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A Milestone in Science: Discovery of the *Porosome*—The Universal Secretory Machinery in Cells

The discovery of a new cellular structure, *'the porosome*,'[1] has dawned a new era in biology and medicine, and given birth to a new field—*'NanoCellBiology.'* More than 5 decades ago, the electron microscope (EM) was the leading tool in discovery of various sub-cellular structures such as ribosomes, lysozomes,[2] and of pathogens such as bacteria and viruses. Similarly, in the past decade the atomic force microscope (AFM) has enabled the discovery of a new cellular structure—*the porosome*,[1] the universal secretory machinery in cells. Besides this seminal discovery of the porosome, the AFM has allowed determination of the porosome structure, its function and dynamics, at nm resolution and in real-time in live cells. The AFM has also helped to determine at great detail the molecular mechanism of SNARE-induced membrane fusion, and the regulated release of intra-vesicular contents during cell secretion.[1] The review by Paknikar and Jeremic in this issue[3] briefly outlines the discovery of the porosome, providing even to the non-specialized reader, the significance of this monumental discovery.

Porosomes are permanent, supramolecular cup-shaped structures at the cell plasma membrane, where secretory vesicles transiently dock and fuse to release intravesicular contents to the outside during cell secretion. Porosomes or fusion pores are often confused with membrane fusion, i.e., the establishment of SNARE-induced continuity between secretory vesicle membrane and the cell plasma membrane.[4] Unlike t-/v-SNARE ring complex formed when v-SNARE-associated liposomes meet t-SNARE-associated membrane;[1] porosomes are permanent supramolecular cup-shaped structures at the cell plasma membrane, where secretory vesicles dock and fuse to release vesicular contents.[1] Precisely, t-SNAREs are located at the base of porosomes, where v-SNARE-associated secretory vesicles temporarily dock and establish continuity between the vesicle lumen and the porosome, during cell secretion. Prior to the discovery of the porosome, there were numerous suggestions that such a structure is initiated following stimulation of cell secretion, which clearly is not the case. Porosomes on the other hand, are permanent cup-shaped structures at the cell plasma membrane, which dilate during secretion to allow for regulated release of intravesicular contents to the outside. At the base of porosomes, membrane-bounded secretory vesicles fuse transiently, and not completely as previously hypothesized. The accumulation of empty and partially empty vesicles following cell secretion can now be accounted for. After almost a century, nanobioscience has helped solve one of Natures fundamental mysteries, i.e., cell secretion, a process required for the very existence of life. It would be interesting to determine the roles of such cellular structures in nanomaterial–cell interactions and their intracellular trafficking.

References and Notes

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