TopoChip reveals the Braille code of cells

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Cells in the human body change shape as they crawl, split, or cling to other surfaces, but while the scientific literature is filled with examples of how cell shapes shift in response to things they touch, little is known about the rules that govern these changes. And there has been no high-throughput way to systematically test different topologies against different types of cells to optimize the surface of something like a medical implant.

"We don't know the Braille codes of cells," said biologist Jan de Boer of the University of Twente in the Netherlands.

To address this gap in understanding, de Boer and his team of researchers have designed a systematic way to discover how a cell changes shape in response to a range of topographies. Their massive screening approach, which uses a platform called the TopoChip, tests thousands of surface patterns and catalogs how cells react to them, similar to the way pharmaceutical companies screen whole libraries of compounds in their search for promising drugs.

De Boer will describe his team's latest findings using the TopoChip, and how this work could influence the design of better surfaces for medical implants, at the AVS 60th International Symposium and Exhibition, to be held Oct. 27-Nov. 1, 2013, in Long Beach, Calif.

"Our unique approach is, we don't design a few surfaces – we design thousands of them," de Boer said. So far they have selected 2,173 patterns out of their library of over 150 million unique topographies and

can make more.

To develop their technique, the team wrote an algorithm that generates unique patterns in silicon: pillars just a few micrometers across with combinations of geometric shapes such as triangles, rectangles, and circles, spaced various distances apart from each other and with differences in size and orientation. The silicon patterns are used as molds to make imprints onto polymeric surfaces, which can be coated with a ceramic or metal when desired. The researchers employ the TopoChip to grow cells on these surfaces, then use high-content imaging to see how the cells respond.

Of the dozen types of cells they have tested, all have responded to at least some of the patterns, though different types of cells respond in different ways. "Sometimes cells sit on top of the pillars, sometimes between them," de Boer said. "Sometimes they wrap themselves around them." These drastic changes in shape are thought to have a biological effect on the cells, for instance by changing behavior such as proliferation rates.

By analyzing the data, the team is now able to predict how that cell will change its shape in response to a particular type of geometric arrangement of the pillars.

Learning the Braille code of cells has potential applications in the world of artificial implants, which include heart valves, dental implants, and artificial joints. Our bodies respond to some of these implants in negative ways, for example forming scar tissue around the foreign object. By creating medical implant surfaces that speak the language of cells, researchers may be able to elicit more positive reactions.

"What is nice about this approach is we don't need coatings. We don't need to change chemistry or biology. All we change is surface

topography," de Boer said. Eventually, he continues, it could be a very powerful approach to improving the performance of medical devices.

Next steps for his team include finding out how many unique patterns there are that can elicit a unique response. De Boer is also beginning to collaborate with genomics researchers to get more insight into what is happening inside the cell as it changes shape. And to facilitate making the TopoChip platform available to medical device manufacturers, de Boer and colleagues have established a spin-off company, Materiomics B.V., to perform individualized screens on request.

More information: Presentation BI-WeM4, "Do Cells Read Braille? High Throughput Screening of Surface Topography-Induced Cellular Responses," is at 9:00 a.m. Pacific Time on Wednesday, Oct. 30, 2013.

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