Scientists discover important step in sperm reprogramming

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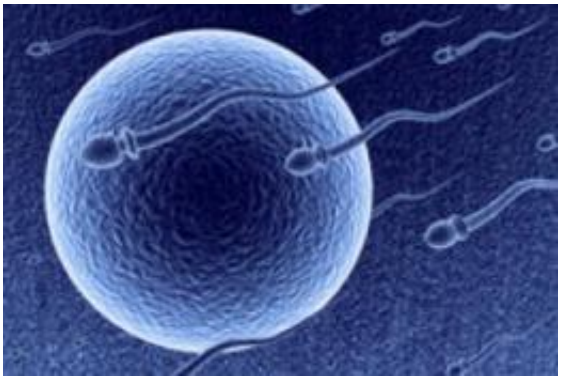

Illustrated here are images of sperm and egg. Credit: NIH

When sperm meets egg, the chemical instructions that tag sperm cells must be erased so that human life can start anew. One way these instructions are erased is through demethylation, the removal of specific chemical tags or methyl groups that dot the underlying DNA of cells. Though scientists have known about this phenomenon for a decade, exactly how such "reprogramming" occurs has proved elusive.

Now, a study from the University of North Carolina at Chapel Hill School of Medicine has illuminated a key step of demethylation, giving stem cell researchers critical information as they try to reprogram adult cells to mimic the curative and self-renewing properties of stem cells.

Previous research had shown that the methyl tags on sperm DNA are

converted to their chemical cousin, hydroxymethyl, before disappearing completely. The current finding, published online in the September 22, 2011, issue of *Science Express*, suggests that the disappearance of these chemical tags in the later steps of demethylation is not an active process catalyzed by an enzyme but is rather a passive process.

"The biological function of this molecular event is not known yet, we are still trying to figure it out," said senior study author Yi Zhang, Ph.D., Kenan distinguished professor of biochemistry and biophysics at UNC and an investigator of the Howard Hughes Medical Institute. "But we do believe it must be important for development, because it happens before the cells committed to any specific cell types." Zhang is also a member of the UNC Lineberger Comprehensive Cancer Center.

Zhang's postdoctoral fellow and co-author Azusa Inoue, Ph.D., developed a technique that enabled him to visualize chromosomes – the threadlike bodies that contain the cell's DNA – at the earliest stage of life. Through a high resolution staining technique, he was able to compare the levels of methyl tags and hydroxymethyl tags in sperm and egg chromosomes at early developmental stages of life.

Their findings confirmed what they already knew – that the sperm DNA goes through a chemical conversion from methyl to hydroxylmethyl while the egg DNA did not. But it also found something new – that the hydroxymethyl tags disappeared passively over time, being diluted out as the DNA divided and the organism doubled from the one-cell to the two- and four-cell stage.

The clinical implications of the finding are still not clear, Zhang says, because researchers still don't know why male DNA undergoes that initial conversion when female DNA does not. It may have something to do with the differential protein structure (chromatin) that packages the DNA of sperm and egg. This is a notion Zhang and others in the field are

actively pursuing.

Provided by University of North Carolina School of Medicine