PON1 and Pesticides

Fundamental Questions

1990

Found that administering the PON1 protein to rats protected against exposure to chlorpyrifos oxon, the toxic breakdown product of the pesticide chlorpyrifos.[1]

1991

Purified human PON1 protein for the first time; cloned human PON1 gene for further study.[2-3]

1993

Observed that mice lacking PON1 were susceptible to organophosphate toxicity and atherosclerosis, or plaque buildup in arteries; found that PON1 protection depends on the type of organophosphate exposure.[6-8]

1999

CHAMACOS was established at the University of California, Berkeley, to investigate the effects of pesticides and other environmental exposures among children living in an agricultural region in California.[9]

Application and Synthesis

1999-2000

Reported that PON1 genotype and protein quantity may better predict organophosphate sensitivity than genotype alone.[10-11]

2003

Demonstrated the validity of a functional genomic assay in detecting PON1 mutations.[12]

2003-2006

Indicated that fetuses and newborns are more sensitive to organophosphate exposure than adults; suggested that PON1 levels plateau between 6 and 15 months of age, with high variability between individuals.[13-16]

2004-2012

Found that chlorpyrifos exposure interfered with brain development in rats and humans.[17-19]

Implementation and Adjustment

2004-2014

Showed that human PON1 variants introduced into mice influenced their sensitivity to organophosphate toxicity; identified associations between PON1 and human birth outcomes and neurodevelopmental effects.[20-27]

2008

Suggested that human PON1 protein expressed in bacteria could be used to treat exposure to diazoxon, a metabolic byproduct of diazinon.[28]

2008

Developed laboratory protocols for determining people's PON1 blood concentrations and activity levels without the use of toxic organophosphates.[29]

2009

Observed that low levels of a less active form of the PON1 protein were associated with the inhibition of butyrylcholinesterase, a protein used to monitor organophosphate exposure.[30]

Policy and Practice

2014

Using mice, found that maternal PON1 protein quantity and activity influenced neonatal sensitivity to chlorpyrifos exposure.[31]

2018

Recommended policy reforms on organophosphate use. [32]

Impact

2021

Informed by NIEHS-funded studies, among others, the EPA banned use of chlorpyrifos on food sold in the United States.[33*]

**No NIEHS funding was used to advocate the EPA for this policy change.*

NIH National Institute of Environmental Health Sciences

NIEHS supported research for all of the milestones highlighted above.