CDB SEMINAR

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16:00~17:30 C1F CDB Auditorium

Beyond the genome: Automated, continuous analysis of embryonic gene expression with cellular resolution in *C. elegans*

Summary

The complete genome sequence of *C. elegans* provides the basis for the systematic description of the network of gene expression. In an effort to realize some of that potential, we have developed a system that permits the automated analysis of the kinetics of gene expression in the worm with cellular resolution during embryogenesis. We collect 3D movies of developing embryos expressing histone-GFP fusion proteins in all nuclei and use computational methods to find nuclei and to trace the lineage. We simultaneously image a histone-RFP reporter driven by a promoter of interest in the same strain. The nuclear positions determined in the lineage tracing allow us to obtain quantitative measurement of expression for each cell at each time point. Because the cell lineage is invariant, we can directly map each independent expression pattern onto the reference lineage to obtain a composite picture of gene activity. We have begun to apply the method systematically to reveal the expression of each transcription factor throughout embryonic development, and have already generated expression patterns for a number of key developmental regulators of embryonic development, including *pha-4* (forkhead), *cnd-1* (NeuroD), *hlh-1* (MyoD) and the GATA factors *end-3, elt-2* and *elt-7*. Comparing the time of onset for genes expressed in the same lineage allows the inference of regulatory pathways. We have begun testing some of these predictions by examining the impact of RNAi knockdown of the regulator on expression levels of predicted targets.

The automated lineage analysis also allows new approaches to the study of development. For example, by comparing multiple lineages, we have begun to quantify the limited levels of stochastic variability in cycle length for each cell. In turn this limited variation of cell cycle length has facilitated a search for genes that alter cell cycle timing.

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