Investigating one of the world's deadliest substances

Luis Wilfrido Atienza
November 18, 2017
lw.atienza@gmail.com

Dioxins are known to be one of the most toxic substances in the world. They are created by several industrial processes but are also created naturally in volcanic eruptions and forest fires. Because of this they are extremely common—found all over the world, in many different ecosystems, including urban environments.

They are classified as persistent organic pollutants, meaning they are extremely resistant to environmental degradation and can be present in an environment for an extremely long time. Humans are mainly exposed to dioxins through food. Dioxins can accumulate in the fat cells of animals, such as chickens, and affect humans who eat them.

Dioxins are carcinogenic to humans and can cause infertility and fetal development damage. The effects of dioxin on other animals differ greatly depending on the species, but the substance is harmful or fatal to a wide variety of species.

Because dioxins are extremely common, harmful, and difficult to manage, the study of these substances, how to manage their presence in environments and mitigate their effects on different organisms, is incredibly important. A large part of understanding this is understanding exactly what the effects of dioxins are not only on environments as a whole but also on the molecular level.

Published in the Archives of Toxicology, work by a team of scientists headed by Dr. Hoa Thanh Nguyen of Ehime University, including Dr. Maria Claret Lauan Tsuchiya of the University of the Philippines Los Baños, has yielded some important insights by examining the effects of a dioxin, TBDD in mice.

The researchers looked at two different strains of mice: one resistant to dioxins, and the other sensitive to them. Their study was focused on the proteomes of these two strains of mice—the network of all the different proteins that they produced—when they were exposed to TBDD.

The scientists exposed groups of mice to TBDD by injecting them with TBDD dissolved in corn oil. They also injected a control group of mice with corn oil with no TBDD. The mice were observed for three days after being exposed; then they were euthanized, and proteins were extracted from their livers.

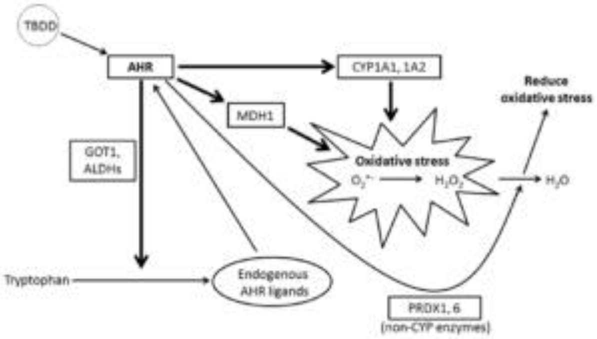
By looking at the different proteins produced by dioxin-sensitive and dioxin-resistant mice after exposure, and the biochemical processes these proteins are involved in, the researchers were hoping to discover what exactly made certain mice sensitive to dioxin, and why some mice were much more resistant to it.

From this the scientists were able to uncover several important points. For example, TBDD makes both dioxin-sensitive and dioxin-resistant mice produce more of certain proteins and less of others. In sensitive mice, more proteins were affected this way than in resistant mice.

Aside from studying how individual proteins were affected, the researchers analyzed the biological processes of which these proteins are a part to get a better idea of how exactly TBDD can cause damage to an entire organism.

TBDD affects cells by interacting with a certain cell receptor, called AHR, causing a chain reaction within the cells, leading to the buildup of harmful oxidative molecules. Genetically, dioxin-resistant mice have less of this receptor than dioxin-sensitive mice. But beyond that, the researchers found that when TBDD did interact with this receptor, sensitive mice produced more of another protein. That protein also interacts with AHR, causing more of the same chain reaction, amplifying the effect of dioxin in sensitive mice.

Many of the proteins affected by TBDD are related to how the body processes amino acids, specifically an amino acid called tryptophan. In sensitive mice, TBDD makes certain processes happen more often, resulting in tryptophan also being converted into oxidative molecules.



A schematic diagram showing the mechanism through which TBDD causes oxidative stress, as proposed by the researchers.

Overall TBDD seems to be harmful to dioxin-sensitive rats because of how it makes cells produce so many of these harmful oxidative molecules. In line with this, other proteins that were more abundant in dioxin-sensitive mice were involved in the creation of antioxidants, and this sheds light on how organisms can adapt to the harmful effects of TBDD.

Aside from studying rats injected with TBDD, the researchers studied a control group of rats that were not injected with TBDD. In comparing their test subjects to this control group, the researchers found that dioxin-resistant and dioxin-sensitive mice differed not only in the amount of certain proteins that they produced but also in the characteristics of those proteins. These slightly different proteins might also help dioxin-sensitive mice defend against oxidative stress.

Understanding the effects of dioxin toxicity by studying the protein profiles of these rats can give us significant insights into why exactly TBDD is so harmful to many different species; this could lead to our finding ways to mitigate its effects or rehabilitating environments that are contaminated with it. This work could also lead to methods that would allow us to identify dioxin resistance in other species, or even the development of genetic therapies that would help sensitive animals cope with dioxin in the environment. Since most human exposure to dioxin happens through the consumption of contaminated food, helping animals such as chickens become resistant to dioxins will reduce human exposure to the toxic substance as well.

REFERENCE

Nguyen HT, Tsuchiya MCL, Yoo J, Iida M, Agusa T, Hirano M, Kim E-Y, Miyazaki T, Nose M, Iwata H. 2016. Strain differences in the proteome of dioxin-sensitive and dioxin-resistant mice treated with 2,3,7,8-tetrabromodibenzo-p-dioxin. Arch Toxicol 2017; 91:1763–82.

Luis Wilfrido Atienza graduated from the Ateneo de Manila University, with a BS in Biology, and a minor in poetry. He currently works as a copywriter for a sustainability agency, and spends some of his free time writing about science.