Protein Important in Blood Clotting May Also Play a Role in Fertility

October 19 2006

A protein known to play a role in blood clotting and other cell functions is also critical for proper sperm formation in mice, according to researchers from the University of North Carolina at Chapel Hill School of Medicine.

Male mice missing both copies of the gene that produces the protein, called CIB1, have testes about half the normal size, have smaller numbers of the cells that give rise to sperm and produce no mature sperm at all, the researchers found. Female mice missing CIB1 were fertile, as were males missing only one copy of the CIB1 gene. Mice, like humans, have two copies of every gene, one from each parent.

The serendipitous discovery occurred when lead study author Dr. Weiping Yuan, intending to study CIB1's role in blood clotting, bred mice missing the CIB1 gene. All male mice bred without both copies of the gene were infertile, said Yuan, UNC research assistant professor of pharmacology.

CIB1 joins a growing list of fertility genes discovered during the course of mice studies of diseases such as cancer, diabetes and heart disease. In 2000, UNC researchers found several genes essential for male mouse fertility while studying how cells transport chloride, sodium and potassium, Yuan notes.

The results appear online in advance of print publication in the journal *Molecular and Cell Biology*. The study was funded by the National

Institute of Child Health and Human Development, part of the National Institutes of Health.

Earlier work by Yuan and his colleagues showed CIB1 helps control blood clotting in humans by keeping blood platelets from sticking together, acting as a natural anti-coagulant to prevent uncontrolled clotting of blood platelets that might lead to heart attacks and strokes.

From initial observations, the CIB1 defect in mice appears to disrupt sperm formation in its final stage, said Dr. Deborah O'Brien, study co-author and an associate professor of cell and developmental biology. "To make a sperm, you have to go from a fairly typical cell to one that has a very distinctive shape and half the number of chromosomes," O'Brien said. "The male mice missing CIB1 appear to have a problem very late in this process, when the cell differentiates into a sperm cell."

Further study would be needed to determine if the finding has implications for human infertility, O'Brien said. "If the protein has the same expression pattern and role in humans, then I would expect that a defect in this protein should have the same effect in humans. Some infertility could be due to a mutation in CIB1, but that's far down the road."

The discovery suggests that CIB1 is a major regulatory protein, active in cell function throughout the body, said Dr. Leslie Parise, senior author, professor of biochemistry and biophysics and pharmacology and chair of the department of biochemistry and biophysics. "This protein is known to regulate cell migration in other cells. Whether that ability is linked to this problem with spermatogenesis, we don't know," said Parise, who discovered CIB1 in 1997. "It will take further research to determine exactly how CIB1 regulates sperm formation."

Study co-authors include assistant professor Dr. Tina Leisner; research

technicians Andrew McFadden and Shantres Clark, all of the department of pharmacology; Dr. Maedo Nobuyo, professor of pathology and laboratory medicine; and Sylvia Hiller, research laboratory specialist in pathology and laboratory medicine.

Source: University of North Carolina at Chapel Hill School of Medicine