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Small details between "in vivo" and "in vitro" studies make for big differences in understanding diabetes and other secretory dysfunctions

Exocytosis, the fundamental process by which cells secrete hormones such as insulin and other useful biological substances, is regulated far differently in life than in laboratory tissue cultures and explanted organs, according to research presented today at the American Society of Cell Biology's 50th Annual Meeting in Philadelphia.

The unexpected findings that exocytosis regulation "in vivo" is not the same as the process long studied "in vitro" is a reminder of the gap between laboratory glassware experiments and the cell biology of living animals -- and humans, said Roberto Weigert, Ph.D., of the National Institutes of Health (NIH), National Institute of Dental and Craniofacial Research (NIDCR).

During exocytosis, a cell internally packs up secretions and ferries them to the plasma membrane (PM) that demarcates the cell from its surroundings.

There, the packages, which are named secretory vesicles, fuse with the PM and then eject their contents. The process has been studied for decades in glassware experiments involving cultured cells and tissues.

Thanks to the optical imaging technology intravital microscopy. Weigert and colleagues were able to determine for the first time how exocytosis

actually occurs in the salivary glands of a living mouse.

According to previous in vitro studies in the salivary glands, multiple secretory vesicles fuse with the PM, forming strings of vesicles in a process stimulated by two classes of chemical switches, muscarinic and beta-adrenergic receptors.

However, when the scientists examined the process in vivo, they saw the secretory vesicles fuse, not in strings, but one by one with the PM and only under stimulation from beta-adrenergic receptors.

Their additional in vivo studies revealed that the fusion step requires the assembly of a scaffold around the membrane of the vesicles.

This scaffold contains actin, a protein that forms filaments, and myosin II, a protein that binds to multiple actin filaments. When assembled, these molecules generate a contractile force that pushes the membranes and drives the fusion process to completion.

The molecular differences between in vivo and in vitro may seem minor but may have a large impact, said Weigert, because exocytosis is fundamental to understanding the basis of secretory dysfunctions such as diabetes in which insulin is transported in secretory vesicles.

Provided by American Society for Cell Biology