Abstract

Metazoan development is a complex and tightly controlled process that not only requires precise cell fate differentiation, but also demands accurate timing of cell division and precise cell migration. Genetic regulation of cell cycle length throughout metazoans embryogenesis is largely unknown, mainly due to the technical hurdle in quantifying cell division timing during development. Caenorhabditis elegans embryogenesis provides an excellent opportunity to study the genetic regulation of division timing because of its invariant cell lineage and widespread division asynchronies between sister cells. A combination of in toto imaging and automated cell lineaging coupled with high throughput RNAi allows genetic screening of genes involved in regulation of Asynchrony of Division between Sister cells (ADS) or cousin cells. One of the most pronounced asynchronies between cousin cells during C. elegans embryogenesis is a significant elongation of division timing in two endoderm progenitor cells, Ea and Ep (E2), versus their cousins MSa and MSp (MS2) that mainly develop into mesoderm organs. Out of a total of 822 essential and conserved genes that were perturbed by RNAi in our previous genetic screening, 53 genes are found to produce significantly reduction specifically in the E2 cell cycle length (p<0.01). Surprisingly, nearly 70% of the 53 genes are involved in mRNA production or its regulation, indicating a differential requirement of transcription for division timing between E2 and MS2. Reduction in E2 cell cycle length is frequently associated with cell migration defect and gastrulation failure. Furthermore, our systematic data on cell division timings upon perturbation of a large cohort of essential genes provide a valuable source for inferring the function of uncharacterized gene. For example, phenotypical clustering based on cell division timings suggested that an essential gene, gad-1, is likely to be involved in general transcription, which is in agreement with its further functional assays. In summary, a combining of the published data with our own demonstrates that E2 specific cell cycle elongation requires robust and earlier zygotic genome activation (ZGA) during C. elegans embryogenesis. The cell-specific elongation might be important for coordinate fate differentiation, division timing and cell migration of E2 to ensure proper intestine development.
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CURRICULUM VITAE