CELL BIOLOGY

Trying out topographies

A new chip and high-content imaging allow thousands of surface patterns to be tested for their influence on cell behavior.

Cells behave differently on different surfaces, but testing these effects systematically has been difficult. Now, researchers led by Jan de Boer at the University of Twente in the Netherlands have developed a chip that allows 2,176 unique surface topographies to be screened, imaged and analyzed over a single course of experiments.

Each topography on the 'TopoChip' consists of randomly grouped features shaped like triangles, long rectangles or circles. To avoid artifacts caused by differences between the edge and center of the chip, patterns are replicated twice per chip and placed in randomized locations. The TopoChips also include four smooth areas as controls.

After manufacturing chips using silicon molds and the polymer poly(D,L-lactic acid), the scientists seeded the devices with human mesenchymal stromal cells and used high-content imaging for analysis. Depending on the surfaces on which cells were plated, their behavior varied markedly in their expression of alkaline phosphatase, a marker of bone differentiation. Cells also differed in levels of proliferation and in morphology, such as whether they took on flat or rounded shapes and how many filopodia they extended.

The way the researchers designed the surfaces was key to the advance, says de Boer. They devised mathematical algorithms to build up topographic features from primitive shapes, which they arranged into imaginary squares with edges of 10, 20 or 28 micrometers. In each square, they grouped and rotated primitive shapes, creating over 154 million possible topographies. Of these, they randomly selected 2,176 topographies to be placed on the TopoChips.

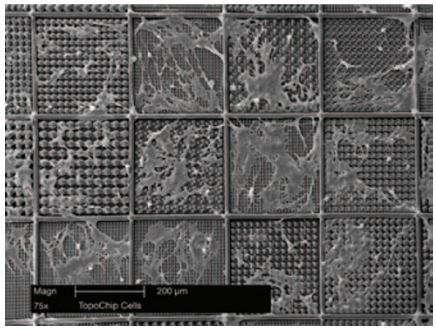
Up until now, says de Boer, most examinations of surface topographies on cell biology have been limited to testing just a few options based on researchers' ideas about what features are most likely to matter. The computational approach can encompass a much broader variety, he says. "You could not have created these patterns if you had designed it in a rational way."

Repeated experiments showed that different surface topographies consistently affected how much the cells were proliferating, but visual inspection could not reveal exactly what features of the topography contributed to this behavior. The researchers devised a machine-learning algorithm to predict features likely to promote proliferation or differentiation. The next step, says de Boer, is to engineer new topographies for additional screens using features of the top-scoring topographies.

The technology will be useful for cell culture and tissue engineering, says de Boer, though he sees the most immediate impact in the design of implantable medical technologies, such as hip replacements, in which certain kinds of cell growth around the medical devices can interfere with their function. "What we made is a platform technology that can be applied for any question. It's almost like having a drug-screening library," says de Boer.

Currently, the researchers are modifying the TopoChip to be compatible with six-well plates so that other researchers will be able to apply the design in their own studies. In addition, de Boer and others have launched a company called Materiomics to commercialize the technology. Already, says de Boer, other scientists have inquired about collaborations to find surfaces for many properties: bacterial adhesion, neural guidance, platelet adhesion and more. "You can basically use it for any application," he says.

Monya Baker



A nanofabricated chip allows thousands of surface topographies to be screened for influences on cell biology. Image courtesy of Hemant Unadkat.

RESEARCH PAPERS

Unadkat, H.V. *et al.* An algorithm-based topographical biomaterials library to instruct cell fate. *Proc. Natl. Acad. Sci. USA* **108**, 16565–16570 (2011).