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Molecular chastity

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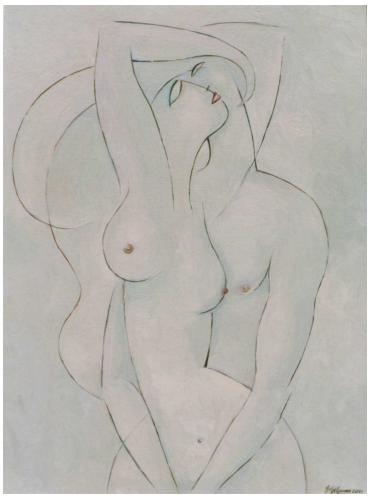
Triggering off the making of a baby may seem a pretty straightforward process. Which it is, from a certain point of view. Yet, before any decisive action is undertaken by a woman and a man in order to unite their gametes, sperm – like ovules – have already been through a very complex series of developmental transformations. Such transformations ensure that only sperm and ovules of the same species get involved with one another, for example, or that once a couple of gametes has united no one else is allowed in. Properties of this sort are expressed on the molecular level both on the sperm's and the ovule's surface. One such molecule is a receptor known as zp3 found in mammals. Zp3 is expressed on the ovule's surface and, though it is just one of many molecules, it is an essential one. Without it, sperm would not only be incapable of binding to the ovule's membrane but they would also most probably miss their target altogether.



'Tenderness' by Vladas Velyvis

Source : http://www.velyvis.com/

Sperm have been fertilizing ovules for millions of years and yet we are only just beginning to understand the rudimentary fundaments involved. Over the millennia, the miracle of conception has occupied some of the most learned minds and, before the existence of the microscope, a vivid imagination was required to make sense out of the liquid men injected into women, which ultimately produced a new version of one of them. A baby boy or a baby girl. Hence the existence of what may seem preposterous theories to us now but which were perfectly sensible in the light of what was then known. For instance, two opposing schools of thought lasted for a very long time. There were those who believed that a complete – but very small version of a human – was contained within one sperm and, once in the woman's womb, it grew to the size of a newborn. And then there were those who believed that a perfectly-shaped baby human was already floating in the ovule and that all it needed was the sperm to trigger off its growth.

Despite an apparent simplistic view of how Nature dealt with things, what had been understood is that both a sperm and an ovule are necessary for conception. Nothing happens in the absence of the other. And that remains a fact. What we know today is that both gametes can be present and, what is more very close to one another, but if there is something faulty on either one's surface, nothing will happen. And this is frequently the cause of infertility – male or female. Gametes have a very specific and intricate makeup. There are molecules on their surface which have a protective role, molecules which recognise the other and molecules which allow them to adhere to one another. Zp3 – for zona pellucida 3 – is a protein receptor which is buried in the matrix which surrounds an ovule, known as the zona pellucida. This is the cushiony part of the cell, full of carbohydrate and protein in almost equal amounts, through which one sperm must find its way to initiate fertilization.

Zp3 is a cell surface receptor which is bound to the ovule's membrane. Typically, the protein backbone of zp3 is covered in O-linked oligosaccharides which make up part of the zona pellucida cushion. These particular carbohydrates are recognised by a receptor found on the sperm's surface. Despite this recognition, scientists believe that the binding of a

sperm to an ovule also involves a host of other molecules. What is clear though is that zp3 and its oligosaccharides are needed to initiate the acrosome reaction – the reaction in which the sperm binds irreversibly to the ovule's membrane and, in so doing, triggers off the chemical process which modifies the supra-molecular structure of the zona pellucida thus forming a barrier to the entry of a second sperm.

Besides discovering the beauty of how life starts on a very small scale, the finer our knowledge is on the molecular processes involved in the moments before and during fertilization, the better we can help men and women faced with infertility problems. Similarly, targeting essential molecules on the surface of sperm or ovules could lead to alternative methods of contraception. Research of the kind has been carried out in the hope of checking the exponential growth of animal populations. Protected from ivory poachers and squeezed into geographical spaces that are getting smaller all the time, elephants are overpopulating game reserves in Africa. Instead of shooting them, a means of birth control would be a more humane solution. Since the 1990s, scientists have been seeking ways of producing antibodies to zp3 for instance, which would create temporary infertility. Some have suggested engineering a virus with a copy of human zp3 and intentionally infecting an animal species whose growth has gone out of control. For instance, mice infected with the virus would produce zp3 antibodies, thereby causing infertility of their host because mouse zp3 is very similar to human zp3. Furthermore, one mouse would infect another mouse, and each infected mouse would in turn become infertile. The problem is: who says the virus won't infect another animal population which is essential to the fauna's equilibrium… It is a risk which cannot be taken.

Likewise, immunity of some kind against zp3 could be an elegant form of contraception for humans. It is common knowledge that, though very useful in many ways, the pill or intrauterine devices can be damaging to women – so any method which could prove to be absolutely harmless is welcome. Recently, some scientists suggested a gene-silencing technique whereby the zp3 gene is not translated. This is done by using a method known as RNA interference. In this case, short RNAi fragments bind to zp3 mRNA thus checking zp3 translation. Consequently, the zp3 receptor does not appear on the ovule's surface and sperm are then unable to bind to an ovule – which is a sure means of avoiding conception. This kind of contraceptive could be administered through a skin patch or by means of a vaginal suppository. And scientists are confident that such treatment will only affect the zp3 receptors of maturing ovules – i.e. the ones that make an appearance once a month – and not the whole reserve in the ovary. It sounds promising and attractive. And far more appealing than a chastity belt.

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