Urology Study Sheds Light on Androgen Deficiency

A laboratory study at the Miller School of Medicine’s Desai Sethi Urology Institute has uncovered new clues about the cellular processes that can lead to deficiencies of androgens (male hormones) such as testosterone.

Himanshu Arora, Ph.D.

Symptoms of testosterone deficiency include low sex drive, erectile dysfunction, depression, and fatigue.

“Although testosterone deficiency may be present in one in five men 40 years or older, the driving factors remain largely unknown,” said Himanshu Arora, Ph.D., assistant professor of urology.

Dr. Arora’s lab examined the effect of different concentrations of leptin—a hormone produced by fat cells—on the microenvironment of the testes, which produce both sperm
and testosterone.

Dr. Arora is lead author of the study “Leptin Secreted from Testicular Microenvironment Modulates Hedgehog Signaling to Augment the Endogenous Function of Leydig Cells,” published in the journal *Cell Death & Disease*.

The research builds on prior studies of how Sertoli and peritubular myoid cells (PMC) in the testicular microenvironment help drive Leydig stem cell differentiation via the cellular desert hedgehog signaling pathway, which transmits information to embryonic cells that guides proper cell differentiation.

In the new study, Dr. Arora and his colleagues extracted cellular samples from men undergoing testes biopsies for sperm retrieval. The researchers found that when the testes microenvironment secreted leptin in low doses, Leydig stem cells differentiated into adult Leydig cells producing normal levels of testosterone. However, higher doses of leptin depressed testosterone levels.

“Our findings identify leptin as a key factor within the testes microenvironment,” said Dr. Arora, adding that the insight “holds important implications for androgen deficiency and could have further application in prostate cancer research.”
Noting that leptin is already used in treating patients for obesity, “Preclinical studies could indicate whether adjusting levels of this hormone would be helpful in patients with testosterone deficiency,” said Ranjith Ramasamy, M.D., study co-author and associate professor and director of the Miller School’s Reproductive Urology Program.

The research was supported by an American Urological Association, the Stanley Glaser Award, the Soffer Family Foundation, and grants from the National Institutes of Health (NIH).

Miller School co-authors were Ranjith Ramasamy, M.D., associate professor of urology and director of the Male Reproductive Medicine and Surgery Program; Joshua M. Hare, M.D., Louis Lemberg Professor of Medicine and founding director, Interdisciplinary Stem Cell Institute; Rehana Qureshi, Ph.D., assistant scientist; Kajal Khodamoradi, Ph.D., research associate; Deepa Seetharam, Ph.D., postdoctoral associate; Madhumita Parmar, M.D; Derek J. Van Booven, senior bioinformatics analyst; and student intern Isabelle Catherine.
Issa.

Content Type article