The lysosomal Ragulator complex activates NLRP3 inflammasome in vivo via HDAC6

Keywords: Inflammatory response, NLRP3 inflammasome, gout, lysosome, Ragulator complex

The cellular activation of the NLRP3 inflammasome is spatiotemporally orchestrated by various organelles, but whether lysosomes contribute to this process remains unclear. Hyota Takamatsu, Atsushi Kumanogoh (Graduate School of Medicine, Osaka University/IFReC), and the research group showed the vital role of the lysosomal membrane-tethered Ragulator complex in NLRP3 inflammasome activation. their results provide novel insights into the role of lysosomes in the activation of NLRP3 inflammasome by the Ragulator complex.

Here, the authors show lysosomal Ragulator complex enhances NLRP3 inflammasome activation via histone deacetylase 6 (HDAC6).

 Deficiency of Lamtor1, an essential component of the Ragulator complex, abrogated



NLRP3 inflammasome activation in vitro and in mice.

- Lamtor1 interacted with NLRP3 and HDAC6.
- HDAC6 enhances the interaction between Lamtor1 and NLRP3.
- DL-all-rac-α-tocopherol, a synthetic form of vitamin E, inhibited the Lamtor1– HDAC6 interaction, resulting in diminished NLRP3 inflammasome activation.
- Article

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