

# Researchers find important clue to immune infertility

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Most of us have never heard of immune infertility, yet it prevents many prospective parents from conceiving.

Immune infertility is one of 80 autoimmune disorders, a group that includes better-known diseases like Multiple Sclerosis and Type 1 Diabetes. This reproductive disorder affects both men and women, causing their immune systems to wage war on sperm.

A recent discovery at the University of Virginia Health System may help pinpoint what molecules assist the immune system in attacking sperm. In the July 2007 issue of *Gene*, UVA researchers reported finding a new human protein, radial spoke protein 44 (RSP44). Exposure to RSP44 caused infertile men to produce antisperm antibodies (ASA) in their serum.

“We’ve spent several years looking for sperm molecules that evoke antibody responses in humans,” says Dr. John C. Herr, director of UVA’s Center for Research in Contraceptive and Reproductive Health. “The identification of RSP44 gives us additional insight into immune infertility and may prove useful in diagnosing the disorder in a subset of men. RSP44 will likely not be a dominant antigen in everyone.”

Researchers believe that RSP44 belongs to a highly conserved and ancient gene family. It can be found in all men, residing in the sperm tail at the center of a structure known as the axoneme. There, it clusters around microtubules involved in sperm movement. Both men and

women have RSP44 in hair-like strands, called cilia, in the bronchioles of their lungs, the ventricles of their brains and the lumens of their thyroid gland.

The discovery of RSP44 also promises to broaden scientific thinking about the causes of immune infertility. Until now, researchers believed that ASA only targeted the surface of the sperm membrane.

“Because RSP44 is located in the heart of the axoneme, it doesn’t appear to be directly involved in ASA binding at the sperm membrane. Identifying RSP44 as an antigen in several individuals indicates it may serve as a useful biomarker of the anti-sperm response,” notes Dr. Jagat Shetty, lead author of the UVA paper. “There may be mechanisms underlying infertility that are yet to be discovered.”

Women with immune infertility produce ASA in their reproductive tracts. These antibodies neutralize sperm by clumping them together and poking holes in their membranes. ASA also coats over receptors involved in sperm-egg binding and fertilization.

An estimated 12 to 15 percent of unexplained infertility in women is linked to ASA. In rare cases, these antibodies have caused women to go into anaphylactic shock upon insemination.

In men, immune infertility has several causes, including vasectomies. After a vasectomy, the body can no longer release sperm and produces antibodies to help engulf and clear them. ASA persist for years in the circulation of vasectomized men and may cause reduced fertility in those who have the procedure reversed (vasovasostomy).

Several therapeutic procedures available through UVA, such as sperm washing and intra-cytoplasmic sperm injection, have proven beneficial to patients with ASA.

Source: University of Virginia

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