Scientists develop new tool for the study of spatial patterns in living cells

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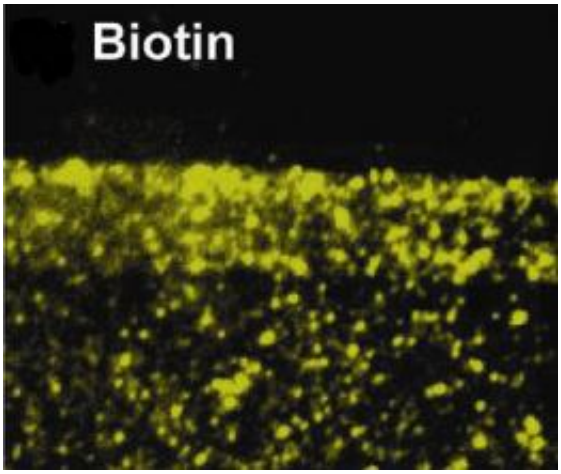

Gold nanoparticles in a lipid membrane can be coupled to biomolecules for the study of specific cellular functions. Here gold nanoparticles have been coupled to biotin (vitamin B7), which plays an essential role in cell growth. Credit: Groves, et. al

(PhysOrg.com) -- Football has often been called “a game of inches,” but biology is a game of nanometers, where spatial differences of only a few nanometers can determine the fate of a cell – whether it lives or dies, remains normal or turns cancerous. Scientists with the U.S. Department of Energy (DOE)’s Lawrence Berkeley National Laboratory (Berkeley Lab) have developed a new and better way to study the impact of spatial patterns on living cells.

Berkeley Lab chemist Jay Groves led a study in which artificial membranes made up of a fluid bilayer of lipid molecules were embedded with fixed arrays of gold nanoparticles to control the spacing of proteins and other cellular molecules placed on the membranes. This provided the researchers with an unprecedented opportunity to study how the spatial patterns of chemical and physical properties on membrane surfaces influence the behavior of cells.

“The gold nanoparticles are similar to the size of a single protein molecule, which gets us to a scale we couldn’t really access before,” says Groves. “As the first example of a biological membrane platform that combines fixed nanopatterning with the mobility of fluid lipid bilayers, our technique represents an important improvement over previous patterning methods.”

Schematic shows gold nanoparticle arrays embedded into a supported lipid bilayer membrane then selectively labeled with specific surface chemistry properties to study living cells that are bound to the nanoparticles and/or lipid bilayer. Credit: Groves, et. al

Groves holds joint appointments with Berkeley Lab’s Physical Biosciences Division and the University of California (UC) Berkeley’s Chemistry Department, and is a Howard Hughes Medical Institute (HHMI) investigator. He is the corresponding author of a paper that reports these results in the journal Nano Letters. The paper is titled “Supported Membranes Embedded with Fixed Arrays of Gold Nanoparticles.”

Spatial patterning of chemical and physical properties on artificial membranes of lipid bilayers is a time-tested way to study the behavior of cultured biological cells. Natural lipid bilayer membranes surround virtually all living cells as well as many of the structures inside the cell including the nucleus. These membranes provide a barrier that restrains the movement of proteins and other cellular molecules, penning them into their proper locations and preventing them from moving into areas where they do not belong. Past spatial patterning efforts on artificial membranes have been done on an all-or-nothing basis – proteins placed on a membrane either had complete mobility or were fixed in a static position.

“Immobile patterning intrinsically defeats any cellular process that naturally involves movement,” Groves says. “On the other hand we need to be able to impose some fixed barriers in order to manipulate membranes in really novel ways.”

Groves is a recognized leader in the development of unique “supported” synthetic membranes that are constructed out of lipids and assembled onto a substrate of solid silica. He and his group have used these supported membranes to demonstrate that living cells not only interact with their environment through chemical signals but also through physical force.

“We call our approach the spatial mutation strategy because molecules in a cell can be spatially re-arranged without altering the cell in any other way,” he says.

However, until now Groves and his group were unable to get to the tens of nanometers length-scales that they can now reach by embedding their supported membranes with gold nanoparticles.

“Our new membranes provide a hybrid interface consisting of mobile

and immobile components with controlled geometry," Groves says. "Proteins or other cellular molecules can be associated with the fluid lipid component, the fixed nanoparticle component, or both."

The gold nanoparticle arrays were patterned through a self-assembly process that provides controllable spacing between particles in the array in the important range of 50 to 150 nanometers. The gold nanoparticles themselves measure about five to seven nanometers in diameter.

Groves and his team successfully tested their hybrid membranes on a line of breast cancer cells known as MDA-MB-231 that is highly invasive. With their hybrid membranes, the team demonstrated that in the absence of cell adhesion molecules, the membrane remained essentially free of the cancer cells, but when both the nanoparticles and the lipid were functionalized with molecules that promote cell adhesion, the cancer cells were found all over the surface.

Groves and his research group are now using their gold nanoparticle membranes to study both cancer metastasis and T cell immunology. They expect to report their results soon.

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