Swimming with sperm

A putative calcium channel specific to sperm tails may be the best target yet for a male contraceptive. The protein, dubbed CatSper, was discovered in a homology search by David Clapham and colleagues of Harvard Medical School, Boston, MA.

CatSper looks like a calcium channel, although Clapham could not detect a calcium current in transfected cells, probably because another component of the channel is missing. CatSper is, however, required for a calcium influx into sperm that is triggered by cyclic nucleotides. Such signaling events may be part of the process by which sperm either gain their initial motility in the epididymis, or augment that motility (in a process called hyperactivation)

move sluggishly (at approximately one third of the normal rate) and can fertilize eggs only if the eggs have been stripped of their protective coat of zona pellucida.

Based on these data, says David Garbers (University of Texas Southwestern Medical Center, Dallas, TX), a CatSper inhibitor might be useful as a male contraceptive. “The problem with going after a male contraceptive is that you have millions of sperm and you have to get them all,” he says. “Amazingly enough, when this channel was gone they got no fertilization. That makes it reasonably attractive as a drug target.” ■

Reference: Ren, D., et al. 2001. Nature. 413: 603–609.

Killing for love

Embryos are at least half foreign to their mothers. Now, George Chrousos (National Institutes of Health, Bethesda, MD) and colleagues have found that the cells that help an embryo implant also kill off some of the mother’s T cells—the ones that might otherwise reject the embryo as foreign.

The pathway begins with corticotropin-releasing hormone (CRH). As a stress hormone in the body, CRH is first proinflammatory (via mast cell degranulation) and then antiinflammatory (via effects in the brain that induce cortisol production). A similar sequence of events may take place during pregnancy. An inflammatory process is needed to initiate implantation of the embryo into the wall of the uterus. But then CRH, as detailed by Chrousos, induces the expression of the death protein FasL.

This results locally in the death of Fas-expressing activated T lymphocytes.

Blockade of this process with a CRH antagonist results in a 50–70% reduction in the number of successful implantations in pregnant rats. This reduction occurs thanks to T cells. In nude rats, which lack T cells, the number of implantation sites returns to normal.■

Reference: Makrigiannakis, A., et al. 2001. Nat. Immunol. 2: 1023–1029.

Arms together, CENs apart

The cohesin complex acts as a glue for sister chromatids, but in some organisms most cohesin is lost from chromosome arms well before anaphase onset. Now, Robin Allshire (MRC Human Genetics Unit, Edinburgh, UK), Jean-Paul Javerzat (CNRS Institut de Biochimie et Génétique Cellulaires, Bordeaux, France), and colleagues show that Swi6, the fission yeast version of heterochromatin protein 1 (HP1), is required for the association of cohesin with centromeres. This provides one explanation for what Swi6 and heterochromatin are doing at the centromere.

“We knew before that mutants in Swi6 lost chromosomes at a high rate and displayed a high frequency of lagging chromosomes on anaphase spindles,” says Allshire. But the explanation for this defect remained unclear. Was Swi6 helping to establish kinetochore structure? Allshire says this remains a possibility, but for now he has established another explanation. Mutants lacking Swi6 maintain cohesion on chromosome arms during a mitotic block but lose cohesion at the centromeres thanks to the loss of a cohesin subunit.

Swi6 is also required for binding of cohesin near telomeres and the silent mating locus—the other heterochromatic regions in fission yeast. This suggests that kinetochore components are not necessary for Swi6-dependent cohesion loading. Only future work will show whether a direct interaction between Swi6 and cohesin is responsible for loading cohesin. ■

Reference: Bernard, P., et al. 2001. Science. 10.1126/science.1064027, http://www.sciencemag.org/cgi/content/abstract/1064027