Chemical and Genetic Approaches to Identify *Caenorhabditis elegans* Spermiogenesis-Related Factors

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Spermiogenesis is the final phase of spermatogenesis in which round spermatids transform into spermatozoa. However, the molecular basis of spermiogenesis is largely unknown in many species. One of the reasons why we use *Caenorhabditis elegans* to study spermiogenesis is that spermatids from this organism do not require any hormones and accessory cells in vitro to become spermatozoa. *C. elegans* spermiogenesis consists of two pivotal events, the pseudopod extension from spermatids and the fusion between the plasma membrane and the intracellular membranous organelles (MOs). In vitro activators such as Pronase (Pron) can induce these two cytological reactions in a simple, chemically defined medium. This advantage enables us to explore compounds that up- and downregulate spermiogenesis, which would be powerful tools for basic research and be the seeds of future drugs for infertility and contraception.

Our aim in this study is to obtain compounds that exhibit significant effects on *C. elegans* spermiogenesis and to clarify how those compounds are involved in the spermiogenesis pathway. Therefore, we screened a chemical library to find out compounds that block Pron-induced spermiogenesis and eventually obtained DDI-1, an interesting compound that blocks the pseudopod extension, but not the MO fusion. Moreover, we introduced random mutations into the *C. elegans* genome with ethyl methanesulfonate, isolated mutant males, and tested if spermatids from those males can activate into spermatozoa by Pron stimulation in the presence of DDI-1. By this genetic screening, we isolated several mutant strains in which the inhibitory activity of DDI-1 is neutralized. Currently, we are trying to figure out the mutated genes that show the suppressive effect.

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