# A protein duo ensures that the chromosomes in reproductive cells find their significant other

October 5 2017

Reproduction is made easier by finding the right partner—and it's no different for the chromosomes inside reproductive cells. Now, an international team of researchers, including A*STAR scientists, has revealed just how chromosomes find their perfect match.

The tightly-wound chromosomes that carry the genetic code inside living cells may float around the cell nucleus on their own, but they all have a genetically similar partner, or homolog, with one inherited from each parent.

During the life cycle of reproductive cells, these homologs need to find and dock to each other to ensure that the DNA is correctly distributed to the sperm or egg: a bad chromosome match can render the entire cell non-functional. Even worse, failure to distribute chromosomes correctly can lead to a variety of inherited disorders.

In 2013, Brian Burke and Colin Stewart from the A*STAR Institute of Medical Biology set out to discover how chromosomes find their match.

They revealed that a protein called KASH5 acts as an adaptor for a molecular motor which shuffles along the microtubule scaffolding of the cell. Mice modified to lack KASH5 were infertile.

The scientists proposed that KASH5 docks to the surface of the nucleus

and teams up with another protein – SUN1 – which locks on to the ends of chromosomes inside the nucleus. With SUN1 and KASH5 attached, the chromosomes inside the nucleus would get dragged along the microtubule scaffolding randomly, allowing for the chromosomes to bump into their homologs.

For this paper, Burke teamed up with scientists at the University of Oklahoma to confirm the theory.

The team stained the DNA in living sperm precursor cells from normal mice and mice lacking KASH5, and imaged the cells' chromosome movements in three dimensions. Specialized algorithms revealed that, unlike normal cells, the chromosomes stop moving when KASH5 is lacking, which confirms the team's model. "This was really gratifying to see," says Burke.

The paper co-authors are now chasing leads on how mutations in either KASH5 or SUN1 could be causing infertility in humans and are investigating how similar protein duos may be working together to distribute the nuclei located in other cell types, such as skeletal muscle cell.

"We have to stop thinking of the nuclear envelope as just sort of a bag for genes which just sit there and do nothing but be transcribed," says Burke. "The whole system is far more dynamic than one would appreciate from reading your average cell biology textbook!"

**More information:** Chih-Ying Lee et al. Mechanism and Regulation of Rapid Telomere Prophase Movements in Mouse Meiotic Chromosomes, *Cell Reports* (2015). DOI: 10.1016/j.celrep.2015.03.045