RTI Author Awards Series

Role of Cytochrome P450 2E1 in the Metabolism of Acrylamide and Acrylonitrile in Mice

Sumner, S.C., **Fennell, T.R.**, Moore, T.A., Chanas, B., Gonzalez, F., et al. (1999). Role of cytochrome P450 2E1 in the metabolism of acrylamide and acrylonitrile in mice. *Chemical Research in Toxicology,* 12 (11):1110-1116.


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Cytochrome P450 2E1 (CYP 2E1) is a protein involved in the oxidative metabolism of hormones, chemicals, and drugs in the body. Because CYP 2E1 polymorphisms occur in humans, it is important to know how chemicals are metabolized in the presence or in the absence of this enzyme. The aim of our study was to determine the role of CYP 2E1 in the metabolism of acrylamide and acrylonitrile. This information can be used in the assessment of risks of human exposure to these chemicals—exposure through cigarette smoke, environmental contamination, or certain foods, or through accidental exposure in occupational settings.

In the early 1990s, a mouse model was developed to be devoid of cytochrome P450 2E1. This provided an opportunity to evaluate the metabolism of acrylamide and acrylonitrile in the absence of cytochrome P450 2E1.Our study results suggest that P450 2E1 is the *only* cytochrome P450 enzyme involved in the oxidative metabolism of acrylamide and acrylonitrile, and that when P450 2E1 is absent, other P450s do not metabolize these chemicals.

Results of our study were used in the development of physiologically based pharmacokinetic models and in assessment of risks associated with exposure to these chemicals. These studies indicate that mice created lacking P450 2E1 are an appropriate model for the investigation of the role of oxidative metabolism in the toxicity or carcinogenicity of acrylamide and acrylonitrile.

Link: http://pubs.acs.org/cgi-bin/abstract.cgi/crtoec/1999/12/i11/abs/tx990040k.html