# Singapore scientists make breakthrough findings on early embryonic development

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Scientists at the Genome Institute of Singapore (GIS) have recently generated significant single cell expression data crucial for a detailed molecular understanding of mammalian development from fertilization to embryo implantation, a process known as the preimplantation period. The knowledge gained has a direct impact on clinical applications in the areas of regenerative medicine and assisted reproduction.

This study, published in *Developmental Cell* on April 20, 2010, is the first of its kind to apply single cell gene expression analysis of many genes to hundreds of cells in a developmental system.

Using the new BioMark microfluidic technology and the mouse preimplantation embryo as a model, the scientists were able to study the expression of 48 genes from individual cells and applied this to analyze over 600 individual cells from the 1-cell to the 64-cell stage of preimplantation development. This high throughput single cell research methodology provides the scientists with the ability to detect dynamic patterns in cellular behaviour, which is unprecedented in the field. Significantly, the findings of the study resolves some of the arguments pertaining to cellular differentiation events and places fibroblast growth factor signalling as the primary event in the later cell fate decisions.

Executive Director at the GIS, a biomedical research institute of the Agency for Science, Technology and Research (A*STAR), Professor Edison Liu said, "This remarkable work by Guoji Guo, Mikael Huss, Paul Robson and colleagues uses new microgenomic technologies to

map, over time, how a single cell decides to permanently become different parts of an embryo. Within one division, cells commit to specific developmental lineages by expressing defined sets of genes. This research now opens the possibility of assessing the genetic triggers for fate determination of individual cells in developmental time. On another level, this work highlights the importance of new microtechnologies in advancing the understanding of early embryonic events. "

Professor Davor Solter, Senior Principal Investigator of the Institute of Medical Biology, A*STAR, added, "This is a real technological tour de force. The authors investigated changes in expression of multiple genes on the single cell level during preimplantation mouse development. They clearly demonstrated gradual and stochastic lineage allocation and absence of predetermination. These results conclusively resolved one of the hotly debated issues in mammalian development and provided important new insight into the mechanism which regulates early development in mammals."

"These are important findings. The team at GIS provided a new look into the complex and little-understood process of early embryo development. It also demonstrates the power of single cell gene expression. It is clear that individual cells and small groups of cells behave differently than the aggregate population, and these differences are key to understanding the biology of the system as a whole." said Gajus Worthington, president and chief executive officer of Fluidigm. "It always provides a special thrill when researchers use the capabilities of Fluidigm's technology to bring insight to the body of scientific knowledge."

The Preimplantation period involves the first cellular differentiation events in mammalian development including the formation of pluripotent cells from where embryonic stem (ES) cells are derived. Being one of the simplest mammalian developmental systems to study, it

can provide comprehensive understanding of the complex molecular control of reprogramming and cell fate decisions.

**More information:** The research findings described in the press release can be found in the April 20, 2010 print issue of Developmental Cell under the title "Resolution of cell fate decisions revealed by single cell gene expression analysis from zygote to blastocyst".

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