New evidence for female control in reproduction

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Adding another layer of competition to the mating game, scientists are reporting possible biochemical proof that the reproductive system of female mammals can “sense” the presence of sperm and react to it by changing the uterine environment. This may be the molecular mechanism behind post-copulatory sexual selection, in which females that have mated with several partners play a role in determining which sperm fertilizes their egg.

Lead author Alireza Fazeli says that the deep new molecular insights into this post-coital “ladies’ choice” has profound implications for in-vitro fertilization (IVF), cloning, and animal breeding. It is also a windfall for evolutionary biology, providing a possible explanation for female promiscuity in the animal kingdom, he adds.

In a first-of-its-kind study scheduled for ACS’ *Journal of Proteome Research*, Fazeli’s international scientific team reports the first chemical evidence of a sperm recognition system in the oviducts of pigs — standard animals for such research because their reproductive systems are similar to humans.

In the traditional view, competition for the egg is male-oriented, with sperm themselves deciding which fertilizes the egg by being the faster swimmer. With post-copulatory sexual selection, the female is in control, her oviducts selecting the “winner”— the best quality sperm from the healthiest male — and rejecting the rest.

“This study clearly shows that the sperm’s arrival in the female reproductive tract triggers a cascade of changes that leads to alteration of protein production in the oviduct and a change in the oviductal environment. We speculate that this is mainly done to prepare oviduct environment for storing sperm, fertilization and early embryonic development,” Fazeli said. However this can also be used as a detection and selection system that alerts females to the presence of different kinds of sperm and then triggers mechanisms in the oviducts that control sperm transport, binding and activation for fertilization.

“We know sperm selection exists in nature, especially in promiscuous species, when females mate with several males,” Fazeli said. “Baboons are a good example. During one reproductive cycle, if the female mates with several males, most of the time the offspring belong to one of the males — not a spread between all of them… We are now seeing what can be the molecular basis for this effect.”

While sperm interaction with oviduct cells has been studied in laboratory cultures, the new research is the first to provide evidence for this poorly-understood process in living animals, Fazeli said. Using minimally invasive techniques, the researchers compared protein changes in the oviductal fluids before and after sperm introduction to the reproductive tract.

The data shows that the mammalian female reproductive tract is a far more tightly regulated environment than once thought — a fact that Fazeli says is “nearly completely ignored by modern IVF.” He believes the new findings have profound implications for the massive IVF industry, which has grown exponentially in the past 25 years, as well as cloning. Both techniques rely on egg fertilization outside of their finely-tuned reproductive environment.

“The female reproductive tract is a very highly organized and regulated

system," Fazeli explained. "With IVF, the embryo can develop into an adult, but the question remains: 'Are we doing the fine-tuning right'? We are not sure if what we are doing, based on differences between in-vitro and in-vivo fertilization, is creating health problems for these babies."

Applications for this research extend into agricultural animal breeding, since it has the potential to improve fertilization rates and reproductive techniques in livestock.

Fazeli suggests that the work his team is doing is also applicable to the artificial insemination industry. Some of the products that a female's oviducts produce in response to sperm are meant to store and keep the sperm alive. This may be an aspect of post-coital sexual selection since sperm may remain viable in the human female's reproductive tract for nearly five days. Other female animals sustain sperm for even longer periods—bats can do so for up to six months.

Fazeli said that another aspect of this work relates to understanding the mechanisms involved in determination of self and non-self by the immune system. Since sperm are a foreign entity in the female reproductive tract, the immune system should attack and destroy them. In reality, however, sperm are protected and stored.

The traditional explanation is that sperm somehow evade the immune response. Fazeli says his data shows that this is not true. He found that the female immune system instead recognizes sperm as a friend, not a foe. Fazeli suggests that the female reproductive tract is equipped with sensory systems that recognize sperm and alert the ancient, non-specific "innate" immune system to dampen its reaction towards them.

"The main message from this work is that the female reproductive tract has a lot more control than previously thought," says Fazeli. "This discovery profoundly influences our understanding of the physiology of

events leading to conception and the bearing of offspring."

Source: American Chemical Society