

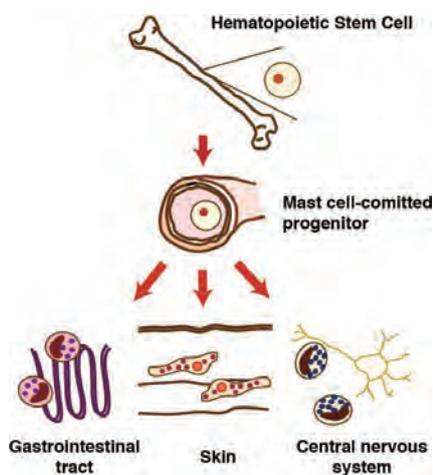
# Establishment of a novel culture model for cutaneous mast cells

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## Background

Mast cells are distributed in almost every vascularized tissue and involved in a wide variety of pathophysiological responses including immediate allergy, contact hypersensitivity, atopic dermatitis and allergic asthma. Since terminal differentiation of mast cells undergo in the tissues, in which they are ultimately resident, there is heterogeneity among tissue mast cells (left panel). Since suitable models of tissue mast cells have not been established, chemical compounds targeting mast cell functions have been evaluated by animal experiments.



## A newly established culture model for cutaneous mast cells

This culture model has been developed by modifying a previously reported model (bone marrow-derived cultured mast cells; BMMCs), which was obtained by prolonged culture of murine bone marrow cells in the presence of interleukin-3 (IL-3). It has been established by co-culture of BMMCs with the murine fibroblastic cell line, Swiss 3T3, in the presence of stem cell factor (SCF). Using the mutant fibroblastic cell line, in which expression of hyaluronan synthase-2 (HAS-2) is genetically suppressed, can further expand the culture scale.

## Advantages of this culture model

The model features characteristics that are not currently found in other models:

1. This model is **highly sensitive to the cationic secretagogues and neuropeptides, such as compound 48/80 and substance P**, resulting in a massive histamine release.
2. This model expresses **significant levels of granule neutral proteases**, such as chymase, tryptase, and carboxypeptidase A.
3. **More than  $\sim 10^8$  cultured mature mast cells** can be obtained by a single experiment using a couple of mice.
4. The process of maturation is **highly reproducible** in this system.

## Application

1. High-throughput screening of therapeutic chemical compounds targeting **cutaneous inflammatory diseases**.
2. High-throughput **screening of toxic chemical compounds that evoke allergy-like reactions** by acting directly on mast cells.

