

Dr. Sergio Grinstein completed his Ph.D. in 1976 at the Centro de Investigacion y Estudios Avanzados, in Mexico City. He then spent two years as a post-doctoral fellow at the Hospital For Sick Children in Toronto, followed by a year in the Department of Biochemistry at the Federal Institute of Technology in Zurich. He is currently working at the Hospital For Sick Children in Toronto and has been Professor of Biochemistry at the University of Toronto since 1988. Dr. Grinstein is interested in the cell physiology and biophysics of innate immunity, particularly phagocytosis and host-pathogen interactions.



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### Abstract

#### **Receptor mobility is regulated by the cytoskeleton connected to an exoskeleton via transmembrane pickets: role in phagocytosis.**

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Phagocytosis initiated by clustering of receptors upon exposure to target particles bearing multiple ligands. Clustering depends on the ability of receptors to move laterally in the plane of the membrane. Intrinsic proteins were originally thought to diffuse freely along the fluid mosaic of the membrane, but more recent observations indicate that mobility can be severely restricted by the existence of a cytoskeletal fence anchored to the plasma lemma via transmembrane “pickets”. However, the molecular nature of these putative pickets, the manner whereby they associate with the cytoskeleton, and their role in phagocytosis have not been investigated.

Based on its abundance and structural features, we surmised that CD44 may serve as a picket in macrophages. We used single-molecule tracking to study its behavior and how it affects the mobility of phagocytic receptors. In addition, because its extracellular domain can bind hyaluronic acid, we found that CD44 serves as a transmembrane connector between the pericellular (glycocalyx) coat, which is akin to an exoskeleton, and the cytoskeleton. The pericellular coat restricts access of particles to phagocytic receptors, which comparatively short molecules. The implications of this transmembrane structural framework to phagocytosis will be illustrated and discussed.