Large scale sorting of C. elegans embryos reveals the composition and dynamics of small RNA expression during early embryogenesis.

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Caenorhabditis elegans is one of the most prominent model systems to study embryogenesis. However, it has been impractical to collect large amounts of precisely staged embryos. Thus, early *C. elegans* embryogenesis has not been amenable to most modern high-throughput genomics or biochemistry assays. To overcome this problem, we devised a method to collect large amounts of cleanly staged *C. elegans* embryos by Fluorescent Activated Cell Sorting (termed eFACS). eFACS can in principle be applied to all embryonic developmental stages up to hatching. As a proof of principle we show that a single eFACS run routinely yields tens of thousands of almost perfectly staged one-cell embryos. Since in animals the earliest embryonic events are driven by post-transcriptional regulation, we combined eFACS with next-generation sequencing technology to systematically profile the embryonic expression of small, non-coding RNAs. We discovered a wealth of complex and orchestrated changes in the expression between and within almost all classes of small RNAs, including miRNAs, during embryogenesis. Our data indicate turn-over of the protein synthesis machinery upon fertilization and also shed light on the expression and genomic organization of the previously under-appreciated 26G-RNAs. Together, our eFACS data suggest that the complexity of small RNA expression dynamics in animals is comparable to the expression dynamics of protein encoding genes.