MedicalXpress

Common herbicide disrupts human hormone activity in cell studies

May 7 2008

A common weedkiller in the U.S., already suspected of causing sexual abnormalities in frogs and fish, has now been found to alter hormonal signaling in human cells, scientists from the University of California San Francisco (UCSF) report.

The herbicide atrazine is the second most widely used weedkiller in the U.S., applied to corn and sorghum fields throughout the Midwest and also spread on suburban lawns and gardens. It was banned in Europe after studies linked the chemical to endocrine disruptions in fish and amphibians.

The UCSF study is the first to identify its full effect on human cells. It is being reported in the May 7 issue of the journal “PLoS ONE.”

In studies with human placental cells in culture, the UCSF scientists found that atrazine increased the activity of a gene associated with abnormal human birth weight when over-expressed in the placenta. Atrazine also targeted a second gene that has been found to be amplified in the uterus of women with unexplained infertility.

In parallel studies of zebrafish, a widely used animal in development studies, the research team showed that atrazine “feminized” the fish population – increasing the proportion of fish that developed into females. In water with atrazine concentrations comparable to those found in runoff from agricultural fields, the proportion of female fish increased two-fold. Environmental factors are known to influence the

sex of zebrafish and many other fish and amphibians as they develop.

“These fish are very sensitive to endocrine disrupting chemicals, so one might think of them as ‘sentinels’ to potential developmental dangers in humans,” said Holly Ingraham, PhD, senior author on the study and a UCSF Professor of Cellular and Molecular Pharmacology. “These atrazine- sensitive genes are central to normal reproduction and are found in steroid producing tissues. You have to wonder about the long-term effects of exposing the rapidly developing fetus to atrazine or other endocrine disruptors.”

Ingraham intends to determine precisely how atrazine affects human and other mammalian endocrine cells and why these cells are particularly sensitive to it. She notes that bisphenol A, a compound in many hard plastic consumer products, is also an endocrine disrupter and is now under increased study for its safety. In April, Canada announced a decision to ban sale of consumer products with bisphenol A.

The lead author of the study is Miyuki Suzawa, a postdoctoral fellow in Ingraham’s lab.

UCSF researchers exposed sexually immature zebrafish to atrazine and other chemicals for different periods of time. They found that exposure to atrazine for 48 hours at concentrations that might be found in water containing agricultural runoff, produced twice as many female fish.

Through genetic analysis, they found that atrazine preferentially activates a class of receptors in the cell nucleus, including two known as SF-1 and LRH-1. SF-1 regulates production of enzymes involved in the synthesis of steroids in the body and development of many endocrine tissues. One of these enzymes, known as Aromatase, plays a role in determining whether lower vertebrates, such as fish will become male or female. Aromatase is known as a feminizing enzyme.

In the human placental cell culture studies, the scientists found that a 24-hour exposure to atrazine activates a cluster of genes involved in hormone signaling and steroid synthesis.

They report, “Endocrine-related cell types with a capacity for steroid generation appear to be especially sensitive (to Atrazine), as demonstrated by the “exquisite” cellular specificity of the atrazine response.”

The finding that a pervasive and persistent environmental chemical appears to significantly change hormone networks means that scientists must take a broader look at this herbicide’s potential effect on human health, Ingraham said. Up to now, much of the focus has been on breast cancer, but since proper development of the endocrine system is important for normal reproduction, stress responses and metabolism, early exposure to this chemical in a fetus or infant might alter normal physiology later in life, she said.

Source: University of California - San Francisco