Study finds neutralizing an immune system gene could improve the success of fertility treatments in women

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Difficulty in conceiving a child is a major challenge for one in seven heterosexual couples in America, especially for those over the age of 35. Now a new discovery by researchers at Tel Aviv University and Chaim Sheba Medical Center at Tel Hashomer could boost the chances of conception in women undergoing in vitro fertilization (IVF) treatments.

Their new research reveals a linkage between the genes of the innate immune system—immunity with which human beings are born, rather than immunity they acquire during their lives—and ovarian longevity.

The study, published recently in the *Proceedings of the National Academy of Sciences*, constituted the doctoral work of Dr. Shiri Uri-Belapolsky of TAU's Sackler School of Medicine. The research was led by Prof. Ruth Shalgi, of the Department of Cell and Developmental Biology at TAU's Sackler School of Medicine, Dr. Yehuda Kamari and Prof. Dror Harats of TAU's Sackler Faculty of Medicine and Sheba Medical Center, and Dr. Aviv Shaish of Sheba Medical Center.

According to research conducted on laboratory mice, the genetic deletion of the protein Interleukin-1 (IL-1), a key player in the innate immune system, could improve the number of eggs available for fertilization as well as improve the ovarian response to hormonal stimulation involved in IVF procedures. This could prove especially effective in women who initially respond poorly to hormonal treatment.

Neutralizing the risks

"We revealed a clear linkage between the genes of the innate immune system and female reproduction," said Dr. Uri-Belapolsky. "The results of our study, which point to neutralizing the effects of the IL-1 protein to slow down the natural processes that destroy the eggs, may set the basis for the development of new treatments, such as an IL-1 blockade that would raise the number of eggs recovered during an IVF cycle and reduce the amount of hormones injected into women undergoing the treatment."

The connection between IL-1 and fertility was discovered by accident in the course of research performed by the scientists on the role of IL-1 in atherosclerosis, the hardening of the arteries. In a surprise result of the research, the fertility lifespan of IL-1-deficient mice was found to be 20% longer than that of control wild-type mice.

Keeping the clock ticking

Female mammals, including humans, are born with a finite number of eggs and are subject to a biological clock that dictates the end of the reproductive lifespan at around 50 years of age. Over the past decade, a trend of postponing childbearing into advanced age has led to a corresponding upward trend in the number of IVF treatments. Inflammation has been reported to affect both IVF outcomes and the ovarian reserve adversely. "Identifying a possible culprit, such as Interleukin-1, may offer new insight into the mechanisms responsible for egg loss as well as practical interventions," the study reports.

"Our revelation is secured with a patent application, and naturally, further study in mice and in humans is required to examine this therapeutic opportunity," said Prof. Shalgi. "I believe we will take this research forward into human clinical trials. However, there is still research to be done before we can start these trials."