SAN DIEGO SCIENTISTS PROVIDE NEW CLUES TO THE BIOCHEMISTRY OF FERTILIZATION

La Jolla, CA. -- A team of researchers at The Scripps Research Institute and UCSD's Scripps Institution of Oceanography has discovered the molecular structure of a key protein that offers insight into the process of human fertilization and reproduction and may lead to the development of a new class of contraceptives.

The finding, to be published in the Dec. 17 issue of the journal Science, elucidates the structure of the protein that allows abalone sperm to fertilize eggs.

"The molecular process by which animal sperm penetrate egg envelopes isn't known. The abalone provides a model system in which to study it," said Victor D. Vacquier, a scientist at UCSD's Scripps Institution of Oceanography who purified a fertilization protein called lysin found in abalone sperm.
Three researchers at The Scripps Research Institute, Andy Shaw, Duncan McRee, and David Stout, solved the three-dimensional structure of abalone lysin using X-ray crystallography. The process involves scanning crystals of lysin with an X-ray beam and then studying the diffraction pattern, or arrangement of spots the crystal creates on film, to construct a picture of how the atoms in each molecule are arranged.

According to David Stout, "This is the first time that a fertilization protein has been visualized. Now that we have determined the structure of the protein, we can conduct experiments to understand how it functions."

Abalone eggs are similar to human eggs in that they are contained within an envelope. The abalone sperm penetrates the envelope by releasing lysin. Whereas scientists had previously postulated that sperm passed through the envelope by releasing an enzyme that destroyed the envelope's integrity, the new work shows that lysin is not an enzyme. It interacts with the surface of the envelope, causing it to disassemble. "The envelope is made up of long, thin fibers that are intertwined in an extremely tight and tough meshwork, and what the lysin protein does is to destroy the cohesiveness of the fibers," Vacquier said.
The mechanism lysin uses to disrupt the structural integrity of the egg envelope remains unclear. It may act, however, by destroying hydrogen bonds or inducing structural changes in envelope molecules that cause them to dissociate. The fact that the process is non-enzymatic is significant, Vacquier said, because similar interactions may be occurring in other processes where cells try to invade each other, including cancer.

According to the scientists, no one has ever looked for surface active proteins being involved in normal development or disease processes.

Because abalone release their sperm and eggs into the sea, survival of the species hinges on the ability of the sperm and egg to successfully recognize and interact with one another.

The researchers observed that lysin appears to be species specific. Sperm of red abalone, for example, were found to be much more capable of penetrating the envelopes of eggs from red abalone than those from the pink abalone.

"We think that changes in the structure of lysin might be part of the speciation process," Vacquier said.

Scientists often conduct fertilization research using marine invertebrates because they can easily obtain the large quantities of eggs and sperm needed for study. Much of the work conducted in marine invertebrates lays the groundwork for understanding fertilization in other animals, including humans.