

1 **Title:** Connective tissue mast cells store and release noradrenaline

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5 **Abstract:**

6 Mast cells are present in mucosal and connective tissues throughout the body. They
7 synthesize and release a wide variety of bioactive molecules, such as histamine, proteases,
8 and cytokines. In this study, we found that a population of connective tissue mast cells
9 (CTMCs) stores and releases noradrenaline, originating from sympathetic nerves.
10 Noradrenaline-storing cells, not neuronal fibers, were predominantly identified in the
11 connective tissues of the skin, mammary gland, gastrointestinal tract, bronchus, thymus,
12 and pancreas in wild-type mice but were absent in mast cell-deficient *W-sash c-kit* mutant
13 *Kit^{W-sh/W-sh}* mice. *In vitro* studies using bone marrow-derived mast cells revealed that
14 extracellular noradrenaline was taken up but not synthesized. Upon ionomycin
15 stimulation, noradrenaline was released. Electron microscopy analyses further suggested
16 that noradrenaline is stored in and released from the secretory granules of mast cells.
17 Finally, we found that noradrenaline-storing CTMCs express organic cation transporter 3
18 (Oct3), which is also known as an extraneuronal monoamine transporter, SLC22A3. Our

- 1 findings indicate that mast cells may play a role in regulating noradrenaline concentration
- 2 by storing and releasing it in somatic tissues.
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