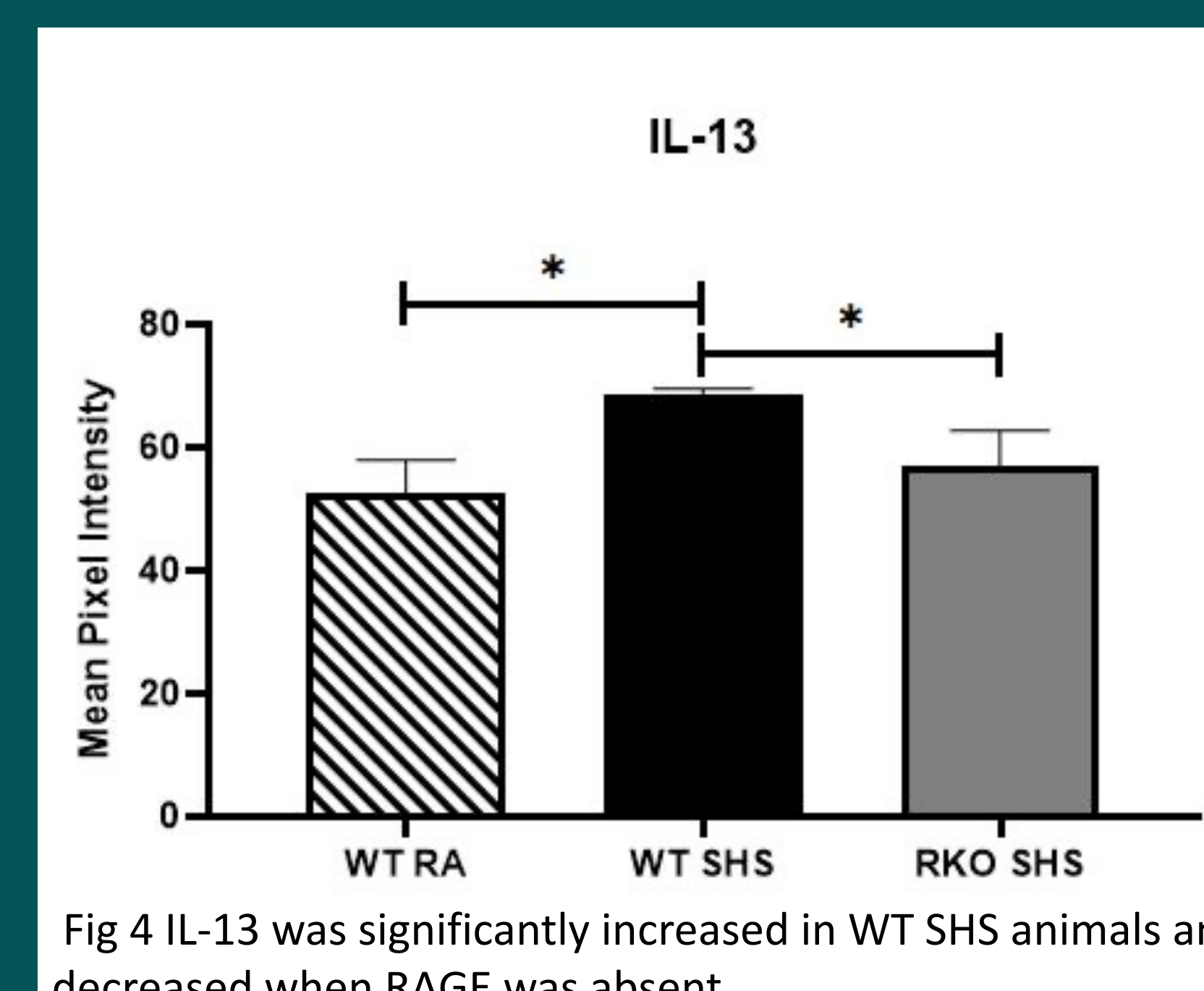


Fig 4 IL-13 was significantly increased in WT SHS animals and decreased when RAGE was absent.

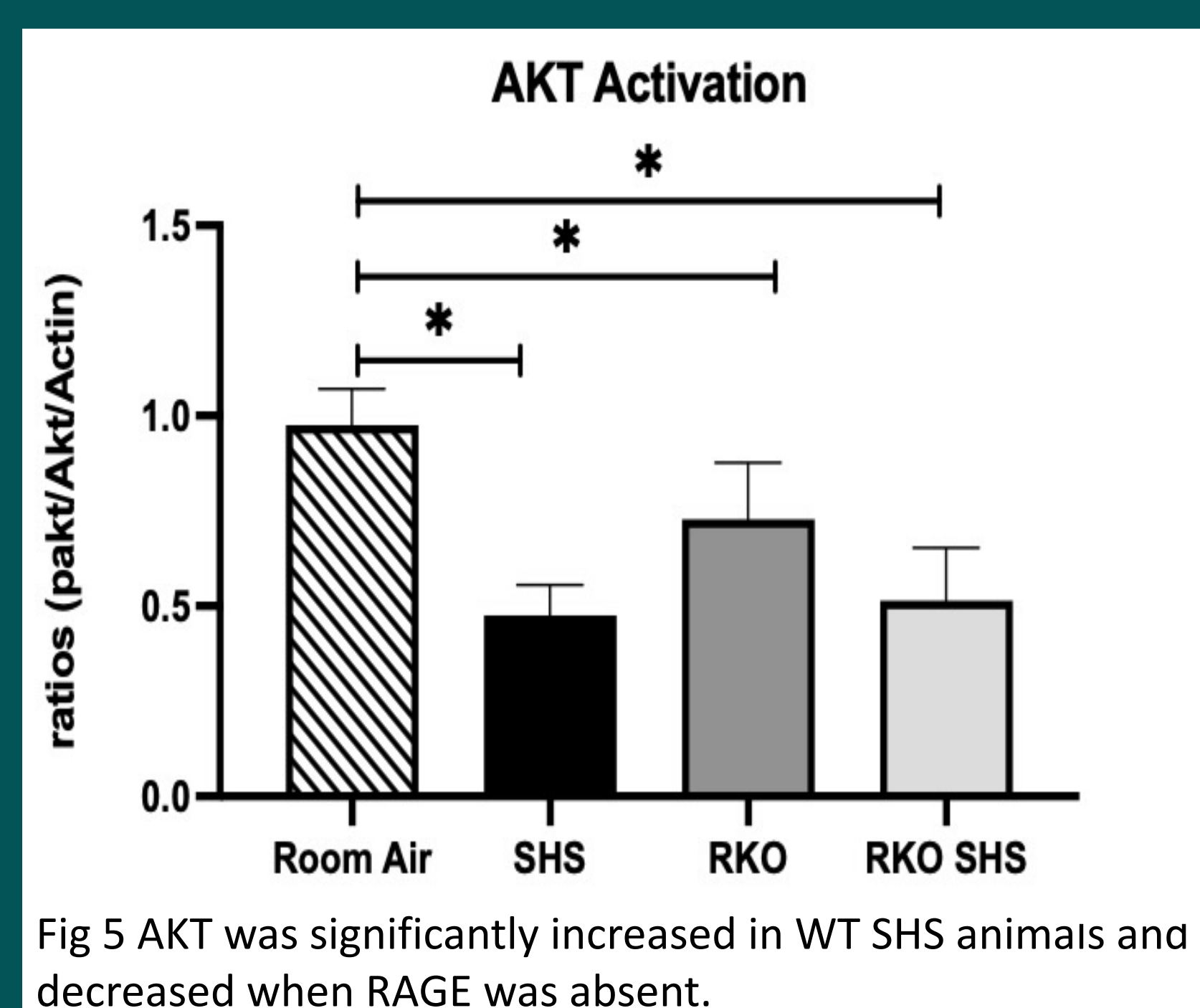


Fig 5 AKT was significantly increased in WT SHS animals and decreased when RAGE was absent.

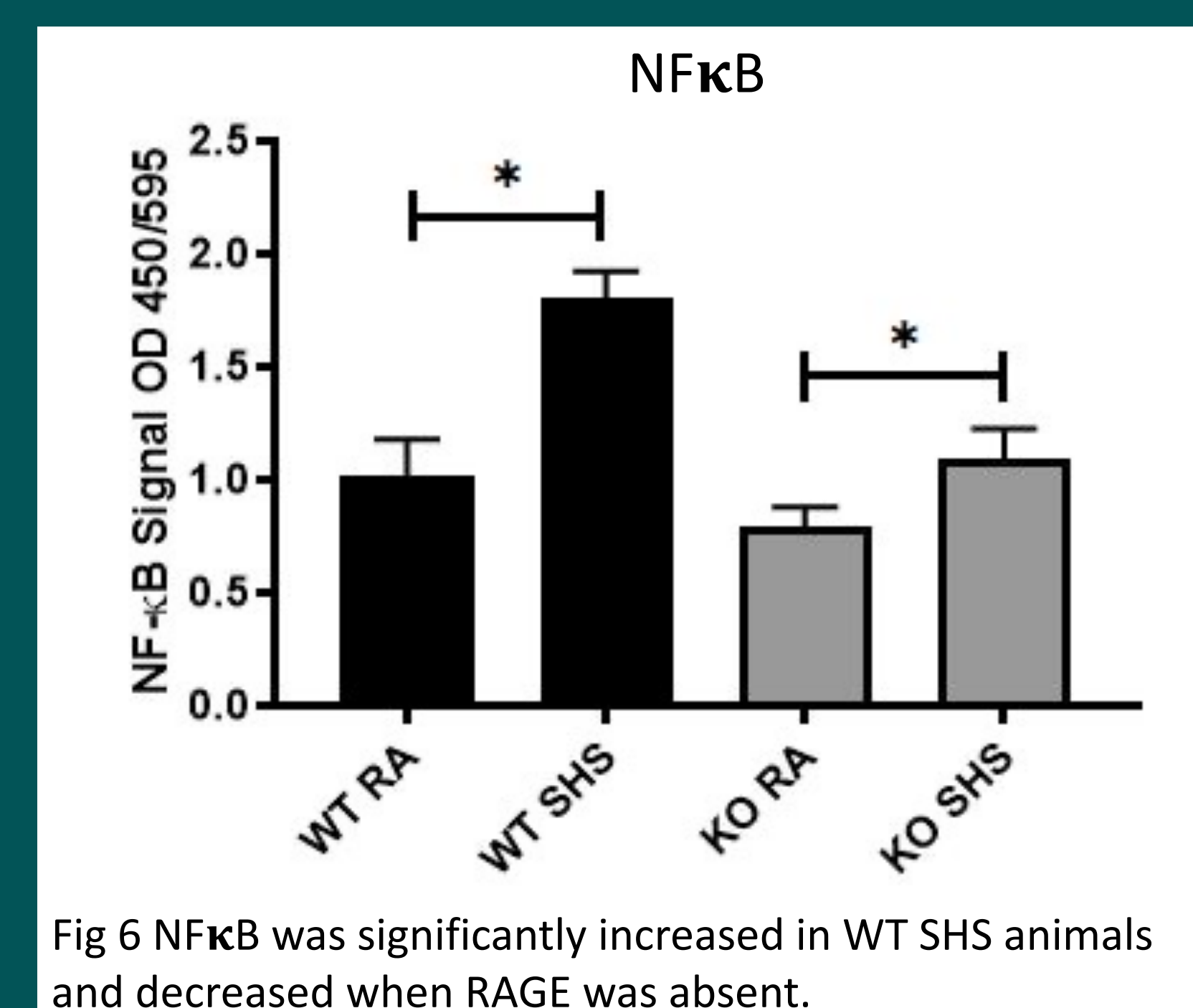


Fig 6 NFκB was significantly increased in WT SHS animals and decreased when RAGE was absent.

