Down-regulation of intracellular vesicle trafficking by the treatment of zoledronate in mast cells

Shuang Liu, Sahid Muhammad, Erika Takemasa, Kazutaka Maeyamma, Masaki Mogi

Pharmacology, Ehime University School of Medicine, Japan

Background Zoledronate is widely used in the treatments of osteoporosis and cancer-related bone disorders. Zoledronate also modulates immunity as results of inhibition of the mevalonate pathway. Our study is undertaken to investigate the effects of zoledronate on antigen-dependent activity in mast cells.

Methods Non-treated RBL-2H3 cells and zoledronate-treated mast cells were sensitized using specific anti-DNP-BSA IgE and stimulated by DNP-BSA. Histamine released from mast cells, a hallmark of mast cell activity, was measured. The exocytotic process in mast cells was screened using a high-throughput quantification system and the trajectory of single functional vesicles was monitored. The possible interactive networks of vesicle-associated proteins were elucidated.

Results Zoledronate inhibits the antigen-dependent histamine release from mast cells. The results of high-throughput quantification screening suggest that the exocytotic process were down-regulated in zoledronate-treated mast cells. Zoledronate detains the velocity of vesicle trafficking and blocks membrane fusion of exocytotic vesicle. Finally, zoledronate suppresses the formations of myosin Va/Rab3a complex and syntaxin4/VAMP7 complex in antigen-activated mast cells.

Conclusions Our finding imply that zoledronate down-regulates the antigen-dependent mast cell activity via disturbing the intracellular vesicle trafficking.