A novel biological role of tachykinins as an upregulator of oocyte growth: identification of an evolutionary origin of tachykinergic functions in the ovary of the ascidian, *Ciona intestinalis*

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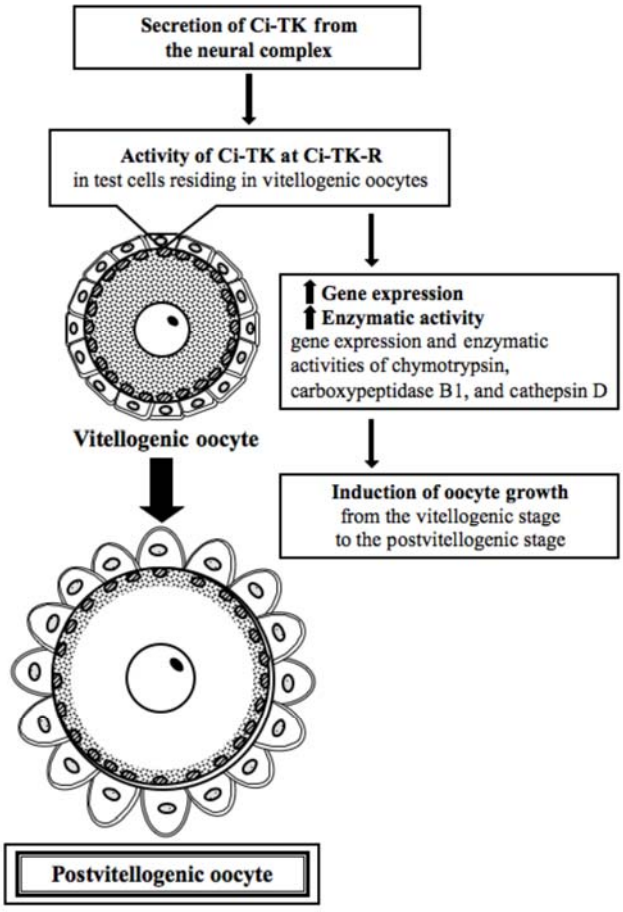
Tachykinins (TKs) and their receptors have been shown to be expressed in the mammalian ovary. However, the biological roles of ovarian TKs have yet to be verified. Ci-TK-I and Ci-TK-R, characterized from the protochordate (ascidian), *Ciona intestinalis*, are prototypes of vertebrate TKs and their receptors. In the present study, we show a novel biological function of TKs as an inducible factor for oocyte growth using *C. intestinalis* as a model organism. Immunostaining demonstrated the specific expression of Ci-TK-R in test cells residing in oocytes at the vitellogenic stage. DNA microarray and real-time PCR revealed that Ci-TK-I induced gene expression of several proteases including cathepsin D, chymotrypsin, and carboxypeptidase B1 in the ovary. The enzymatic activities of these proteases in the ovary were also shown to be enhanced by Ci-TK-I. Of particular significance is that the treatment of *Ciona* oocytes with Ci-TK-I resulted in progression of growth from the vitellogenic stage to the postvitellogenic stage. The Ci-TK-I-induced oocyte growth was blocked by a TK antagonist or by protease inhibitors. These results led to the conclusion that Ci-TK-I enhances growth of the vitellogenic oocytes via upregulation of gene expression and enzymatic activities of the proteases. This is the first clarification of the biological roles of TKs in the ovary and the underlying essential molecular mechanism. Furthermore, considering the phylogenetic position of ascidians as basal chordates, we suggest that the novel TK-regulated oocyte growth is an 'evolutionary origin' of kinergic functions in the ovary.



Scheme of the novel molecular mechanism underlying the growth of vitellogenic oocytes triggered by Ci-TK-I. Ci-TK-I activates Ci-TK-R specifically expressed in test cells residing within vitellogenic oocytes, and then upregulates gene expressions and enzymatic activities of chymotrypsin, carboxypeptidase B1, and cathepsin D. The resultant increased protease activities enhance growth of oocytes from the vitellogenic stage (stage II) to the postvitellogenic stage (stage III).