Identification and molecular control of diapause-inducing signal in silkworm

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Diapause is a programmed developmental arrest in insects to survive unfavorable environmental conditions. Diapause research is most advanced in the domestic silkworm *Bombyx mori*, and they induce embryonic diapause beyond generations as a maternal effect. Offspring diapause is determined by the environmental temperature and photoperiod during the embryonic development of the mother moths. Female moths destined to produce diapause eggs release diapause hormone (DH) into hemolymph during the pupal-adult stages. DH acts on a DH receptor in the ovaries to induce offspring diapause. Recently, *pnd* (*pigmented and non-diapausing*) and *pnd-2* have been identified as the downstream factors of DH signaling.[1] However, the molecular mechanism of diapause regulation through the PND and PND-2 signals is still unclear.

We began by bioinformatic analysis which led us to discover that PND and PND-2 are structural homologs of mammalian interleukin-17 (IL-17) and its receptor (IL-17R), respectively. Transient expression analysis in *B. mori*-derived cells demonstrated that PND-2 localized on the cell membrane and PND co-localized with PND-2. Protein-protein interaction between PND and PND-2 was shown with a NanoBiT split luciferase complementation assay. These results indicated PND and PND-2 may act as a ligand-receptor pair to induce diapause in silkworm. We have further shown that cyanidin, an IL-17 signaling inhibitor, can inhibit PND/PND-2 interaction, meaning the cyanidin may work as a diapause inhibitor.[2] Our SAR study revealed the critical structure of cyanidin to inhibit PND/PND-2 interaction and identified a cyanidin derivative with at least ten times more active than cyanidin. These findings lead to the complete control of silkworm diapause and the development of diapause-disrupting pesticides.

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