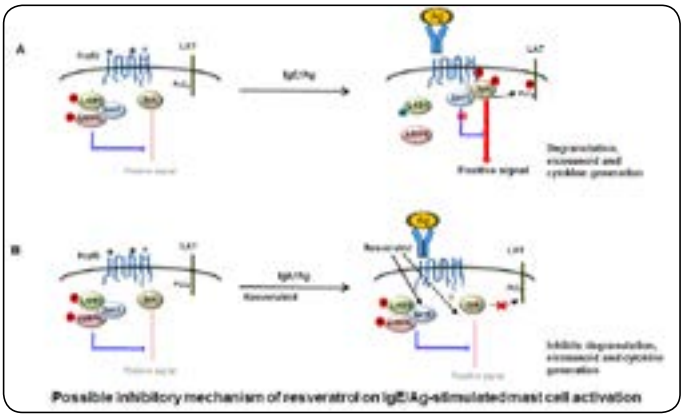
Hyeun Wook Chang et al., J Clinic Toxicol, 2018, Volume 8
DOI: 10.4172/2161-0495-C1-028

Resveratrol inhibits FcεRI-mediated mast cell activation through Sirt1 dependent and -independent pathways

Hyeun Wook Chang, Xian Li and **Young Na Park**
Yeungnam University, Republic of South Korea

Crosslinking of FcεRI-bound IgE with antigen on mast cells trigger release of various chemical mediators such as histamine, eicosanoids and cytokines which cause allergic-inflammation responses. Previous reports showed that Fyn-regulated LKB1/AMPK axis plays an important a role in shutting down FcεRI-dependent mast cell activation and thereby limiting allergic reactions. Resveratrol, a well-known Sirt1 activator showed various beneficial effects on cardiovascular disease, disorder of glucose metabolism but also exhibited antioxidant, anti-inflammatory and anti-allergic properties *in vitro* and *in vivo* models. However, the role of resveratrol in regulating mast cell activation in context of Sirt1-LKB1-AMPK pathway has not been well understood. The anti-allergic effects of resveratrol was evaluated using mouse bone marrow-derived mast cells (BMMCs) from AMPKα2$^{-/-}$ or Sirt1$^{-/-}$ mice, or BMMCs transfected with siRNAs specific for AMPKα2, Sirt1 or protein tyrosine phosphatase 1B (PTP1B). AMPKα2$^{-/-}$ and Sirt1$^{-/-}$ mice were used to confirm the anti-allergic effect of resveratrol in passive cutaneous anaphylaxis (PCA). Resveratrol inhibited FcεRI-mediated degranulation and production of LTC_4, PGD_2, TNF-α, IL-6 and increase of intracellular Ca^{2+} in a dose dependent manner, but these inhibitory activities were diminished by the siRNA knockdowns of AMPKα2 or Sirt1. Moreover, secretion of chemical mediators were partially recovered by gene knockout (or knockdown) of Sirt1 and AMPKα2, which indicated that resveratrol inhibits mast cell activation by Sirt1 dependent and independent pathways. In addition, oral administration of resveratrol dose dependently suppressed anaphylaxis in wild mice, but the enhanced anaphylaxis in gene knockout of Sirt1 or AMPKα2 mice were less sensitive to resveratrol compared with wild type mice. Furthermore, we also found that resveratrol stimulated the inhibitory Sirt1-LKB1-AMPK axis, with reciprocal suppression of the stimulatory PTP1B/Syk axis, thus potently inhibiting anaphylaxis. In conclusion, resveratrol attenuates FcεRI-mediated mast cell signaling through the activation of inhibitory Sirt1-LKB1-AMPK pathway and inhibition of the stimulatory PTP1B/Syk pathway.



Possible inhibitory mechanism of resveratrol on IgE/Ag-stimulated mast cell activation

Recent Publications:

1. Chang H W et al. (2013) AMP-activated protein kinase negatively regulates FcεRI-mediated mast cell signaling and anaphylaxis in mice. J. Allergy Clin. Immunol. 132(3):729-736.
2. Chang H W et al. (2014) ERK1/2 antagonize AMPK-dependent regulation of FcεRI-mediated mast cell activation and anaphylaxis. J. Allergy Clin. Immunol. 134(3):714-721.

3. Chang HW et al. (2016) NecroX-5 suppresses IgE/Ag-stimulated anaphylaxis and mast cell activation by regulating the SHP-1-Syk signaling module. Allergy. 71(2):198-209.

Biography

Hyeun Wook Chang focuses his research on the investigation of underlying mechanisms for allergy and inflammatory reactions in mast cells and development of new therapies for related various allergic diseases. In recent years, he has published his research results in the *Journal of Allergy and Clinical Immunology* which provide a basis for novel approaches to clinical intervention in allergic diseases. He has provided evidences that AMP-activated protein kinase (AMPK), an intracellular energy sensor, might be useful for treatment of not only metabolic syndrome but also allergic diseases.

hwchang@ynu.ac.kr

Notes: