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Review Article

Mast cells as tissue-embedded signal converters in barrier and neuroimmune networks: molecular and genetic perspectives

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Abstract: Mast cells are tissue-resident immune cells that act as versatile sources of signaling rather than solely as passive responders in IgE-mediated allergy. Recent studies have identified distinct mast cell states across epithelial, neural, stromal, metabolic, and vascular niches, with roles in anaphylaxis, host defense, pain modulation, tissue repair, and organ homeostasis. Local immune, neural, stromal, vascular, and metabolic cues, together with cell-intrinsic molecular programs, shape context-dependent mediator release and interactions with neighboring cells. This narrative review synthesizes recent evidence on mast cell heterogeneity in neuroimmune and stromal networks, with particular attention to extracellular granules, vesicular signaling, and molecular mechanisms that link tissue context to mast cell function. We further discuss how emerging single-cell and spatial technologies may help identify pathogenic or protective mast cell states and inform selective therapies that preserve beneficial mast cell functions.

Keywords: Mast cell heterogeneity, signal converters, neuroimmune circuits, stromal-immune crosstalk, tissue-resident immunity

Introduction

Mast cells occupy barrier and perivascular tissues, where they integrate immune and nonimmune cues. Their activation can support host defense, tissue repair and tissue homeostasis, yet dysregulated activation can promote allergy, pain and chronic inflammation [1, 2]. In this review, "tissue-embedded signal converter" describes the ability of mast cells to translate local immune, neural, stromal, vascular and metabolic inputs into context-dependent mediator release and cellular interactions. By integrating evidence across neuroimmune and stromal networks, this review highlights how tissue context, receptor signaling and cell-intrinsic transcriptional programs jointly shape mast cell states. It also identifies the need to connect molecular and genetic determinants of mast cell differentiation and activation with tissue-specific functional outcomes, providing a rationale for selective therapies that preserve protective mast cell functions.

Tissue microenvironments shape mast cell phenotype

Mast cells have traditionally been recognized for their rapid release of histamine and other mediators after IgE-FcεRI engagement. This paradigm remains important, but it does not encompass all aspects of mast cell behavior. Recently, single-cell and tissue-specific studies have shown that mast cells are composed of phenotypically distinct subpopulations with different functions in different developmental stages and tissues [1, 2]. Human mucosal mast cells are a typical case: TGF-β can regulate differentiation into a mucosal tryptase-rich state with altered receptor and protease profiles and lipid mediator secretion [3]. Simultaneously, mucosal mast cells can interact directly with epithelial cells to promote gasdermin-C-mediated type 2 immunity [4]. Therefore, the idea of mast cells as a single line of effector cells has been modified; now, they are regarded as self-contained signal processing units that continu-

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ously change their output according to the local microenvironment.

Studies using primary human mast cells show that distinct cytokine stimuli (IFN-γ, IL-4/IL-13, IL-33, and TGF-β) induce receptor, mediator and transcriptional patterns observed in skin and respiratory disease samples [5]. Local exposure history also shapes these responses. Prolonged IL-33 stimulation shifted activated human mast cells toward a TGF-β1-secreting state, indicating that the duration of local signaling may influence downstream effects [6]. Integrated single-cell and spatial analyses of human colonic biopsies have identified a TMEM176B-positive mast cell subset that is abundant during relapse in both ulcerative colitis and colitis associated with primary sclerosing cholangitis [7]. Together, these findings indicate that regional cues and activation history shape functionally distinct mast cell states, rather than merely altering protease-marker expression.

Reciprocal circuits at the neuroimmune interface

The signal-converter concept is also relevant at neuroimmune junctions. Maternal anxiety may alter fetal mast cell induction and sensory-neuron maturation, creating a persistent cutaneous neuroimmune environment and increasing susceptibility to early-onset eczema [8]. Sensory neurons and mast cells communicate to trigger inflammation, itch and pain after tissue injury [9]. Scratch-induced events, for example, stimulate nociceptors and trigger substance-P-mediated activation of MrgprB2-labelled mast cells, thereby enhancing allergic responses and strengthening the local defense against Staphylococcus aureus [10]. Mast cells can also contribute to postoperative nociception through a metabolic pathway involving tetrahydrobiopterin and serotonin [11]. Interactions at these junctions are not limited to the soluble mediators described above. Exosomes are now known to regulate the coordination of epidermal and immune cells in normal and diseased skin, providing a broader context for exploring mast cell-neuron and mast cell-epithelial signaling [12].

Neuroimmune interactions may prolong symptoms after initial healing. Research on recurrent urinary tract infections has linked sensory nerve sprouting and persistent bladder symptoms to neurotrophic factors released by recruited monocytes and local mast cells, and experimental interventions have validated this pathway in rodents [13]. In contrast, mast-cell-derived proteases accelerated the resolution of inflammatory pain in laboratory systems [14]. Together, these findings suggest that neuroimmune signaling can sustain pain or promote its resolution, depending on the organ, mediator, and stage of the response.

This framework also applies to the meninges. Rodent dural mast cell degranulation affects cerebrospinal fluid flow at arachnoid cuff exit sites and helps prevent microbial invasion during meningitis [15]. MrgprB2-dependent meningeal mast cell activation promoted neutrophil migration from skull marrow across the dura into the brain; pharmacological inhibition reduced inflammation and improved neurological outcomes [16]. Thus, the anatomical location of mast cells at barrier interfaces can have different consequences in infection and sterile injury.

Functional duality in barrier tissues

Studies in barrier tissues indicate that mast cell functions in disease and defense are context dependent. Cysteinyl leukotrienes released by intestinal mast cells are the main mediators of systemic responses to dietary allergens and directly link local lipid signaling with anaphylactic reactions [17]. However, these cells also help organize the microenvironment of the Peyer's patch required for effective mucosal IgA production [18]. They regulate eosinophil homeostasis and are involved in the acute innate immune response to respiratory syncytial virus in the respiratory tract [19]. Therefore, the same cells may cause harmful hypersensitivity in one environment but maintain antimicrobial or mucosal immunity in another. This functional duality has practical implications. Current biomaterial-based methods for allergy increasingly focus on altering allergen dispersion, immunological training and tissue-specific responses instead of merely inhibiting downstream inflammation [20]. Therefore, it is necessary to identify the pathogenic mast cell phenotype specifically before applying broad-spectrum pharmacological inhibition.

Further studies have identified local pathways that regulate these responses. Impaired T-cell regulation, disrupted microbiome dynamics and elevated intestinal IL-4 in DOCK8-null mice were associated with mast cell expansion and exacerbated oral anaphylaxis, and the underlying mechanisms were validated in vivo [21]. Mast cell-derived ST2 regulates IL-33-induced type 2 inflammation in the respiratory tract via prostaglandin E2 [22], and sustained CysLT2-receptor activation inhibits mast cell activity through a cAMP-dependent mechanism [23]. In patients with diarrhea-predominant irritable bowel syndrome, a low-FODMAP diet improved colonic barrier function and altered mast cell activation [24].

Instructive roles of stromal and vascular niches

Stromal and vascular compartments also regulate mast cells through additional mechanisms. A lipid-driven paracrine network among mast cells and fibroblasts regulates mast cell maturation and anaphylactic responses; thus, stromal cells actively shape the identity of mast cells rather than just offering structural support [25]. Conditional ablation studies have also shown that dermal fibroblasts and perivascular cells provide the KIT ligand required for mast cell homeostasis in normal mouse skin [26]. This view is consistent with the general function of PDGFRα-positive stromal populations in maintaining tissue-specific niches and regulating repair, fibrosis, and chronic injury [27]. Metabolic disorders provide a clear example: mast-cell-specific inactivation of SIRT6 promotes adipose fibroinflammation through galectin-3-mediated signaling [28], illustrating how a cell-intrinsic genetic perturbation can couple metabolic context to tissue pathology.

At sites of vascular injury, platelets can activate perivascular mast cells and promote progression to septic shock in mice with sepsis [29]. A feedback loop mediated by IL-33 in platelet-mast cell interactions has been shown in experimental airway inflammation, involving mast cell leukotrienes and platelet-derived nucleotides [30]. The NLRP3 inflammasome has functions beyond conventional cytokine processing [31], and mast cell degranulation requires recruitment of NLRP3, ASC, NEK7 and other factors into a distinct granule-associated structure [32]. Together, these observations place mast cells at the center of integrated stromal, metabolic and vascular networks.

Local inputs are further shaped by cell-intrinsic organization and feedback mechanisms. In rat basophilic leukemia (RBL) cells, a mast cell model, nanoscale imaging showed that membrane microvilli and organized lipid domains coordinate redistribution of FcεRI, Lyn and LAT after stimulation [33]. Increased expression of RGS1 or GEM in cultured primary human mast cells reduced both IgE- and MRGPRX2-driven degranulation, indicating a shared intracellular checkpoint across activating receptors [34]. Therefore, tissue environmental signals and cell-intrinsic molecular programs work together to determine whether a stimulus is converted into mediator release.

Rethinking mast cell secretion

Mast cell extracellular granules can form bioactive condensates of heparin and polyamines that protect and spatially organize pro-inflammatory mediators after release [35].

Granule contents can act as instructive signals for the target cells. Secretome analysis found CSF1 in mouse and human mast cell granules, and functional experiments linked its secretion to macrophage differentiation [36]. Independently, internalization of intact extracellular granules remodeled macrophages toward a mixed functional phenotype in mouse studies and human-cell or skin preparations [37]. Live imaging of peritoneal injury showed an additional mechanism: mast cells stimulated by sensory neurons transferred extracellular aggregates to adjacent macrophages via cytonemes, promoting their clustering and repair functions [38]. Granule release can therefore alter neighboring-cell responses and may support either inflammation or tissue repair, depending on context.

Extracellular vesicles can also carry packaged signals, and they have recently been linked to the regulation of allergic immune responses [39]. Although studies of mesenchymal-cell-derived vesicles do not establish mast cell physiology, they illustrate how tissue-derived vesicles can convey signals between epithelial and immune compartments [40]. Technologies

for high-precision isolation and identification of small extracellular vesicles, such as acoustofluidic platforms, may help separate mast-cell-derived vesicular signals from complex tissue fluids [41]. Together, granule biology and vesicle profiling suggest that mast cell secretion is not a single event but a process of rapid degranulation and spatially and temporally regulated extracellular information transfer.

Direct mast cell evidence now supports the vesicular model. IgE priming without degranulation altered the quantity and composition of released extracellular vesicles. Vesicles containing surface IgE transferred functional sensitization to previously unsensitized mast cells in vitro [42]. This distinguishes the spread of allergic responsiveness from immediate degranulation and provides a framework for studying tissue-specific vesicle signaling.

Therapeutic implications and future directions

These findings support selective pharmacological modulation rather than nonspecific suppression of mast cells. Activation of the glutamate receptor GluK2 reduced dermal mast cell activation and cutaneous inflammation in experimental models [43], and potent MRGPRX2/MrgprB2 antagonists inhibit non-IgE-mediated mast cell reactions in human mast cells and disease models [44]. An orally administered MRGPRX2 inhibitor also reduced inflammation in a human-MRGPRX2 knock-in mouse model of atopic dermatitis [45].

Current clinical research distinguishes mast cell inhibition from mast cell depletion. The two-stage REMIX phase 3 trial showed that the BTK inhibitor remibrutinib reduced symptoms of urticaria in antihistamine-resistant chronic spontaneous urticaria [46]. Anti-KIT barzolvolimab has also been evaluated in a randomized phase 1b trial for prurigo nodularis [47], but a separate study found that eliminating mature mast cells did not eliminate mast cell precursors [48]. These studies illustrate the distinction between inhibiting mast cell signaling and depleting mature mast cells, but they do not yet define which pathogenic mast cell states should be targeted in individual tissues.

Studies in human cancer samples and experimental models indicate that mast cell function is not unidirectional. Within gastric malignancies, CD38-expressing mast cells hindered CD8+ T-cell cytotoxicity via adenosine-mediated pathways [49]. Antigen-presenting mast cells were associated with anti-tumor T-cell activity in triple-negative breast cancer, and a subsequent phase II trial investigated cromolyn in combination with PD-1 inhibition for treatment-resistant cases [50]. Engineering IgE-primed mast cells to deliver oncolytic viruses can enhance tumour killing in vitro [51]. Such studies expand the rationale for adapting therapeutic strategies to different mast cell phenotypes in various tissues.

Future work should link these molecular markers with specific mast cell phenotypes in intact tissues. Single-cell micromanipulation and inflow microscopy could enable functional characterization of individual cells [52], although these approaches have not yet been specifically applied to mast cells. Combining spatial transcriptomics with secretome profiling and perturbation experiments may help determine whether specific mast cell subsets should be inhibited, preserved or reprogrammed. Because multiple immune-cell populations contribute to allergic disease [53], therapeutic strategies should account for the anatomical microenvironment, activating stimuli and functional outcomes.

Conclusion

Mast cell behavior depends on tissue location, exposure history and interactions with nearby cells. Recent mechanistic and clinical studies support this context-dependent view, but much of the causal evidence comes from experimental models. Human spatial studies linked to functional assays are needed to identify which mast cell states should be suppressed, preserved or reprogrammed in specific diseases.

Disclosure of conflict of interest

None.

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References

[1] Pahima HT and Dwyer DF. Update on mast cell biology. J Allergy Clin Immunol 2025; 155: 1115-1123.

[2] St John AL, Rathore APS and Ginhoux F. New perspectives on the origins and heterogeneity of mast cells. Nat Rev Immunol 2023; 23: 55-68.
[3] Derakhshan T, Hollers E, Perniss A, Ryan T, McGill A, Hacker J, Bergmark RW, Bhattacharyya N, Lee SE, Maxfield AZ, Roditi RE, Bankova L, Buchheit KM, Laidlaw TM, Boyce JA and Dwyer DF. Human intraepithelial mast cell differentiation and effector function are directed by TGF-β signaling. J Clin Invest 2025; 135: e174981.
[4] Yang L, He H, Guo XK, Wang J, Wang W, Li D, Liang S, Shao F, Liu W and Hu X. Intraepithelial mast cells drive gasdermin C-mediated type 2 immunity. Immunity 2024; 57: 1056-1070, e5.
[5] Tontini C, Bahri R, Higham A, Singh D, Simpson A and Bulfone-Paus S. Microenvironment-driven mast cell plasticity: insights from cytokine-activated gene signatures in skin and respiratory diseases. Allergy 2025; 80: 3077-3094.
[6] Teufelberger AR, Költgen C, Babina M and Wolf P. Prolonged IL-33 exposure switches the secreted mast cell cytokine profile from pro-inflammatory to pro-tolerant. Allergy 2026; 81: 720-733.
[7] Tearle JL, Sviriaeva E, Zhang F, Jackson KJ, Kaye J, Tavakoli P, Koentgen S, Warren J, Liang RR, Malhotra P, Williams C, Haque A, Arzivian A, Sudhakar KK, Neavin D, Tedla N, Kim A, Haifer C, King HW, Hold GL, Ghaly S and James KR. Primary sclerosing cholangitis displays distinct colonic mucosa topography yet a shared mast cell state with ulcerative colitis. Nat Commun 2026; 17: 10107.
[8] Serhan N, Abdullah NS, Gheziel N, Loste A, Ekren R, Labit E, Gonzalez AA, Oliva G, Tarot P, Petitfils C, Payros G, D'Avino P, Voisin A, Tinsley HFG, Gentek R, Brosseau C, Bodinier M, Reber L, Val P, Akdis CA, Mitamura Y, Andiappan AK, Chan JKY, Ginhoux F, François A, Cénac N, Basso L and Gaudenzio N. Maternal stress triggers early-life eczema through fetal mast cell programming. Nature 2025; 646: 161-170.
[9] Han C, Zhu X and Sokol CL. Neuroimmune circuits in allergic diseases. Annu Rev Immunol 2025; 43: 367-394.
[10] Liu AW, Zhang YR, Chen CS, Edwards TN, Ozyaman S, Ramcke T, McKendrick LM, Weiss ES, Gillis JE, Laughlin CR, Randhawa SK, Phelps CM, Kurihara K, Kang HM, Nguyen SN, Kim J, Sheahan TD, Ross SE, Meisel M, Sumpter TL and Kaplan DH. Scratching promotes allergic inflammation and host defense via neurogenic mast cell activation. Science 2025; 387: eadn9390.
[11] Starkl P, Jonsson G, Artner T, Turnes BL, Gail LM, Oliveira T, Jain A, Serhan N, Stejskal K, Lakovits K, Hladik A, An M, Channon KM, Kim H, Köcher T, Weninger W, Stary G, Knapp S, Klang V, Gaudenzio N, Woolf CJ, Tikoo S, Jain R, Penninger JM and Cronin SJF. Mast cell-derived BH4 and serotonin are critical mediators of postoperative pain. Sci Immunol 2024; 9: eadh0545.
[12] Wang J, Yuan S, Tu Y, Lv Z, Cheng H and Ding X. Extracellular vesicles in skin health, diseases, and aging. Interdisciplinary Medicine 2024; 2: e20240011.
[13] Hayes BW, Choi HW, Rathore APS, Bao C, Shi J, Huh Y, Kim MW, Mencarelli A, Bist P, Ng LG, Shi C, Nho JH, Kim A, Yoon H, Lim D, Hannan JL, Purves JT, Hughes FM Jr, Ji RR and Abraham SN. Recurrent infections drive persistent bladder dysfunction and pain via sensory nerve sprouting and mast cell activity. Sci Immunol 2024; 9: eadi5578.
[14] de Souza S, Laumet S, Hua H, Inyang KE, Sim J, Folger JK, Moeser AJ and Laumet G. Mast cell-derived chymases are essential for the resolution of inflammatory pain in mice. Pain 2025; 166: 1811-1822.
[15] Mamuladze T, Zaninelli TH, Smyth LCD, Wu Y, Abramishvili D, Silva R, Imbiakha B, Verhaege D, Du S, Papadopoulos Z, Gu X, Lee D, Storck S, Perrin RJ, Smirnov I, Dong X, Hu S, Diamond MS, Pinho-Ribeiro FA and Kipnis J. Mast cells regulate the brain-dura interface and CSF dynamics. Cell 2025; 188: 5487-5498, e16.
[16] Kothari R, Abdulrahim MW, Oh HJ, Capuzzi DH, Kilgore CB, Nair SK, Zhang Y, Limjunyawong N, Saini SS, Kim JE, Caplan JM, Gonzalez FL, Jackson CM, Bettegowda C, Huang J, Ganesh BP, Tan C, Koehler RC, Tamargo RJ, McCullough LD, Xu R and Dong X. A mast cell receptor mediates post-stroke brain inflammation via a dural-brain axis. Cell 2025; 188: 5499-5515, e20.
[17] Bachtel ND, Cullen JL, Liu M, Erickson SA, Kutyavin VI, El-Naccache DW, Florsheim EB, Lim J, Sullivan ZA, Imaeda R, Hudak A, Zhang C and Medzhitov R. Intestinal mast cell-derived leukotrienes mediate the anaphylactic response to ingested antigens. Science 2025; 389: eadp0246.
[18] De Giovanni M, Vykunta VS, Biram A, Chen KY, Taglinao H, An J, Sheppard D, Paidassi H and Cyster JG. Mast cells help organize the Peyer's patch niche for induction of IgA responses. Sci Immunol 2024; 9: eadj7363.
[19] Hebbandi Nanjundappa R, Liwski CR, Edgar A, Castonguay M, Haidl ID and Marshall JS. Mast cells support lung eosinophil homeostasis and the acute innate immune response to respiratory syncytial virus. Nat Commun 2026; 17: 6776.
[20] Tian Y, Wu X, Sun X, Rong L and Han K. Engineered strategies for the allergic disease

therapy. Interdisciplinary Medicine 2025; 3: e20240115.
[21] Janssen E, Das M, Butts J, Alasharee M, Mukherjee S, Lozano GL, Rao C, Livingston AF, Woods B, Smith E, Peters Z, Milin E, Beamer MA, Wilkie H, Leyva-Castillo JM, Kam C, Sobh A, Dasouki M, Wakim RH, Dbaibo G, Al-Herz W, Chatila TA, Finkelman FD, Rakoff-Nahoum S and Geha RS. DOCK8 in T cells promotes Th17 and Treg cell functionality to restrain mucosal mast cells and limit susceptibility to oral anaphylaxis. Immunity 2025; 58: 1794-1810, e5.
[22] Alhallak K, Nagai J, Zaleski K, Marshall S, Salloum T, Derakhshan T, Hayashi H, Feng C, Kratchmarov R, Lai J, Kuchibhotla V, Nishida A, Balestrieri B, Laidlaw T, Dwyer DF and Boyce JA. Mast cells control lung type 2 inflammation via prostaglandin E(2)-driven soluble ST2. Immunity 2024; 57: 1274-1288, e6.
[23] Nagai J, Hastings MM, Nishida A, Majumdar S, Zaleski K, Marshall SA, Lin J, Saliman MAS, Tani Y, Murakami Y, Feng C, Perniss A, Wong C, Bankova LG, Inoue A, Barrett NA and Boyce JA. Mast cell-specific CysLT2 receptor signaling inhibits cysteinyl leukotriene-dependent mast cell activation and type 2 allergic lung inflammation. Cell Rep 2026; 45: 116758.
[24] Gao J, Lee AA, Abtahi S, Turner JR, Grover M, Schmidt A, Schmidt TM, Nee JW, Iturrino J, Lembo A, Chey WD, Wiley JW and Singh P. Low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols diet improves colonic barrier function and mast cell activation in patients with diarrhea-predominant irritable bowel syndrome: a mechanistic trial. Gastroenterology 2026; 170: 132-147.
[25] Taketomi Y, Higashi T, Kano K, Miki Y, Mochizuki C, Toyoshima S, Okayama Y, Nishito Y, Nakae S, Tanaka S, Tokuoka SM, Oda Y, Shichino S, Ueha S, Matsushima K, Akahoshi N, Ishii S, Chun J, Aoki J and Murakami M. Lipid-orchestrated paracrine circuit coordinates mast cell maturation and anaphylaxis through functional interaction with fibroblasts. Immunity 2024; 57: 1828-1847, e11.
[26] Martzloff P, Testroet F, Salatino A, Ahmed A, Manke T, Biggs LC, Rognoni E, Bajénoff M, Mihlan M and Lämmermann T. Mast cell homeostasis depends on KIT ligand from dermal fibroblasts and perivascular cells in mouse skin. J Invest Dermatol 2026; 146: 2486-2503, e7.
[27] Kang X, Zhao K, Huang Z, Fukada SI, Qi XW and Miao H. Pdgfrα(+) stromal cells, a key regulator for tissue homeostasis and dysfunction in distinct organs. Genes Dis 2024; 12: 101264.
[28] Song MY, Jeon YG, Do Yang J, Moon YJ, Kim JB, Bae EJ and Park BH. Sirt6 deficiency in mast cells promotes adipose fibroinflammation in obesity through galectin-3 signaling. Nat Commun 2026; 17: 57.
[29] Choi HW, Noh JH, Iskarpatyoti J, Zhu X, Bao C, Abraham M, Hoffmann U, Privratsky JR, Lee RH, Bergmeier W, Tsalik EL, Fiorino C, Yao J, Abraham SN and Karhausen J. Platelet-mediated activation of perivascular mast cells triggers progression of sepsis to septic shock in mice. Nat Commun 2025; 17: 270.
[30] Nishida A, Nagai J, Hastings M, Zaleski K, Sasaki M, Samir O, Lai J, Marshall SA, Hayashi H, Majumdar S, Alhallak K, Feng C, Liu T and Boyce JA. Platelets engage mast cells in a bilateral IL-33-driven feed-forward loop. Proc Natl Acad Sci U S A 2025; 122: e2512193122.
[31] Que X, Zheng S, Song Q, Pei H and Zhang P. Fantastic voyage: the journey of NLRP3 inflammasome activation. Genes Dis 2023; 11: 819-829.
[32] Mencarelli A, Bist P, Choi HW, Khameneh HJ, Mortellaro A and Abraham SN. Anaphylactic degranulation by mast cells requires the mobilization of inflammasome components. Nat Immunol 2024; 25: 693-702.
[33] Ghosh S, Wagenknecht-Wiesner A, Desai S, Vyphuis J, Ramos MS, Grazul JL and Baird BA. Synergy between membrane topography and domains to control signaling protein localization in mast cells facilitates their activation. Proc Natl Acad Sci U S A 2025; 122: e2424427122.
[34] Folkerts J, van Tienen P, de Bruijn MJW, van IJcken WFJ, Hendriks RW, Stadhouders R, Tam SY and Galli SJ. Identification of shared regulators of IgE- and MRGPRX2-dependent degranulation in human mast cells. Allergy 2026; 81: 2979-2983.
[35] Xiong Y, Tomares DT, Guo J, Sato K, Zeng L, Tian Y, Su M, Albis A, Pant A, Pappu RV and Su X. Mast cell extracellular granules are bioactive condensates assembled by heparin and polyamine. Nat Chem Biol 2026; 22: 1120-1131.
[36] Kovacs D, Heger K, Giansanti P, Iuliano C, Meissner F, Mann M, Böttcher J, Öllinger R, Rad R, Tammer F, Gölling V, Zeng T, Masjedi A, Groll T, Roers A, Babina M, Robles MS, Moser M, Kaesler S, Steiger K, Biedermann T and Schmidt-Supprian M. Mast cells modulate macrophage biology through release of prestored CSF1. J Allergy Clin Immunol 2025; 156: 1260-1276.
[37] Katsoulis-Dimitriou K, Schmidt J, Roder M, Dudeck J, Philipsen L, Koch JP, Cattelan M, Schmitter L, Biskou O, Hoffmann A, Mihlan M, Sharma R, Kotrba J, Voss M, Abedi M, Sauerland I, Frischbutter S, Zielinski CE, Geffers R, Lämmermann T, Müller AJ, Kahlfuß S and Dudeck A. Ingestion of mast cell granules boosts macrophages and drives atypical programming. J Allergy Clin Immunol 2025; 156: 774-789.

[38] Salm L, Lopez MA, Jenkins E, Shim R, Tejada O, Abou Mehrem B, Huang S, Etemadi Nezhad P, Derakhshani A, Lee WY, Nusse Y, Mewburn JB, Noskovicova N, Bayer J, Rashid MU, Li X, Baltaci Z, Young D, Carneiro MB, Fritzsche M, Jakubzick CV, Peters NC, Deniset JF, Zindel J, Dufour A, Yipp BG, Ditlev JA, Dustin ML, Canton J and Kubes P. A nerve and mast cell sentinel system releases extracellular condensates to induce macrophage repair. J Exp Med 2026; 223: e20260410.

[39] Wu J, Wang Y, Wang Y, Ribaudo J, Li S, Hu S, Tang M, Chen Y and Long Y. Interplay between extracellular vesicles and allergic diseases: current insights and future perspectives. Interdisciplinary Medicine 2025; 3: e20240049.

[40] Luo H, Birjandi AA, Ren F, Sun T, Sharpe PT, Sun H and An Z. Advances in oral mesenchymal stem cell-derived extracellular vesicles in health and disease. Genes Dis 2023; 11: 346-357.

[41] Liu JF, Xia J, Rich J, Zhao S, Yang K, Lu B, Chen Y, Ye TW and Huang TJ. An acoustofluidic device for sample preparation and detection of small extracellular vesicles. Cyborg Bionic Syst 2025; 6: 0319.

[42] Pfeiffer A, Bandara G, Pardo K, Cooper G, Schwarz B, LaCroix IS, Bohrnsen E, Zektser E, Pham L, Young FD, Sellers BA, Meyer E, Langowski TJ, Li MJ, Chatman L, Laky K, Luker A, Smelkinson MG, Metcalfe DD, Frischmeyer-Guerrerio PA and Olivera A. IgE-sensitized mast cells release extracellular vesicles that transfer IgE and spread allergic sensitization. J Allergy Clin Immunol 2026; [Epub ahead of print].

[43] Zhang YR, Keshari S, Kurihara K, Liu J, McKendrick LM, Chen CS, Yang Y, Falo LD Jr, Das J, Sumpter TL and Kaplan DH. Agonism of the glutamate receptor GluK2 suppresses dermal mast cell activation and cutaneous inflammation. Sci Transl Med 2024; 16: eadq9133.

[44] Al Hamwi G, Alnouri MW, Verdonck S, Leonczak P, Chaki S, Frischbutter S, Kolkhir P, Matthey M, Kopp C, Bednarski M, Riedel YK, Marx D, Clemens S, Namasivayam V, Gattner S, Thimm D, Sylvester K, Wolf K, Kremer AE, De Jonghe S, Wenzel D, Kotańska M, Ali H, Herdewijn P and Müller CE. Subnanomolar MAS-related G protein-coupled receptor-X2/B2 antagonists with efficacy in human mast cells and disease models. Signal Transduct Target Ther 2025; 10: 128.

[45] Wollam J, Solomon M, Villescaz C, Srinivasan S, Charlot B, Vest A, Napora J, Cavarlez C, Vasquez A, Dvorak L and Viswanath V. MRGPRX2 antagonist treatment prevents inflammation and disease in a mouse model of atopic dermatitis. J Invest Dermatol 2026; 146: 2727-2735, e8.

[46] Metz M, Giménez-Arnau A, Hide M, Lebwohl M, Mosnaim G, Saini S, Sussman G, Szalewski R, Haemmerle S, Lheritier K, Martzloff ED, Seko N, Wang P, Zharkov A and Maurer M; REMIX-1 and REMIX-2 Investigators; REMIX-1 Investigators; REMIX-2 Investigators. Remibrutinib in chronic spontaneous urticaria. N Engl J Med 2025; 392: 984-994.

[47] Metz M, Ständer S, Moiin A, Nattkemper L, Bloom B, Alvarado D, Rogalski M, Lu Y, Hawthorne T, Bili A, Meltzer-Podolske M and Yosipovitch G. Safety and efficacy of barzolvolimab, an anti-KIT monoclonal antibody, in adults with moderate-to-severe prurigo nodularis: a randomized phase 1b intravenous single dose study. J Am Acad Dermatol 2025; 93: 1596-1599.

[48] Moñino-Romero S, Mahnke NA, Terhorst-Molawi D, Grekowitz EM, Kiefer LA, Alvarado D, Metz M, Siebenhaar F, Scheffel J and Maurer M. Depletion of mast cells with barzolvolimab, an anti-KIT antibody, does not affect mast cell progenitors. J Eur Acad Dermatol Venereol 2025; 39: e970-e972.

[49] Zhao J, Feng D, Zhang F, Cai S, Xiong Y, Pan G, Ma J, Tan J, Zhong M, Lin Z, Zhuang Y, Wang W, Zhou H, Zhou S, Cheng A, Xu M, Ye W, Chen H, Song Y, Wang Z and Hong X. Activated CD38(+) mast cells promote gastric cancer progression by suppressing CD8(+) T cell cytotoxic activity through adenosine metabolism. Cell Rep 2026; 45: 116863.

[50] Wu SY, Jin X, Liu Y, Wang ZY, Zuo WJ, Ma D, Xiao Y, Fu T, Xiao YL, Chen L, Liu XY, Fan L, Wang ZH, Shen M, Liu R, Chai WJ, Shao ZM and Jiang YZ. Mobilizing antigen-presenting mast cells in anti-PD-1-refractory triple-negative breast cancer: a phase 2 trial. Nat Med 2025; 31: 2405-2415.

[51] Xu Y, Zhang X, Han X, Huang H, Meng C, Yang Y, Sheng T, Ren E, Shi J, He K, Cen D, Zhao P, Fang W, Li H, Zhang Y, Cai X, Liu F, Yu J and Gu Z. Sensitized mast cells for targeted drug delivery and augmented cancer immunotherapy. Cell 2026; 189: 872-886, e23.

[52] Filippi J, Casti P, Lacconi V, Antonelli G, D'Orazio M, Curci G, Ticconi C, Rago R, De Luca M, Pecora A, Mencattini A, Neale SL, Campagnolo L and Martinelli E. ODEP-based robotic system for micromanipulation and in-flow analysis of primary cells. Cyborg Bionic Syst 2025; 6: 0234.

[53] Tiligada E, Gafarov D, Zaimi M, Vitte J and Levi-Schaffer F. Novel immunopharmacological drugs for the treatment of allergic diseases. Annu Rev Pharmacol Toxicol 2024; 64: 481-506.