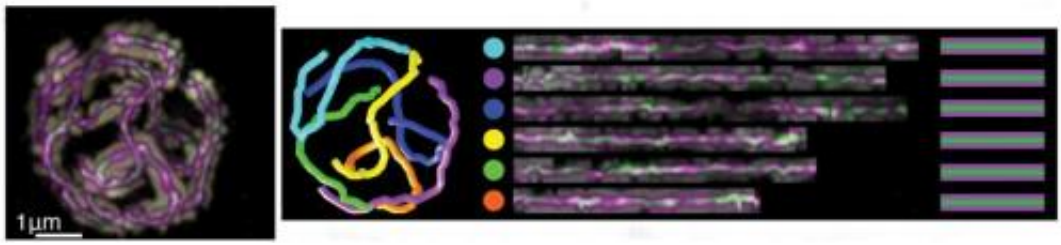
Scientists uncover how protein ensures reproductive success

October 23 2014



Super-resolution microscope image of DNA in the nucleus of a reproductive cell. Credit: Peter Carlton, Kyoto University's iCeMS

An international team of researchers from Japan and the UK has discovered how a single protein, called PP4, oversees the processing of DNA during sperm and egg generation for successful fertilization. This protein's activity becomes even more paramount during aging. The study, published in the journal *PLOS Genetics*, may one day help scientists to understand the mechanisms underlying age-related fertility declines in humans.

While a typical adult human cell contains 46 DNA strands, or chromosomes, that carry our complete genetic information, reproductive cells such as sperm and eggs receive half of this number during a highly intricate process known as "meiosis." How chromosomes are mixed, matched and distributed into reproductive cells accurately is essential for successful fertilization and the development of diverse new life.

However, errors in the system can lead to infertility.

To understand which proteins help meiosis run smoothly, the researchers from Kyoto University's Institute for Integrated Cell-Material Sciences (iCeMS) and Tohoku University in Japan, and Imperial College in London, used a tiny worm known as Caenorhabditis elegans to look into the role of PP4.

The researchers genetically engineered the worm so that PP4 was functionally disabled, and then observed the consequences of its absence on chromosome regulation during meiosis. The researchers used a super-resolution microscope, which takes pictures at twice the level of detail compared to a normal microscope.

"We found that when PP4 was missing, chromosomes failed to assemble correctly and DNA recombination, an important step for genetic diversity, did not occur," said Aya Sato-Carlton a researcher involved in the study from iCeMS. "The resulting eggs were defective, and the embryos inside could not survive after fertilization," added Sato-Carlton.

Surprisingly, the authors observed that the effects of defective PP4 became even worse as the worms aged, indicating an age-related dependence.

Because the PP4 DNA of worms is over 90% identical with that of humans, it is possible that the protein plays a similar role in all animals as a universal regulator of meiosis, particularly as an organism ages.

"However, it's too early to say for certain that PP4 has a similar kind of role in humans", said Peter Carlton, the principal investigator of the study from iCeMS. "The next step is to see whether we observe the same kind of phenomenon in mice."

Provided by Kyoto University