Researchers improve technology to save sperm stem cells

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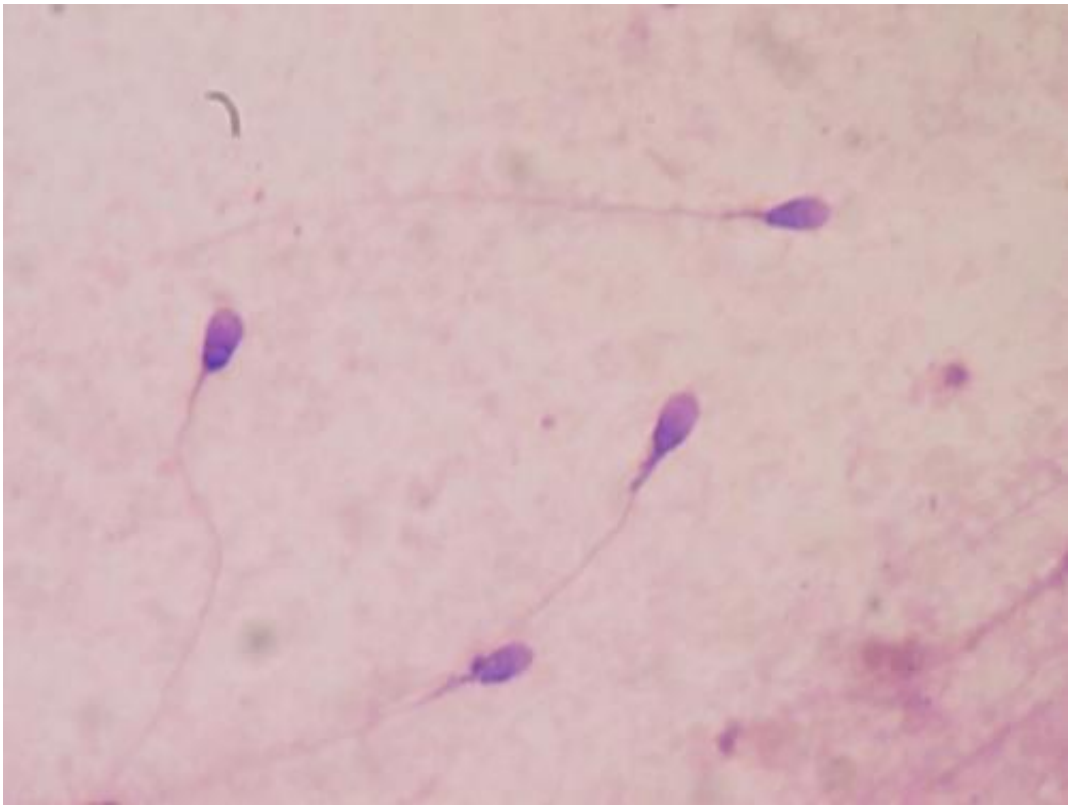

Human sperm stained for semen quality testing in the clinical laboratory. Credit: Bobjgalindo/Wikipedia

Washington State University researchers have found a promising way to preserve sperm stem cells so boys could undergo cancer treatment without risking their fertility.

Adult men can have their sperm frozen before undergoing radiation or chemotherapy, both of which can render sperm infertile. But boys who haven't been through puberty can only have sperm stem cells removed and frozen in anticipation of technology that could culture the cells and place them back in the testes, where they produce sperm after puberty.

Jon Oatley, an associate professor in the WSU School of Molecular Biosciences and director of the Center for Reproductive Biology, said he and his colleagues are well on their way to developing such a technology.

"I think it's going to become the standard by which everybody cultures their cells, including trying to develop conditions for human cells," said Oatley. He and his colleagues—graduate student Aileen Helsel and lab manager Melissa Oatley—report on the new technique in the journal *Stem Cell Reports*.

Stem cell can produce 5,000 sperm

Fewer than 1 percent of the nation's cancer cases involve children, according to the American Cancer Society, which estimated that a little more than 10,000 children under the age of 15 would be diagnosed with cancer last year. Better than four out of five survive five years or more, but prepubescent boys risk getting azoospermia, a lack of viable sperm.

"After the cancer is controlled, the quality of life, which often includes the ability to have a normal child, becomes a major issue," said Marvin Meistrich, a University of Texas oncologist, writing in the journal Pediatric Blood & Cancer.

With each heartbeat, mature, fertile men produce some 1,300 sperm cells. They come from a pool of self-renewing spermatogonial stem cells that are present at birth. As each stem cell differentiates, it can produce some 5,000 sperm.

Eight-fold improvement in viable sperm stem cells

Working with prepubescent mouse pups, Oatley and his colleagues put a fluorescent tag on a gene specific to stem cells. This let them in effect watch the process of a stem cell differentiating to create the progenitors that eventually become sperm.

Early in the process, they saw the stem cells creating energy through one method, called glycolysis, then switching to another method. The second method, called oxidative phosphorylation, produces free radicals, reactive forms of oxygen that can be particularly harmful to a cell's DNA.

"If you're a stem cell that is going to give rise to sperm essentially through the whole lifetime of an individual, you want to have a pristine genome," said Oatley. "You don't want it damaged by reactive oxygen species. That's why we think glycolysis is important for the stem cell. So we tried to change the culture environment to favor glycolysis."

By lowering the oxygen in the culture—adding nitrogen to cut it by more than half—the researchers found they could dramatically improve the percentage of stem cells capable of making normal sperm when put back into the testes. Where before only 5 percent of the cells remained viable after six months, now 40 percent were viable.

"We're getting an eight-fold improvement," Oatley said.

Next steps: Epigenetic, human tissue studies

The WSU researchers still have a host of challenges to confront. Working with Marisa Bartolomei at the University of Pennsylvania, they plan to see if the cultured stem cells undergo changes to their

epigenome, which determines if genes are turned on and off. The team also will investigate whether the technique will work with human tissues.

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