Human Mast Cells Adhere to Extracellular Matrix Proteins through Their Selective Expression of β 1 Integrins

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Key Words

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Mast cells are usually found in association with vascular structures within tissues, where they interact with the endo-thelium and its surrounding basement membrane. How human mast cells localize at specific perivascular sites is unknown. One hypothesis is that the tissue localization of mast cells is influenced by the composition of the extracellular matrix.

Previous studies have shown that activated mouse bone-marrow-derived mast cells attach to the extracellular matrix proteins laminin and fibronectin [1,2]. They also bind spontaneously to vitronectin [3]. However, whether human mast cells adhere to the extracellular matrix is presently unknown.

Integrins are heterodimers located in the cell membrane where they function both as cell-matrix and cell-cell adhesion receptors [4]. The expression of integrins in human mast cells has been only partially investigated. In particular, human uterine and lung mast cells express receptors for fibronectin (VLA-4 and VLA-5) [5, 6]. However, these studies did not address the function of these molecules.

We have studied the adhesion of skin mast cells to several components of the extracellular matrix (plasma fibronectin, laminin, collagen types I and IV) and evaluated whether these cells express the β 1 integrins potentially involved in the adhesion to these proteins. We found that human skin mast cells ($5.1 \pm 1.5\%$ pure, $n = 6$) spontaneously adhered to fibronectin and laminin ($0.1-10 \mu\text{g/ml}$) immobilized on plastic surfaces (e.g., 14 ± 7.2 and $14 \pm 4.4\%$ adhesion at $10 \mu\text{g/ml}$, respectively). Similar results were obtained with a 90% pure mast cell preparation. In contrast, skin mast cells did not adhere to collagen type I ($1.6 \pm 0.5\%$ adhesion) or type IV ($1.2 \pm 0.8\%$ adhesion). Mast cell adhesion to fibronectin was optimal after an incubation period of 60-90 min ($t_{1/2} = 28.2 \pm 6.2$ min), whereas adhesion to laminin was faster ($t_{1/2} = 9.5 \pm 1.4$ min) and nearly optimal after a 15-min incubation period. Dual-color immunofluorescence and flow cytometry were used to evaluate whether human skin mast cells ($51.3 \pm 3.9\%$ pure, $n = 6$) express β 1 integrins that may mediate cell adhesion to extracellular

matrix proteins. Mast cells were found to express VLA-3 [75.3 ± 35.6 specific fluorescence intensity (SFI)] and, to a lesser degree, VLA-4 and VLA-5 receptors (8.0 ± 2.5 and 6.9 ± 3.2 SFI, respectively). In contrast, VLA-1, VLA-2, and VLA-6 integrins were not expressed. Monoclonal antibodies (mAbs) to VLA-3, VLA-4, and VLA-5 each inhibited skin mast cell adhesion to fibronectin by about 70%. mAbs to VLA-3 nearly abol-

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ished mast cell adhesion to laminin, whereas anti-VLA-4 and anti-VLA-5 were ineffective. Finally, the immunosuppressants cyclosporin A (100 nM) and FK-506 (10 nM) partially inhibited (24-55% inhibition) mast cell adhesion to both fibronectin and laminin. The present studies are the first to show that human mast cells can adhere to extracellular matrix proteins. Our studies also identify some of the cellular structures (β 1 integrins) that mediate this adhesion process. Furthermore, pharmacologic studies suggest possible intracellular pathways involved in this mast cell-substrate adhesion. Interactions between these β 1 integrins and extracellular matrix proteins may be involved in perivascular tissue localization of human mast cells in vivo.

References

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Thompson HL, Burbelo PD, Segui-Real B, Yamada Y, Metcalfe DD: Laminin promotes mast cell attachment. *J Immunol* 1989;143:2323-2327.

Dastyk J, Costa JJ, Thompson HL, Metcalfe DD: Mast cell adhesion to fibronectin. *Immunology* 1991;73:478-484.

Bianchini PJ, Burd PR, Metcalfe DD: IL-3-dependent mast cells attach to plate-bound vitronectin: Demonstration of augmented proliferation in response to signals transduced via cell surface vitronectin receptors. *J Immunol* 1992; 149:3665-3671.

Albelda SM, Buck CA: Integrins and other cell adhesion molecules. *FASEB J* 1990;4:2868-2880.

Guo CB, Kagey-Sobotka A, Lichtenstein LM, Bochner BS: Immunophenotyping and functional analysis of purified human uterine mast cells. *Blood* 1992;79:708-712. Sperr WR, Agis H, Czerwenka K, Klepetko K, Kubista E, Boltz-Nitulescu G, Lechner K, Valent P: Differential expression of cell surface integrins on human mast cells and human basophils. *Ann Hematol* 1992;65:10-16.