New Nanoparticles Could Revolutionize Therapeutic Drug Discovery

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Understanding the structure of proteins is a vital first step in developing new drugs, but to date, researchers have had difficulty studying the large number of proteins that are normally embedded in the cell membrane, a family of proteins that includes those involved in cancer-related signaling processes. However, using nanoparticles, scientists from the University of Birmingham in the United Kingdom have found a way to preserve membrane proteins intact, enabling detailed analysis of their structure, molecular functions, and interaction with potential anticancer agents.

Michael Overduin, Ph.D., who led the study that was published in the Journal of the American Chemical Society, explained: “We have shown how a polymer can wrap around and preserve membrane proteins intact in stable nanoparticles. Membrane proteins are the most valuable but technically challenging targets for drug discovery. Finding a gentle solution that preserves their structure and activity, yet is robust enough for experimental interrogation, has eluded scientists for decades, but is now available.”

The key to stabilizing membrane proteins turns out to be a polymer made of styrene and maleic acid. This copolymer is able to envelope membrane proteins in an environment that closely mimics that of the cell membrane while simultaneously forming stable nanoparticles that the researchers call styrene maleic acid lipid particles (SMALPs). The investigators found that not only did the proteins maintain their folded structure and binding and enzyme activities in the SMALPs, but also

using the nanoparticles allowed them to be used in virtually any type of laboratory analysis.

Timothy R. Dafforn, Ph.D., who jointly ran the study, noted: “In the past, studies have concentrated largely on soluble proteins since membrane proteins are so difficult to make. However, the discovery of the SMALPs removes this barrier and opens up access to membrane proteins. This has exciting clinical implications since it may enable drug discovery on receptors that are currently too difficult to produce or to study by current methods.”

This work is detailed in the paper “Membrane proteins solubilized intact in lipid containing nanoparticles bounded by styrene maleic acid copolymer.” An investigator from the University of Warwick, United Kingdom, also participated in this study. An abstract of the paper is available at the journal's Web site.

Source: National Cancer Institute (news : web)