Toxic chemicals affect steroid hormones differently in humans and invertebrates

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In a study with important consequences for studies on the effects of chemicals on steroid responses in humans, a team of French and American scientists, including Michael E. Baker, PhD, professor in UC San Diego's Department of Medicine, Division of Nephrology-Hypertension, have found that - contrary to earlier assumptions - enzymes used for the synthesis of steroids in insects, snails, octopuses and corals are unrelated to those used in humans.

The research, led by a team at the Université de Lyon, ENS Lyon, provides insight into the evolution of steroid hormone signaling and the relationship of steroid synthesis to enzymes that detoxify harmful chemicals in the environment. Their findings will be published the week of June 29, 2009 in the advance online publication of the *Proceedings of the National Academy of Sciences (PNAS.)*

"The toxic effects of chemicals on snails and corals remain a major area of environmental concern," said Vincent Laudet, professor in the Institute of Functional Genomics of Lyon, Division of Molecular Zoology. "For a long time, it has been thought that many invertebrate animals share with humans the same steroid hormones and enzymes that synthesize steroids. However, our research indicates that the method by which toxic chemicals effect the steroid hormone signaling of snails, corals, insects and other invertebrates can't be extrapolated to human disease."

Steroids hormones are key to many vital physiological responses in

humans, ranging from anti-inflammatory agents to regulating events during pregnancy. They are also the target of many chemical pollutants, known as endocrine disruptors. As part of a program to understand the evolution of steroid hormone signaling, Laudet - along with Gabriel Markov, a student in the Institute of Functional Genomics, initially trained by Raquel Tavares at Université de Lyon, characterized the evolutionary relationships between proteins that synthesize steroids in animals. They traced the origin of such enzymes from vertebrates, insects, snails and jelly fish and interpreted these results through extensive discussions with Baker, Chantal Dauphin-Villemant at Université Paris 6, and Barbara Demeneix from the National Museum of Natural History in Paris.

Through an analysis of several invertebrate genomes, the scientists discovered that snails and insects utilize steroid-synthesizing enzymes that are not vertebrate-related, but instead belong in an invertebrate family. Moreover, these invertebrate steroidogenic enzymes have a strong evolutionary connection to enzymes that detoxify chemicals (called xenobiotics).

This unexpected finding led them to hypothesize that these steroid-synthesizing enzymes arose independently from specific pathways used by snails and worms for detoxifying environmental chemicals.

"This finding shows that, if we want to really understand the effects of environmental chemicals on steroid synthesis in snails, worms, octopuses and such animals, we must switch from a human-centered viewpoint to snail-centered viewpoint. This is the best way to accumulate knowledge that could be useful to human health," said Laudet, adding that this emphasizes the need for more cross-disciplinary studies between toxicologists, endocrinologists and zoologists.

Source: University of California - San Diego (news : web)