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Perspective

Battle of the sexes over paternity

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Reproductive behaviors have evolved through severe inter-sexual competition. We have recently described a behaviour in post-mated female *Drosophila melanogaster* that controls ejaculate retention and sperm storage, and is a possible mechanism by which females who have mated with several partners can choose which sperm that is stored and used for fertilization. This behaviour can also regulate exposure of the female to harmful effects of male SFP that are present in the ejaculate. Our study identified the neural pathway functioning in the female brain that regulates this behaviour. [BMB Reports 2015; 48(0): 0-0]

It is common place in the Animal Kingdom for females to mate with more than one male. These polyandrous mating systems can increase female fitness by reducing the risk of infertility and, when sperm from different males co-reside in the female, can provide opportunities for competition between sperm from different ejaculates and for females to bias paternity towards the sperm of a preferred male, a phenomenon known as CFC. It is now recognized that both of these examples of PCSS can have profound biological impact in driving evolutionary change. A remarkable example of CFC was demonstrated in the domestic fowl where sperm from socially subordinate males is preferentially ejected from the female reproductive tract (henceforth, sperm ejection).

The reproductive success of males, on the other hand, will often depend upon avoidance of sperm competition by preventing mated females from copulating and receiving sperm from other male suitors. In *D. melanogaster*, males use SFP to construct a mating plug in the female reproductive tract to block insemination by other males. Other *Drosophila* SFP also confer a competitive advantage to males by altering female behavior (e.g. rejection of courting males). SFP can however compromise female fitness and even shorten her life-span. This cost to the female is the basis of sexual conflict in *Drosophila*, an evolutionary arms race between the sexes. Under these circumstances, females are expected to evolve mechanisms to control exposure to the male ejaculate in order to maximize fitness by balancing the positive and negative impacts of SFP.

The fruit fly *D. melanogaster* has become a model *par excellence* to study many behavioral and developmental paradigms, including PCSS. It is well known that some *D. melanogaster* SFP compromise female fitness, driving sexual conflict. Despite advances in our understanding of the male strategies in the sexual arms race, we know very little about how female flies counter the male tactics, and the underlying mechanisms linking female behavior to sperm storage, sperm competition and the defense against male seminal substances toxic to the female. In our recent study, we discovered that *D. melanogaster* females actively eject sperm and seminal substances with a stereotypic behavior after they store a fraction of received sperm, and that this sperm ejection behavior is regulated by a highly conserved brain signaling pathway, composed of a neuropeptide Dh44 and its receptor (Dh44R1). Flies lacking Dh44 or Dh44R1 eject sperm precociously, and cannot store sperm. In contrast, enhancing activities of Dh44 or Dh44R1 delays sperm ejection. We mapped Dh44 function to a subset of neurons located in specific brain region, which we name as Dh44-PI neurons. Dh44 is the insect counterpart of the vertebrate CRF, which has a plethora of biological functions, including ones associated with systemic stress responses in mammals. Remarkably, we also found that salt induced kinase 2, a known regulator of mammalian CRF expression, is also expressed in the fly Dh44-PI neurons. The strong and multi-level conservation between Dh44 and CRF signaling pathways suggests an intriguing possibility that CRF may function in vertebrate reproductive biology in a similar way to that of Dh44 in insect reproduction.

Male ejaculate substances including SFPs play a critical role in determining the fertilization success of *Drosophila* males. However, such efforts to ensure paternity might not be in the reproductive interest of promiscuous females who wish to

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Abbreviations: CFC, cryptic female choice; CRF, corticotrophin releasing factor; diruretic hormone 44 (Dh44); PCSS, post-copulatory sexual selection; SFP, seminal fluid protein

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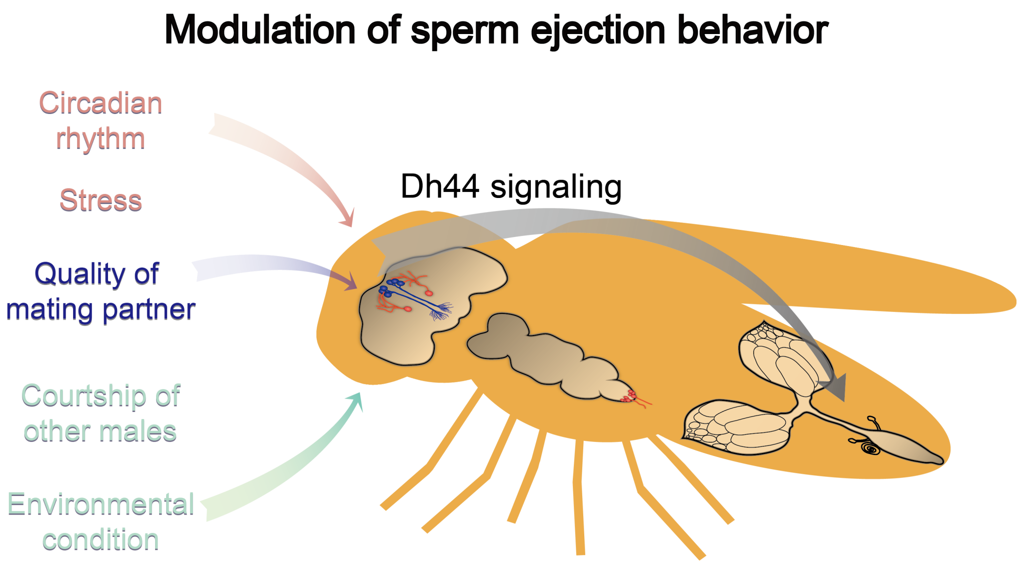

Fig. 1. To maximize their fitness, polyandrous females can bias the use of sperm from multiple mates by modulating the temporal delays to sperm ejection according to various external (courtship quality of male mates, social interactions etc.) and internal cues (internal clock, nutritional and physiological states etc.). The brain Dh44 pathway may serve as a brain center that integrates multiple internal and external cues and modulates the post-copulatiory sperm ejection decision.

choose their mates. In our study, we noted strong positive correlation between sperm ejection latency and sperm storage. Consistent with this, the timing of plug and sperm ejection by the female has been shown to have a direct influence on paternity. Delayed sperm ejection by a female after a second mating results in biased paternity in favour of the second male compared to individuals with a shorter sperm retention time. Thus, active regulation of the timing of sperm ejection could provide a mechanism by which females select sperm from different ejaculates to improve reproductive success.

The major factor that has a strong and direct influence on PCSS is the social environment of females, which is mainly shaped by courting males before and even after copulation. Physical environments, such as food source, may also be important for PCSS, because females mate with multiple partners in the presence, but not the absence of food. In addition, internal physiological states such as those associated with nutrition and reproduction are also likely to be important in modulating PCSS. Thus, identification of the brain pathway that regulates timing of sperm ejection offers a new avenue to study how the female brain integrates multi-modal sensory cues and internal state-coding signals, for coordinating behavioral decisions at neuronal and molecular levels (Fig. 1).

Although we have noted the importance of the Dh44 pathway as a mechanism for females to control the timing of sperm ejection and the period of exposure to harmful SFP, we speculate that, as a result of sexual conflict, males may have evolved measures to manipulate the Dh44 pathway. For example, it is possible that some SFP that promote sperm storage might activate the female Dh44 pathway. It is also equally possible that males might have evolved SFP that inhibit the Dh44 pathway, because accelerating removal of the second mate sperm would favor the first mate sperm releasing the inhibitory SFP in sperm competition. Thus, it is yet too early to conclude which sex has won the battle over paternity.

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