Unlocking the key to human fertility

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Scientists at Leeds and Bradford have discovered a unique 'DNA signature' in human sperm, which may act as a key that unlocks an egg's fertility and triggers new life.

Drs David Miller and David Iles from the University of Leeds, in collaboration with Dr Martin Brinkworth at the University of Bradford, have found that sperm writes a DNA signature that can only be recognised by an egg from the same species. This enables fertilisation and may even explain how a species develops its own unique genetic identity.

Dr Iles says, "What we have discovered is a previously unrecognised DNA packaging 'signature' in mammalian sperm that may be essential for successful fertilisation of the egg and development of the embryo. We think it may also be ancient in origin."

Without the right 'key', successful fertilisation either cannot occur, or if it does, development will not proceed normally. Notably, disturbances in human sperm DNA packaging are known to cause male infertility and pregnancy failures.

This 'lock and key' mechanism has other profound implications. Not only does it explain why some otherwise healthy men produce sperm that is sterile, but it also explains how different species evolve and retain their own identity.

Says Dr Miller, "Up until now, Doctors have struggled to understand

idiopathic male infertility. Our latest research offers a plausible explanation for why some sperm malfunction or fail to function correctly."

If the DNA carried by a sperm cell was unwound and stretched out, it would actually measure more than a metre in length. In order to fit all this DNA into the microscopic space within the head of the sperm cell, the DNA needs to be very tightly coiled, or packaged. The Leeds study showed that in human and mouse sperm, not all of the DNA is packaged in the same way. Whilst most of the paternal DNA is compressed in an extremely compact fashion, some is packaged less tightly.

"There is a definite pattern to the way DNA is packaged in sperm cells and we can see that this pattern is the same in unrelated fertile men. It is different in the sperm of infertile men. This implies that there is a significance to the packaging of DNA that has a direct relevance to male fertility," says Dr Iles.

Detailed analyses of the DNA in the 'open', less tightly packaged conformation, showed this DNA carries much of the information critical for activating genes essential for directing the development of the embryo. Further investigations showed the same conformation to exist in the sperm of several unrelated human donors and remarkably, highly similar packaging patterns to exist in the sperm of mice.

DNA regions in the 'open' conformation may therefore be more vulnerable to damaging toxins, such as those in cigarette smoke and certain anti-cancer drugs, than those that are tightly packaged. As Dr Brinkworth says, "this might mean that anything capable of causing genetic damage to sperm could have particular significance for the development of the embryo".

The findings also help explain why inter-species breeding is so rarely

successful.

Where the locks and keys of two species do not match, however similar their DNA is, no viable offspring can be born. Occasionally, for example, with horses and donkeys, offspring are produced - but because the sperm and egg signatures are incompatible, their development as embryos is abnormal and any offspring are almost always infertile.

The research team believes that the same mechanism must also have played a role during human evolution. In the ancient history of mankind, Neanderthals co-existed with modern humans over many thousands of years. Sexual encounters between these two closely related species cannot be ruled out, yet there is no evidence in our DNA of a legacy from such couplings. It is possible that if offspring were produced, they either did not survive long or if they did, they were unable to breed.

Source: University of Leeds (news : web)