SOUTHWESTERN NEWS

Media contacts: Heather Stieglitz or Ann Harrell
(214) 648-3404
or e-mail: heather.stieglitz@email.swmed.edu
or ann.harrell@email.swmed.edu

EMBARGOED FOR RELEASE June 28, 5 p.m. ET

SCIENTISTS SHOW HORMONE INVOLVED IN CRYPTORCHIDISM

DALLAS — June 29, 1999 — Cryptorchidism – impaired testicular descent – is a congenital abnormality that affects 2 percent to 3 percent of full-term human males at birth. Scientists at UT Southwestern Medical Center at Dallas have found, in mice, that a hormone is involved in the regulation of testicular descent.

Their experiments, reported in the July issue of *Nature Genetics* by Dr. Luis Parada, director of UT Southwestern's Center for Developmental Biology, and postdoctoral fellow Dr. Serge Nef, show that fluctuations in the level of the hormone Insl3 greatly influence the state of testicular descent. They believe the same hormone regulates cryptorchidism in humans.

Cryptorchidism has serious implications for males if the condition is not corrected – usually by surgery – before the age of two. Studies have shown that boys born with undescended testes have an increased risk of testicular cancer and reduced fertility.

"It would be so much better if by taking an additional dose of hormone, we could eliminate surgery and the risk of cancer in these boys," said Parada.

Normal testicular descent consists of two stages – transabdominal descent into the inguinal canal and then descent into the scrotum. Parada and Nef created mice that had one or both copies of the *Insl3* gene inactivated. Those born with no Insl3 activity, which normally is expressed in the testes, had bilateral cryptorchidism. Although testes were present, they remained in the abdomen and resulted in sterility in every case. However, the mice exhibited normal androgen-dependent sexual behavior, had normal male accessory organs and normal serum testosterone levels.

(MORE)

The researchers determined that the cause of the cryptorchidism in mice with no Insl3 activity was the underdevelopment of the gubernaculum, a fetal ligament that is believed to guide the descent of the testis into the scrotum, thus blocking transabdominal descent.

Previous studies showed that an unknown factor released from testes regulates gubernaculum differentiation and proliferation. Parada and Nef believe that factor is Insl3.

Seventy-five percent of the mice born with some Insl3 activity (one active gene) had partial unilateral or bilateral cryptorchidism that self-corrected after birth.

"This is very similar to what happens in most cases of human cryptorchidism," said Parada, who also directs the Kent Waldrep Foundation Center for Basic Neuroscience Research. The researchers are now studying Insl3 levels in humans with the condition.

Female mice with both *Insl3* genes inactivated appeared normal but had impaired fertility, which Parada and Nef determined was due to an increased estrus cycle. While in males Insl3 mediates transabdominal testicular descent, in females Insl3 may be responsible for a barren and extended estrus cycle.

The study was supported in part by a grant from the Swiss National Science Foundation and by an Excellence in Education Grant.

###