Metabolites' maternal effect on the initiation ofmaternal-to-zygotic transition in *C. elegans*

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Our health and development are the results of our ingestion of foods. Recent studies have identified many metabolites as key factors for normal development of the animals. It is known that maternal diet affects the growth rate of their offsprings. Hence, these metabolites potentially affect the development of the next generations. However, analyzing the effects of each metabolite (direct approach) is time-consuming. Thus, the causative mechanism involved in maternally loaded metabolites remains elusive. To address this question, we are particularly focused on embryonic development shortly after fertilization; embryos must consume their stored metabolites to proceed with their development until outside energy becomes provided. One of the critical processes in this period is maternal-to-zygotic transition (MZT), the autonomous initiation of zygotic gene expression. The mechanism of MZT has been extensively studied. Yet, little is known how the MZT are autonomously activated; particularly, which and how maternally provided metabolites contribute to the initiation of MZT.

Here we report that two metabolites transgenerationally affect the MZT initiation in *C. elegans*' embryonic development. We fed worm various types of bacteria and recorded their embryonic development from pre-single-cell stage for quantifications. We reduced the number of candidate substances by experimental/informatics searches (indirect approach). As a result, we found that worms fed particular type of bacteria produced embryos exerting abnormal development; their development temporarily stagnated at two-cell stage (one cell-cycle prior to the initiation of worm' MZT). The stagnation held up to 20% (roughly two hours) of normal embryonic development. We identified two substances, a fatty acid and a metabolite, independently causing the cell-stagnation. Furthermore, we also revealed a gene regulatory network that leads to the phenotype. Our results show how maternally loaded metabolites could transgenerationally affect the early development. We will discuss our latest discovery in this symposium.