

New 3D model shines light on key aspects of early development

From a biological standpoint, the earliest stages of life are the most mysterious. A developing human embryo undergoes a flurry of rapid changes, and these changes are exceedingly difficult to study because they transpire within the confines of a womb.

But with new technology, it might soon be possible to fill important gaps in our understanding of early pregnancy and development.

Rockefeller scientists recently used stem cells to create a 3D model of early embryonic tissues, allowing them to simulate developmental processes as they occur in time and space. The researchers hope that this tool, whose utility they recently demonstrated in a report in *Nature Cell Biology*, will make it possible to further elucidate the processes that guide embryonic growth, and ultimately lead to innovations that promote healthy pregnancies.

Dimensions of development

The concept of using stem cells to model early embryonic development was first developed in labs of Ali H. Brivanlou, the Robert and Harriet Heilbrunn Professor, and Eric D. Siggia, the Viola Ward Brinning and Elbert Calhoun Brinning Professor, who published their initial research on the topic in 2014. Despite making several crucial discoveries since that time, Brivanlou and Siggia knew that his system was, in some ways, limited: conventional stem cell models are two dimensional and do not take on the actual shape of an embryo, therefore prohibiting researchers from asking key questions related to its structure.

For example, scientists are highly interested in the process by which embryos attach to the uterus--a crucial first step to a successful pregnancy. And according to Mijo Simunovic, a Simons Junior Fellow in Siggia's lab, it is practically impossible to study this complex phenomenon in a two-dimensional system.

"Attachment is inherently a 3D problem," he says.

To address this issue, Brivanlou, Siggia, and Simunovic used an interdisciplinary approach to develop a 3D model simulating an approximately fourteen-day-old human embryo--the stage of development during which a key milestone of embryonic development called "gastrulation" takes place.

"We combined several techniques--bioengineering, physics, and developmental biology--to create this model," explains Simunovic, who notes that this research would not have been possible without the unique, longstanding collaboration between the Siggia and Brivanlou labs. "We now have a 3D system that mimics not only the embryo's genetic fingerprint, but also its shape and size."

Of course, it is not enough to make a model that simply looks like a real embryo: it must also act like one. Accordingly, the researchers tested whether their system could simulate one of the most fundamental processes in animal development--a phenomenon known as symmetry breaking.