

Scientist observes surprising behavior of cells during blood-vessel formation

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Biologists tend to look at cells in bulk, observing them as a group and taking the average behavior as the norm -- the assumption is that genetically identical cells all behave the same way. In a paper to be published in the online Early Edition of *Proceedings of the National Academy of Sciences* the week of March 7, 2011, Sam Sia, assistant professor of biomedical engineering at Columbia Engineering, presents the results of his four-year tissue-engineering study that show a surprising range of variation in how individual cells behave during formation of a blood vessel. Sia and his team used a new method to painstakingly observe and track individual behaviors, characterizing, for the first time, what happens when human endothelial cells move from an initial dispersed state to the formation of capillary-like structures.

"We were really surprised by this behavior," says Sia, who was named one of the world's top young innovators for 2010 by MIT's Technology Review for his work in biotechnology and medicine. "In contrast to the population-averaged behavior that most studies report, most individual [cells](#) followed distinct patterns of cell-shape changes that were not reflected in the bulk average."

This is one of the first explicit studies to look at the variations between cells during tissue formation, and overturns the assumption that genetically identical cells behave in generally similar ways. Using a systematic approach to quantifying the changes in cell shape and movement for every single endothelial cell over time, the Columbia Engineering team found unexpected hidden patterns in behavior. In

addition to discovering that most cells behave differently from the average, the team also observed that groups of cells behaved in similar fashions, and that some of these clusters of behavior resulted in distinct structural roles in the final blood-vessel network.

The origins of the variations in behavior are not known right now. Sia notes that "one possibility is simply random noise or naturally occurring fluctuations, which have been shown by other researchers to be important in producing biologically significant variations in gene expression and other subcellular processes. It's also possible there are subtle local variations in the extracellular environment that we're not aware of yet."

Sia says an application of this work is to exploit his technique to identify new drugs that modify angiogenesis. "A lot of drugs that either help or hinder blood-vessel formation have unknown mechanisms. This technique can potentially unravel some of those mechanisms, and help identify compounds that modulate specific aspects of how [blood vessels](#) form." In addition, knowledge of how individual cells behave will help in high-precision [tissue engineering](#), an ongoing field of research in Sia's lab. "Knowledge of how individual cells or groups of cells behave enhances our understanding of how native tissues self-organize," he says. "This could ultimately enable more precise approaches for engineering complex multicellular tissues."

Sia was also named in 2010 by NASA as one of the ten innovators in human health and sustainability. In 2008, he received a CAREER award from the National Science Foundation that included a \$400,000 grant to support his other research specialty in three-dimensional tissue engineering. A recipient of the Walter H. Coulter Early Career Award in 2008, Sia participated in the National Academy of Engineering's U.S. Frontiers of Engineering symposium for the nation's brightest young engineers in 2007.

His research is focused on developing new high-resolution tools to control the extracellular environments around cells, in order to study how they interact to form human tissues and organs. His lab uses techniques from a number of different fields, including biochemistry, molecular biology, microfabrication, microfluidics, materials chemistry, and cell and tissue biology.

Provided by Columbia University

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