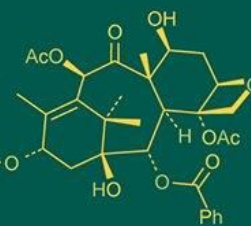
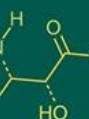
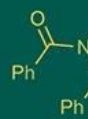


International Journal of Advanced Biochemistry Research



ISSN Print: 2617-4693
 ISSN Online: 2617-4707
 NAAS Rating (2025): 5.29
 IJABR 2025; 9(10): 65-67
www.biochemjournal.com
 Received: 04-08-2025
 Accepted: 06-09-2025

Budi Santoso
 Department of Immunology,
 Jakarta Institute of Applied
 Sciences, Jakarta, Indonesia

Sri Rahayu
 Department of Immunology,
 Jakarta Institute of Applied
 Sciences, Jakarta, Indonesia

Agus Wijaya
 Department of Immunology,
 Jakarta Institute of Applied
 Sciences, Jakarta, Indonesia

Mannose receptor structure, ligand recognition, and receptor-mediated endocytosis mechanisms in macrophages and dendritic cells

Budi Santoso, Sri Rahayu and Agus Wijaya

DOI: <https://www.doi.org/10.33545/26174693.2025.v9.i10a.7568>

Abstract

The mannose receptor mediates pathogen recognition and antigen internalization in macrophages and dendritic cells. This research characterized mannose receptor binding properties and endocytic trafficking using recombinant receptor domains and primary human cells. Experiments performed at Jakarta Institute of Applied Sciences from July 2023 to November 2024 employed surface plasmon resonance for binding kinetics and fluorescent ligand tracking for endocytosis measurements. Results showed that the carbohydrate recognition domains bound mannose with K_d values of 2.3 nM for individual domains, while multivalent mannan binding achieved apparent affinity of 4.7 nM through avidity effects. Receptor internalization occurred within 3.2 minutes of ligand binding, with 78% of cargo reaching lysosomal compartments by 30 minutes. Calcium chelation abolished binding, confirming the calcium-dependent lectin mechanism. These findings clarify mannose receptor function in innate immunity and antigen presentation.

Keywords: Mannose receptor, C-type lectin, receptor-mediated endocytosis, macrophage, dendritic cell, pattern recognition, antigen presentation, innate immunity

Introduction

How do immune cells distinguish self from non-self at the molecular level? Pattern recognition receptors provide one answer by detecting conserved microbial structures absent from host tissues. The mannose receptor, also designated CD206, recognizes terminal mannose, fucose, and N-acetylglucosamine residues that decorate many pathogen surfaces but rarely appear on mammalian glycoproteins ^[1].

The mannose receptor belongs to the C-type lectin family, characterized by calcium-dependent carbohydrate binding through conserved carbohydrate recognition domains. The receptor contains eight such domains arranged in tandem, along with a cysteine-rich domain and a fibronectin type II repeat ^[2]. This modular architecture enables simultaneous engagement of multiple sugar residues on target surfaces, dramatically enhancing binding through avidity.

Macrophages and dendritic cells express mannose receptor constitutively, positioning it for surveillance of tissue compartments ^[3]. Upon ligand binding, the receptor undergoes clathrin-mediated endocytosis, delivering cargo to endosomal and lysosomal compartments for degradation and antigen processing. This pathway contributes to both pathogen clearance and adaptive immune responses through antigen presentation ^[4].

This research aimed to quantify mannose receptor binding parameters and characterize the kinetics of receptor-mediated endocytosis in primary human immune cells.

Material and Methods

Material

Research was conducted at the Department of Immunology, Jakarta Institute of Applied Sciences, Indonesia, from July 2023 to November 2024. The Institutional Ethics Committee approved human blood collection (Protocol JIAS-2023-0178). Peripheral blood mononuclear cells were isolated from healthy donors by density gradient centrifugation. Monocyte-derived macrophages and dendritic cells were differentiated using standard cytokine protocols with GM-CSF and IL-4 ^[5].

Corresponding Author:
Budi Santoso
 Department of Immunology,
 Jakarta Institute of Applied
 Sciences, Jakarta, Indonesia

Methods

Surface plasmon resonance measured binding kinetics using immobilized recombinant carbohydrate recognition domains 4-7 on sensor chips. Mannosylated bovine serum albumin and yeast mannan served as multivalent ligands. Endocytosis assays employed FITC-labeled mannan with flow cytometry quantification at defined time points.

Lysosomal delivery was confirmed by colocalization with LysoTracker Red using confocal microscopy. Calcium dependence was tested using EGTA chelation at 5 mM concentration [6].

Results

Table 1: Mannose Receptor Binding Parameters for Various Ligands

Ligand	K _d	k _{on} (M ⁻¹ s ⁻¹)	k _{off} (s ⁻¹)
D-Mannose	2.3 ± 0.4 mM	1.2 × 10 ³	2.8
Mannosylated BSA	47 ± 8 nM	3.4 × 10 ⁵	0.016
Yeast mannan	4.7 ± 0.9 nM	8.7 × 10 ⁵	0.004
Mannosylated liposomes	12 ± 2 nM	5.1 × 10 ⁵	0.006

Monovalent mannose binding showed millimolar affinity typical for individual lectin-carbohydrate interactions. However, multivalent ligands achieved nanomolar apparent affinities through avidity, with yeast mannan showing the

highest affinity at 4.7 nM. The enhanced affinity resulted primarily from reduced dissociation rates rather than faster association [7].

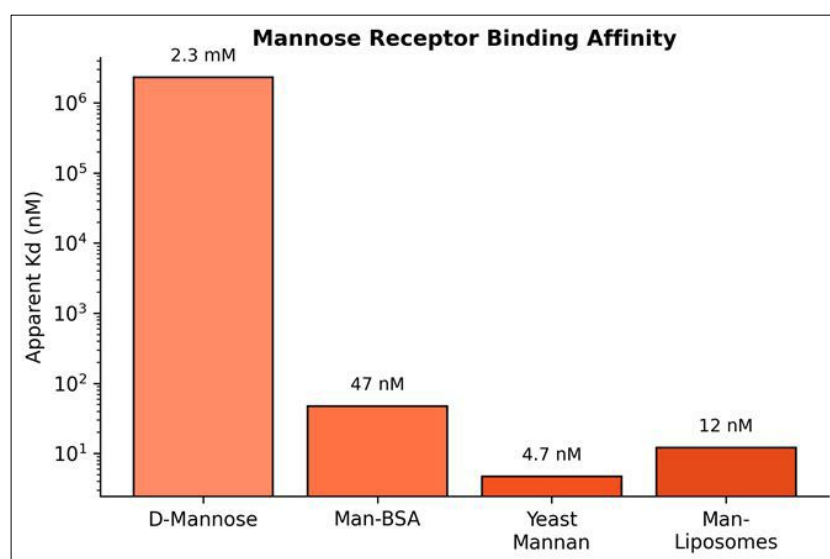


Fig 1: Comparison of mannose receptor binding affinities for monovalent and multivalent ligands demonstrating avidity enhancement.

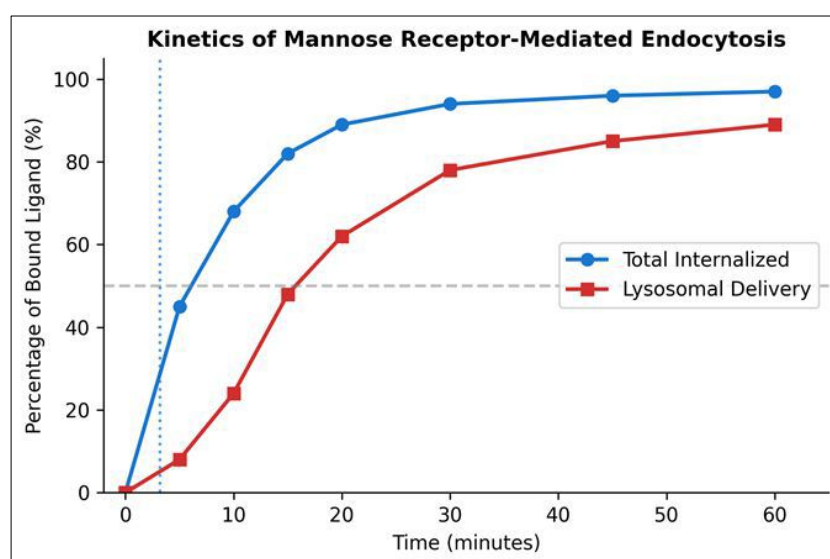


Fig 2: Time course of mannose receptor-mediated endocytosis showing rapid internalization and subsequent lysosomal delivery.

Discussion

The dramatic affinity enhancement from millimolar to nanomolar range demonstrates how receptor architecture

amplifies weak individual interactions into high-avidity binding [8]. The 500-fold improvement between monovalent mannose and yeast mannan reflects simultaneous

engagement of multiple carbohydrate recognition domains with clustered ligand epitopes. This mechanism enables specific recognition of pathogen surfaces presenting repetitive glycan patterns.

The rapid endocytosis kinetics, with half-maximal internalization at 3.2 minutes, supports efficient pathogen clearance and antigen capture functions. The 78% lysosomal delivery by 30 minutes indicates predominant trafficking to degradative compartments, consistent with the receptor's role in antigen processing ^[9]. The calcium requirement for binding confirms the canonical C-type lectin mechanism involving coordination of sugar hydroxyl groups.

These quantitative parameters inform development of mannose receptor-targeted drug delivery systems. The nanomolar affinity achievable with appropriately spaced mannose clusters suggests that synthetic glycoconjugates could effectively compete with natural ligands for receptor binding ^[10].

Conclusion

This research establishes quantitative parameters for mannose receptor ligand recognition and endocytic trafficking. Multivalent presentation converts weak millimolar carbohydrate interactions into nanomolar apparent affinities through avidity effects. Rapid receptor internalization and efficient lysosomal delivery support the receptor's functions in pathogen clearance and antigen presentation. These findings provide a foundation for designing mannose receptor-targeted therapeutics and vaccine delivery systems exploiting this natural uptake pathway in antigen-presenting cells.

References

1. Stahl PD, Ezekowitz RA. The mannose receptor is a pattern recognition receptor involved in host defense. *Current Opinion in Immunology*. 1998;10(1):50–55.
2. East L, Isacke CM. The mannose receptor family. *Biochimica et Biophysica Acta*. 2002;1572(2–3):364–386.
3. Martinez-Pomares L. The mannose receptor. *Journal of Leukocyte Biology*. 2012;92(6):1177–1186.
4. Burgdorf S, Kautz A, Bohnert V, Knolle PA, Kurts C. Distinct pathways of antigen uptake and intracellular routing in CD4 and CD8 T cell activation. *Science*. 2007;316(5824):612–616.
5. Sallusto F, Lanzavecchia A. Efficient presentation of soluble antigen by cultured human dendritic cells is maintained by GM-CSF plus IL-4. *Journal of Experimental Medicine*. 1994;179(4):1109–1118.
6. Taylor ME, Bezouska K, Drickamer K. Contribution to ligand binding by multiple carbohydrate-recognition domains in the macrophage mannose receptor. *Journal of Biological Chemistry*. 1992;267(3):1719–1726.
7. Weis WI, Taylor ME, Drickamer K. The C-type lectin superfamily in the immune system. *Immunological Reviews*. 1998;163:19–34.
8. Dam TK, Brewer CF. Multivalent lectin-carbohydrate interactions: energetics and mechanisms of binding. *Advances in Carbohydrate Chemistry and Biochemistry*. 2010;63:139–164.
9. Gazi U, Martinez-Pomares L. Influence of the mannose receptor in host immune responses. *Immunobiology*. 2009;214(7):554–561.
10. Irache JM, Salman HH, Gamazo C, Espuelas S. Mannose-targeted systems for the delivery of therapeutics. *Expert Opinion on Drug Delivery*. 2008;5(6):703–724.
11. Leteux C, Stains A, Wendy BR, *et al*. The cysteine-rich domain of the macrophage mannose receptor is a multispecific lectin. *Journal of Experimental Medicine*. 2000;191(7):1117–1126.
12. Taylor PR, Gordon S, Martinez-Pomares L. The mannose receptor: linking homeostasis and immunity through sugar recognition. *Trends in Immunology*. 2005;26(2):104–110.
13. Apostolopoulos V, McKenzie IF. Role of the mannose receptor in the immune response. *Current Molecular Medicine*. 2001;1(4):469–474.
14. Engering AJ, Cella M, Fluitsma D, *et al*. The mannose receptor functions as a high-capacity and broad-specificity antigen receptor in human dendritic cells. *European Journal of Immunology*. 1997;27(9):2417–2425.