New method for gene expression experiments a kin to watercolor painting in water

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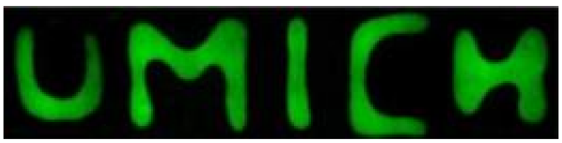

University of Michigan research demonstrate their technique for sketching experiments on a canvas of live cells by writing “UMICH” with a fluorescent water-based solution on cells growing in another water-based medium. Credit: Courtesy of Hossein Tavana

Like oil and water, two water-based liquids can mingle without mixing in a new University of Michigan technology developed for biological experiments.

The new "micropatterning" method is useful in gene expression studies, which essentially turn genes on or off in cells in order to help researchers understand the function of those genes.

"If you take a brush with watercolor paint and move it around in a dish of water, you usually just wash away the paint in the water and get no picture. That's what happens with water-soluble biological reagents in typical cell culture experiments as well. The reagents just diffuse everywhere with no localization," said Shuichi Takayama, associate professor of biomedical engineering and macromolecular science and engineering.

"But we have a system in which you can actually have aqueous solutions that don't mix with each other. Rather than getting a murky dish of washed-away paint, we can create watercolor pictures at the bottom of a dish of water. And when the paint includes gene expression and silencing reagents, we can sketch biological experiments directly onto a canvas of living cells."

Gene expression and silencing reagents are substances that tell cells in an experiment which genes to turn on or off.

In a paper published online on Aug. 16 in *Nature Materials*, Takayama and his colleagues, led by postdoctoral researcher Hossein Tavana, demonstrate their technique by writing "UMICH" with a fluorescent water-based solution on cells growing in another water-based medium.

They also painted reagents on breast cancer cells to make them turn fluorescent proteins on and off in different patterns, and caused a group of cells in a layer of normally non-invasive cells to become invasive, like cancer cells, by turning on a particular gene.

Today, scientists know the sequence of various genomes including humans. They even have reagents to express or silence any gene of interest in living cells. This patterning water in water technique is motivated by the need for a more efficient way to understand the roles of different genes.

"What would help is to be able to use smaller amounts of reagents and cells, to pack more experiments into the same area or plate of experiments, and to be able to study cells in complex microenvironments that mimic living organisms more than typical dishes do," Tavana said. "Our technology, which provides the ability to localize nanoliter droplets of reagents over cells in high density arrays without the need to have segregating physical walls or the limits of having to print on a dry substrate, satisfies these needs."

The new technology allows researchers to use hundreds of times less reagent than is used in comparable experiments under the current methods. Also, cells and reagents permanently remain in a wet environment, which is preferable.

"Life is about micropatterns," Takayama said. "Tissues and organs and even living organisms are patterns of cells put together. All cells in our bodies have essentially the same DNA blueprint, but which genes are expressed or suppressed make a cell function as an eye or cheek or liver, or as a normal cell versus a cancer cell.

"Being able to pattern gene expression and silencing reagents on cells grown on native-like surfaces in a more efficient and versatile manner will help us better understand how living organisms function or how diseases like cancer progress."

The paper is called, "Nanolitre liquid patterning in aqueous environments for spatially defined reagent delivery to mammalian cells." The research is funded by the National Institutes of Health and a gift from J. Passino. Researchers from the University of Michigan Health System and the Life Sciences Institute also contributed, including Stephen Weiss, chief of molecular medicine and genetics in the Department of Internal Medicine; Gary Luker, assistant professor of radiology, and microbiology and immunology. The university is pursuing patent protection for the intellectual property, and is seeking commercialization partners to help bring the technology to market.

Source: University of Michigan (news : web)