proteinspotlight
> ONE MONTH, ONE PROTEIN <

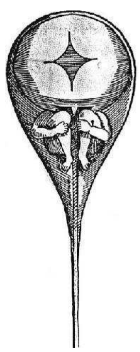
Issue 62, September 2005

www.proteinspotlight.org

Shackled sperm

Vivienne Baillie Gerritsen

We are all looking for attention. One way or another. Even spermatozoa. In its race to fertilise, a spermatozoon modifies the egg's surface thereby demolishing the hope of millions of its kind. It may lack fair play but it certainly is an effective way of grabbing attention. This is exclusiveness on the level of sperm. However, scientists are beginning to realise that semen also has its ways: coagulation. What better way to hinder the advancement of a supplementary troop of sperm than by the erection of a biological fortification? When semen is ejaculated, it coagulates almost instantly to then liquefy slowly, unshackling spermatozoa in the process. A number of chemical entities are involved, one of which is semenogelin, the protein which forms the coagulate scaffold.



Shackled sperm?

A human sperm cell
Nicolas Hartsoeker (1656-1725)

There are not many spermatozoa swimming around in semen. It varies from species to species but, on the whole, less than 10% of mammalian seminal fluid is made up of sperm. What makes up the other 90%? Semen is a cocktail of molecules synthesized in various organs – the testes, the prostrate gland and the seminal vesicle to name but three – and which are decanted into the urethra prior to ejaculation. All sorts of ions, peptides and proteins along with millions of spermatozoa form a mucous fluid, and it is their mingling which triggers off a number of biological processes either before ejaculation or after.

Semenogelins are the major structural proteins found in semen and are actively involved in creating a scaffold which traps spermatozoa in the female tract. They are synthesized in the seminal vesicle – a vesicle situated not far from the prostrate gland. Upon ejaculation, semenogelins as well as a host of other components interact, first to cause semen coagulation and then, minutes later, semen liquefaction.

How semen coagulates and then liquefies is still a mystery but fragments of information are beginning to give a picture. The main instigator of coagulation is most likely zinc. Zinc binds to semenogelins and in doing so probably brings about conformational changes thereby causing them to bind to one another – though it is still not clear – or to fibronectin, a protein also synthesized in the seminal vesicle. The net result is the formation of a solid scaffold which hinders sperm motility.

Whether the semenogelins actually dock to sperm or not is still unknown. They could bind to the sperm membrane via its phospholipids and in doing so allow the passage of ions which ultimately immobilise sperm. Or they could bind to membrane receptors which trigger off biological processes which in turn block sperm movement. Or perhaps the scaffolding they form is sufficient enough to prevent sperm from wriggling. Or maybe they can actually enter the sperm and tamper with the dynein machinery in their flagella… There seem to be as many hypotheses as there are spermatozoa.

The fact that zinc ions are lapped up in this coagulation process enables a protease – known as prostrate-specific antigen or PSA – to function, since it is inhibited in the presence of zinc. It does so by slicing the semenogelins into small peptides. This is the process of semen liquefaction. As a result, the spermatozoa are free to go and the zinc ions free again to inhibit the protease thus avoiding further – and perhaps harmful – degradation of semenogelins.

Why is it that further degradation of semenogelins could be harmful since they have performed their purpose, i.e. coagulation? Besides their capacity to form a semen gel, processed semenogelins may also be involved in sperm motility, sperm capacitation or even egg-binding. What is more, there may be receptor sites for these bioactive peptides within the female tract where they could be involved in immunosuppressive reactions or muscle contraction to pave the sperm's way. To date though, all this is speculation.

Trapping sperm when the whole point of ejaculation is to fertilise an egg in the first place seems a bit of a paradox. There are a number of hypotheses. Spermatozoa smothered in seminal fluid are protected from an immune response that could be triggered off by the recipient female. The semenogelin scaffold could also prevent spermatozoa from changing their mind and heading back from where they came. A coagulated semen cocoon could also act as a means of protection as spermatozoa begin their long journey towards the egg.

Another interesting postulate – and which seems to be gaining ground – has to do with female promiscuity and sperm competitiveness. When semen coagulates in the female tract, it forms a barrier – or natural chastity belt – against subsequent insemination by a second male. Evolutionary studies using semenogelins as candidates have shown that primates such as chimpanzees – where the females are promiscuous (polyandrous) – display semen which, upon ejaculation, forms a firm coagulate. Gibbons on the other hand are satisfied with one partner and their ejaculate remains liquid. Humans are in between. There seems, therefore, to be some kind of correlation between sexual behaviour and the type and quantity of semenogelin in male semen.

Certain types of infertility probably arise from semenogelin dysfunction. If semen liquefaction is hindered, spermatozoa are not released and cannot approach the egg. On the other hand, even following liquefaction, some semenogelin peptides could enter the spermatozoa and affect their motility irreversibly. Obviously, a greater understanding of the proteins will lead to novel therapies in the diagnosis and treatment of infertility. Antibodies that recognise semenogelins have already been commercialised and used in forensic specimens to detect semen. Treatments against prostrate cancer could also be imagined. PSA, for instance, could be tricked into recognising semenogelin peptides which carry drugs. Such prodrugs would be cleaved within the prostrate and subsequently delivered. Whatever the outcome, semenogelins are of growing interest, be it to conquer infertility or to discover our ancestors' sexual behaviour.

Cross-references to Swiss-Prot

Semenogelin-1, *Homo sapiens* (human) : P04279
Semenogelin-2, *Homo sapiens* (human) : Q02383

References

1. Robert M., Gagnon C.
   Semenogelin I: a coagulum forming, multifunctional seminal vesicle protein
   Cell. Mol. Life Sci. 55:944-960(1999)
   PMID: 10412373

2. Jensen-Seaman M.I., Li W.H.
   Evolution of the hominoid semenogelin genes, the major proteins of ejaculated semen
   J. Mol. Evol. 57:261-270(2003)
   PMID: 14629036