'Nano-Keys' Bind Cell Receptors and Trigger Allergic Reactions

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The tumblers of life continue to click as Cornell University researchers have fabricated a set of "nano-keys" on the molecular scale to interact with receptors on cell membranes and trigger larger-scale responses within cells -- such as the release of histamines in an allergic response.

How cell membranes control cellular function has long been studied but with ambiguous results. However, nanotechnology now gives researchers new tools to understand the role of cell membranes in activating responses within cells.

Barbara Baird, Cornell professor of chemistry and chemical biology, reported this research today (Feb.16) at the annual meeting of the American Association for the Advancement of Science. She is the director of Cornell's Nanobiotechnology Center, which is funded by the National Science Foundation.

One day, Baird said, scientists might use these insights to develop new drug therapies for allergies and other immune responses, high cholesterol and perhaps viral infections.

By understanding a membrane's role in cell function, she explained that these nano-keys could interfere with responses via the membrane interactions, rather than just targeting proteins to block responses. This could lead to designing ligands (molecules that bind to receptors) that trigger a desired response or inhibit an allergic reaction and preventing the release of histamines and other inflammatory mediators.

In her presentation, "Design and Fabrication of Stimuli to Reveal Spatial Regulation of Cellular Signaling," she explained, "We want to understand how the receptors on cell surfaces mediate cellular responses, how cells work on a molecular level."

To study how receptors on cell membranes jump-start cellular responses, Baird and her colleagues chose to work with mast cells. They were chosen because mast cells secrete chemicals and histamines (substances released in allergic reactions that cause runny nose, watery eyes and other characteristic allergy symptoms) and they are the gatekeepers for the allergic immune response. This system can be manipulated experimentally.

Specifically, Baird works with immunoglobulin E (IgE) antibodies, which mount membrane proteins on mast cells to form receptor complexes that sense the environment and sensitize the cell to allergens, which are substances that cause an allergic reaction. Typically, two or more receptors cluster together when they bind with an antigen (allergen or foreign body), and this causes transmembrane activation of enzymes within the cell that eventually lead to the release of histamines.

Such processes begin on the nanoscale (a nanometer equals one-billionth of a meter) -- at the molecular level on the cell's surface and lead to a system-wide response. At present, very little is known about the structural changes caused by receptor clustering that allow cells to sense their outer environment and start cellular processes within the cell.

The so-called nano-keys are surfaces of silicon with a layer of polymer or a thin lipid (fatty molecules that make up cell membranes) bilayer. The surfaces, which are engineered on the micron scale (0.000001 meter; there are 25,400 microns in an inch), are arranged in patterns that contain antigens and cause IgE-receptors to cluster when the cells attach to the surface. This activates the cell's inner machinery.

Said Baird: "In this way, we can control what the cell sees. The cells are binding to the engineered surfaces and getting turned on. We can then see how the cell is organizing itself due to the stimulus."

Collaborators include: David Holowka, Cornell senior scientist in chemistry; and the research groups of Harold G. Craighead, Cornell professor of applied and engineering physics; Dan Luo, Cornell assistant professor of biological and environmental engineering; Christopher Ober, Cornell professor of materials science and engineering; Watt Webb, Cornell's Eckert Professor in Engineering; and Ulrich Wiesner, Cornell professor of materials science and engineering.

Source: Cornell University