

Focus on Ecogenetics #1

The PON 1 enzyme and susceptibility to toxicity from exposure to organophosphate pesticides

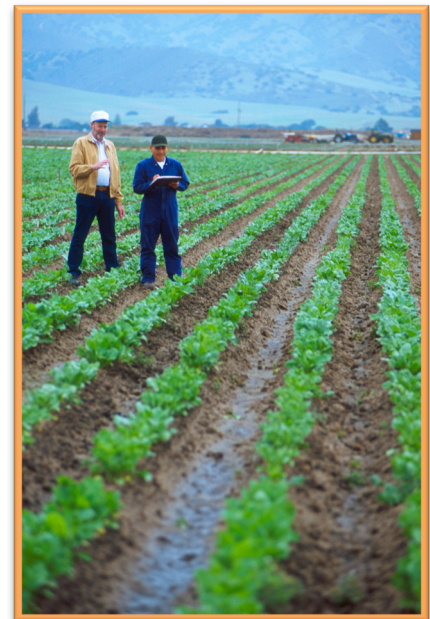
Summary of the Science

Center researchers **Clement Furlong**, **Harvey Checkoway** and **Lucio Costa** are studying human PON1, an **enzyme** that metabolizes organophosphate (OP) pesticides. There are several polymorphisms or forms of the PON1 gene, and PON1 activity varies widely, by up to 50-fold in different individuals. Those with low PON1 activity are more **susceptible to** the toxic effects of OP pesticides. Furthermore, individuals with low PON1 activity are at risk for other health conditions involving **oxidative stress**, including cardiovascular disease, diabetes, and Alzheimer's disease.

A PON1 polymorphism is an inherited genetic factor that cannot be readily changed. However, the effect of this polymorphism is influenced by environmental factors. Some drugs and antioxidants have been shown to increase the activity of PON1 and thus protect people from disease. These include cardiovascular drugs such as statins, anti-diabetic drugs, Vitamins C and E, green tea, blueberries, and grape seed extract. Certain antibiotics such as sodium ampicillin and ciprofloxacin have the opposite effect and inhibit PON1 activity, putting people at higher risk for adverse health effects.

PON1 activity is low from before birth until about age two and decreases again later in life, making young children and older adults more susceptible to the toxic effects of OP pesticides. Also, men have lower PON1 activity and higher susceptibility to OP toxicity than women.

Agricultural workers are at high risk for exposure to OP pesticides as they prepare, apply, and work with it in fields where OP pesticides are used. Worker's spouses and children may also be exposed to pesticide residue carried home from the workplace in cars and on boots and clothing. Besides experiencing harmful exposures, agricultural workers may have less access to resources to protect themselves if they are low income, non-English speakers, and/or undocumented workers.



Courtesy of USDA-ARS Archive
Photo by Scott Bauer

Exploring Ethics

What we are learning about the role of PON1 in metabolizing OP pesticides raises many ethical issues, such as:

- Who should be tested for PON1 status? Should all agricultural workers be tested? Who decides?
- Should employers be informed of a worker's PON1 status once they have taken the test?
- What is the best way to inform agricultural workers of their PON1 status?
- What is the best way to teach non-English speakers and illiterate workers how to protect themselves from OP toxicity?
- Do workers have access to protection from OP pesticides exposure, such as personal protective equipment (PPE) and training in their native language to use it properly? Does the workplace culture encourage the use of PPE?
- Are workers given information about PON1 such as how PON1 activity is affected by other diseases, and the drugs, foods, and vitamins that can protect them?
- Do workers have access to health care and medications that increase PON1 activity?
- Since low PON1 activity suggests increased risk of cardiovascular disease, should everyone be tested for PON1 status?

References

1. *Human PON1, a biomarker of risk of disease and exposure.* Center researchers Furlong, Checkoway, Costa. PMID 20338154
2. *Pharmacological and dietary modulators of PON1 activity and expression: the hunt goes on.* Center researchers Costa, Furlong. PMID 21093416

Glossary of Terms

- **Ecogenetics:** The study of how genetics and the environment interact to influence human health.
- **Enzyme:** A protein that produces chemical changes in the body.
- **Oxidative stress:** Free radical oxygen that causes damage that can lead to disease.
- **Susceptible to:** More likely to be affected or harmed by.