Red ginseng extracts attenuate skin inflammation in atopic dermatitis through p70 ribosomal protein S6 kinase activation

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[Background] Atopic dermatitis (AD) is an important chronic or relapsing inflammatory skin disease characterized by itching. Blood basophils and mast cells mediate chronic allergic inflammation, such as that in AD, that is dependent on the high affinity Immunoglobulin E (IgE) receptor type I (FcεRI). A recent report showed that impaired tight junctional protein expression contributed to barrier dysfunction in AD. Interferon-γ (IFN-γ) was shown to increase cellular permeability through downregulating tight junctional proteins. In specially epidermal keratinocytes and basophils have primary roles in amplification of skin inflammation, IFN-γ is known to be the most potent activator of the proinflammatory functions of keratinocytes. Activation of the mammalian target of rapamycin (mTOR)/p70 ribosomal protein S6 kinase (p70S6K) signaling is known to occur in the inflammatory regions of AD skin. We previously demonstrated that red ginseng extract (RGE), as an anti-inflammatory agent, had potential for treating AD. However, it is still unclear whether RGE inhibits mTOR/p70S6K signaling, Thus, we examined the anti-inflammatory effects of RGE on IgE or IFN-γ activated signaling pathways.

[Methods & Results] To examine whether IgE activated the mTOR/p70S6K signaling pathway in human basophils, KU812 cells were incubated with an anti-FcεRIα antibody for 45 min. In KU812 cells, activation of FCεRI, also known as the high affinity IgE receptor, induced phosphorylation of both mTOR and p70S6K. Moreover, levels of phosphorylated p70S6K (p-p70S6K), but not p-mTOR, were decreased by RGE. We next examined whether IFN-γ activated the mTOR/p70S6K signaling pathway in a human keratinocyte line, NHEK (NB). RGE also decreased p-p70S6K levels in IFN-γ-stimulated human keratinocytes, suppressing the IFN-γ induced increase in levels of C-C chemokine ligand 2 (CCL2) mRNA. These results suggested that RGE suppressed the increase in CCL2 mRNA levels by IFN-γ via inhibition of p70S6K phosphorylation. Similar to IgE-dependent p70S6K activation in basophils, Rg3 and Rh1 strongly suppressed p70S6K phosphorylation in IFN-γ-stimulated human keratinocytes. Furthermore, the increased p70S6K phosphorylation in skin lesions of AD model mice was attenuated by RGE treatment.

[Conclusion] RGE is an inhibitor of the p70S6K signaling pathway and a potential therapeutic agent against inflammatory responses involving activation of p70S6K signaling in AD.