Improved way to assess cancer risk of pollutants

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Susan Tilton. Credit: Gail Wells.

Scientists at Oregon State University have developed a faster, more accurate method to assess cancer risk from certain common environmental pollutants.

Researchers found that they could analyze the immediate genetic responses of the skin cells of exposed mice and apply statistical approaches to determine whether or not those cells would eventually become cancerous.

The study focused on an important class of pollutants known as polycyclic aromatic hydrocarbons, or PAHs, that commonly occur in the environment as mixtures such as diesel exhaust and cigarette smoke.

"After only 12 hours, we could predict the ability of certain PAH mixtures to cause cancer, rather than waiting 25 weeks for tumors to develop," said Susan Tilton, an environmental toxicologist with OSU's College of Agricultural Sciences.

For at least some PAH mixtures, the new method is not only quicker but produces more accurate cancer-risk assessments than are currently possible, she said.

"Our work was intended as a proof of concept," said Tilton, who is also affiliated with the OSU's multidisciplinary Superfund Research Program, a center funded by the National Institute of Environmental Health Sciences (NIEHS).

"The method needs to be tested with a larger group of chemicals and mixtures. But we now have a model that we can use to develop larger-scale screening tests with human cells in a laboratory dish."

Such a method will be particularly useful for screening PAHs, a large class of pollutants that result from combustion of organic matter and fossil fuels. PAHs are widespread contaminants of air, water and soil. There are hundreds of different kinds, and some are known carcinogens, but many have not been tested.

Humans are primarily exposed to PAHs in the environment as mixtures, which makes it harder to assess their cancer risk. The standard calculation, Tilton said, is to identify the risk of each element in the mix - if it's known - and add them together.

But this method doesn't work with most PAH mixes. It assumes the risk for each component is known, as well as which components are in a given mix. Often that information is not available.

This study examined three PAH mixtures that are common in the environment - coal tar, diesel exhaust and cigarette smoke - and various mixtures of them.

They found that each substance touched off a rapid and distinctive cascade of biological and metabolic changes in the skin cells of a mouse. The response amounted to a unique "fingerprint" of the genetic changes that occur as cells reacted to exposure to each chemical.

By matching patterns of genetic changes known to occur as cells become cancerous, they found that some of the cellular responses were early indicators of developing cancers. They also found that the standard method to calculate carcinogenic material underestimated the cancer risk of some mixtures and overestimated the combined risk of others.

"Our study is a first step in moving away from risk assessments based on individual components of these PAH mixtures and developing more accurate methods that look at the mixture as a whole," Tilton said. "We're hoping to bring the methodology to the point where we no longer need to use tumors as our endpoint."

Tilton collaborated on the research with Katrina Waters of the Pacific Northwest National Laboratory, and others. Their findings appeared in a recent edition of *Toxicological Sciences*.

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