

Involvement of histamine in mast cell maturation

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[Introduction] Recent studies have demonstrated the expression of histamine receptors in mast cells, although the function of these receptors remains to be clarified. We previously found the aberrant granules in mast cells of the histidine decarboxylase (HDC)-deficient mice, which raised the possibility that histamine modulates mast cell maturation. We investigated the effects of histamine on mast cell maturation in this study.

[Results] Microarray analyses demonstrated drastic changes in gene expression of peritoneal mast cells in between the wild type and HDC-deficient mice, although there were no differences in morphology and gene expression between them in IL-3-dependent bone marrow-derived cultured mast cells (BMMCs). Impaired granule maturation in the absence of HDC was reproduced in the differentiated mast cells, which were obtained through co-culture of BMMCs with a fibroblastic cell line in the presence of stem cell factor. Granule maturation of the HDC-deficient mast cells was restored by exogenously added histamine. Exogenous histamine was efficiently accumulated in the granules of the HDC-deficient BMMCs, whereas the inhibition of granule uptake of histamine by a specific inhibitor of vesicular monoamine transporter-2, tetrabenazine, did not affect granule maturation of the wild type BMMCs. Restoration of granule maturation by histamine was mimicked by an H₄ agonist, clobenpropit.

[Conclusion] Our results strongly suggest that histamine modulates the granule maturation of mast cells by acting on its specific membrane receptors in an autocrine fashion.