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Scientists May Have Solved Mystery Of Carcinogenic Mothballs

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Chemical compounds in household products like mothballs and air fresheners can cause cancer by blocking the normal process of "cell suicide" in living organisms, according to a new study spearheaded by the University of Colorado at Boulder.

Naphthalene in mothballs and para-dichlorobenzene, or PDCB, found in some air fresheners, were shown to block enzymes that initiate programmed cell death, or apoptosis, said Associate Professor Ding Xue of CU-Boulder's molecular, cellular and developmental biology department. Apoptosis is a normal function of certain cell groups that acts as a "brake" to prevent unchecked cellular proliferation similar to the process that triggers the formation of cancerous tumors, said Xue.

While naphthalene and PDCB have been shown to cause cancer in rodents and are classified by the National Toxicology Program and the International Association for Research on Carcinogens as potential human carcinogens, their biochemistry has not been well understood, said Xue. But using a common, eyelash-sized worm known as C. elegans, the research team has shown that naphthalene can cause the inactivation of a group of enzymes known as caspases -- which control cell suicide -- by oxidizing them.

The study appears in the June issue of *Nature Chemical Biology*. It was authored by Xue and David Kokel of CU-Boulder's MCD biology department and Yehua Li and Jun Qin of the Baylor College of Medicine in Houston.

"This study shows why mothballs and some air freshener products may be harmful to humans," said Xue. "And, for the first time, we have developed a systematic way to screen virtually any potential cancer-causing chemical that may affect humans using these nematodes as animal models."

In the study, caspase enzymes from both nematodes and from humans were blocked after exposure to naphthalene, indicating a "comparable pharmacology" between worms and humans, said Xue.

Understanding how carcinogenic compounds can trigger tumor growth is important for federal regulatory agencies that deal with human exposure to hazardous chemicals, said Xue. More than 1 million pounds of naphthalene and PDCB are used by consumers annually, according to the study.

The nematodes were grown on a culture medium coated with a soybean-based oil that is harmless to the worms but which can dissolve naphthalene and PDCBs, said Xue. When the chemicals were added to the culture, they deactivated the caspases, resulting in the survival of "extra" cells in the tiny worms that normally would have been eliminated by apoptosis, said Xue.

Apoptosis is an essential process in animal development and occurs in many tissues, said Xue. In amphibians it rids frogs of tails as they develop from larvae to adults, and in humans it removes cells that make up "webbing" tissue between the fingers and toes of embryos during development, he said.

"Apoptosis serves as a checking mechanism to ensure that the right amount of cells are generated in the body," Xue said. In Alzheimer's disease and Parkinson's disease, too much apoptosis is occurring, while in cancer and autoimmune disorders, too little apoptosis is occurring, he

said.

Popular with scientists in research labs around the world, C. elegans worms have essentially the same basic biological processes as humans even though their average lifespan is less than three days, he said. Xue's team currently is using C. elegans as an animal model "bioassay" to test common industrial chemicals like biphenyl, toluene and benzene that are suspected to be carcinogens.

"The power of C. elegans' molecular genetics, in combination with the possibility of carrying out large-scale chemical screens in this organism, makes C. elegans an attractive and economical animal model for both toxicological studies and drug screens," the researchers wrote in Nature Chemical Biology.

"Bioassays involving lab rats can take two years to complete," he said. "But we can do the same kind of bioassays with nematodes in two weeks, and we can do them at our lab benches instead of animal care facilities."

Source: University of Colorado at Boulder