

## How Toxic Environmental Chemical DBT Affects the Immune System

October 28, 2008 |

An international team of researchers at the University of California, San Diego School of Medicine and the University of Basel in Switzerland have issued a report on the mechanism of toxicity of a chemical compound called Dibutyltin (DBT).

DBT is part of a class of high toxic and widely distributed chemical compounds called organotins, DBT is most commonly used as an anti-fouling agent in paint, for example in the fishing and shipbuilding industries. It is also used in the production of polyvinyl chloride (PVC) plastic tubes and bottles.

According to co-lead investigators Michael E. Baker, PhD, researcher in UC San Diego's Department of Medicine, Division of Nephrology-Hypertension, and Alex Odermatt, PhD, at the University of Basel, DBT is closely related to tributyltin (TBT), another well-known pollutant. Concern about the side effects of TBT led the United Nations' International Maritime Organization to organize a global ban on its use.

"TBT is metabolized by the body's liver into DBT," the scientists explained. "Humans are also exposed to DBT by drinking water from PVC pipes. Because it is poorly broken down, DBT remains in the environment and it appears that its toxic effects are more rapid and more pronounced than those of TBT."

Symptoms of organotin exposure can include irritated skin, dizziness, difficulty breathing, and flu-like symptoms. Although long-term effects in humans are uncertain, large doses of certain organotins have been shown to damage the reproductive and central nervous systems, bone structure, the liver and immune system in mammals.

Combining studies of the effect in cell culture of DBT on the function of a key class of steroid hormone, glucocorticoids, with computer-based analyses of the molecular interaction of DBT and the glucocorticoid receptor (GR), the U.S. and Swiss scientists explained the mechanism by which DBT inhibits transcriptional activity of the GR.

The GR is expressed in almost every cell in the body. Besides important functions in energy metabolism, the GR helps to regulate genes that control the body's immune system. The

researchers propose that by blocking GR activation, DBT disrupts the appropriate response of the immune system during inflammation, providing an explanation for some of the toxic effects of this organotin.

Alex Odermatt is from the Division of Molecular and Systems Toxicology, Department of Pharmaceutical Sciences at the University of Basel. Additional contributors to the paper include first author Christel Gummy of the University of Basel and the University of Berne; Anna A. Dzykanchuk and Denise V. Kratschmar, University of Basel; and Charlie Chandsawangbhuwana, UC San Diego Department of Bioengineering. The work was supported in part by grants from the Swiss National Science Foundation.

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Media Contact: Debra Kain, 619-643-6163, [ddkain@ucsd.edu](mailto:ddkain@ucsd.edu)

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