Gene Activity during Embryonic Development

NICHD

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Eric Wieschaus
Focus on the Future
(unanswered questions)

Gene activity, transcription networks and pattern

Gene activity and cellular mechanics
Understanding Early Development

Patterning - Maternal gradients provide positional cues

Transcriptional response at MBT controls cell fate
Understanding Early Development

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Biophysical measurements of input Bcd concentration and HB transcriptional output (Gregor et al 2007)
How do transcriptional patterns arise in mammalian embryos?
In flies, pattern of the embryo comes from pre-determined distributions in the unfertilized egg.

Is this possible in mammalian eggs where only a tiny fraction of the maternally supplied RNA and protein is incorporated into the inner cell mass and embryonic epiblast?

Where does the embryonic pattern come from in human embryos?
Localized patterns of expression arise in the inner cell mass through a gradual process cell communication circuits and sorting out.

Anna-Katerina Hadjantonakis, Sloan-Kettering Institute
Can cell signaling within the epiblast also account for the establishment of the head-tail axis in mammalian embryos?
Can cell signaling circuits generate patterns where no patterns previously existed?
cell signaling networks in sea urchins
A systems biological approach
David McClay-Eric Davidson
Can physical properties and mechanical aspects provide the spatial cues that pattern gene expression?
RL patterning in mouse or fish require motile cilia in the node or in Kupfer’s vesicle

Primary cilia in the mouse node
Cliff Tabin Harvard Med School
(Micrographs - K. Sulik & T. Poe, U North Carolina.)

cilia in the zebrafish Kupfer’s vesicle
(Rebecca Burdine, Princeton)
Defects in cilia motility affect asymmetric gene expression

Schottenfeld, Sullivan-Brown and Burdine, Development 2007
Gene Activity => Cellular Mechanics
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Cell fate choices are translated into cell behaviors
Infolding of mesoderm precursors during Drosophila gastrulation

Mesoderm precursors are internalized by formation of a ventral furrow
Epithelial folds during formation of neural tube

Kathryn V. Anderson
Sloan-Kettering Institute
Are there universal biophysical properties that govern cell shape changes and epithelial folding?
Constriction of the apical surface in ventral cells is associated with local accumulation of Myosin II.

Myosin II accumulates in a network of interconnected spots on the apical surface of constricting cells.
Changes in apical cell diameters drive furrow formation

Membrane-GFP (Spider)
Testing cytoplasmic properties by injection of biologically inert fluorescent beads

Bing He, Konstantin Doubrovinsky, Oleg Polyakov
EDGE – Michael Gelbart & Matthias Kaschube
Very suitable for planar cell sheets
Performs tracking in space and time
Computational representations vertex based--Nth-order neighbors
Allows to integrate additional channels (nuclei, myosin, …)
Global flow of cytoplasm follow patterns predicted by Navier–Stokes equations

This is surprising because the equations assume that the fluid being studied is infinitely divisible and not composed of particles (or cells!)