

Extramural papers of the month

By Nancy Lamontagne

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Superfund Research Program
Research Brief. New issues
are published on the first
Wednesday of each month.

Broccoli sprout beverage helps detoxify air pollutants

Research funded in part by NIEHS has shown that drinking a broccoli sprout beverage daily can enhance the detoxification of some airborne pollutants. This inexpensive food-based intervention may provide a way to decrease the long-term health risks of air pollution.

The researchers conducted a clinical trial that included 291 men and women living in a rural farming community in Jiangsu Province, China, which experiences high levels of air pollution, due to its proximity to Shanghai. Broccoli sprouts provide a good source of glucoraphanin, which is converted to sulforaphane in the body. Sulforaphane has been shown to increase levels of enzymes involved in detoxification. During the 12-week trial, the researchers asked one group of study participants to drink a broccoli sprout-derived beverage that provided daily doses of 600 micromol glucoraphanin and 40 micromol sulforaphane, while a control group of participants consumed a drink that did not contain broccoli sprouts.

For participants receiving the broccoli sprout beverage, the rate of excretion of the carcinogen benzene increased 61 percent on the first day and was maintained throughout the 12 weeks. The rate of excretion of the irritant acrolein rapidly increased 23 percent during the 12-week trial. Additional analyses indicated that sulforaphane might activate the signaling molecule NRF2, which increases the capacity to adapt to and survive a broad range of environmental toxins.

Citation: Egner PA, Chen JG, Zarth AT, Ng D, Wang J, Kensler KH, Jacobson LP, Munoz A, Johnson JL, Groopman JD, Fahey JW, Talalay P, Zhu J, Chen TY, Qian GS, Carmella SG, Hecht SS, Kensler TW.
(<http://www.ncbi.nlm.nih.gov/pubmed/24913818>)

2014. Rapid and sustainable detoxication of airborne pollutants by broccoli sprout beverage: results of a randomized clinical trial in China. *Cancer Prev Res*; doi:10.1158/1940-6207.CAPR-14-0103 [Online 9 June 2014].

The effects of early-life air pollution exposure on brain development

A study by an NIEHS grantee and colleagues provided new insights into mechanisms by which early-life exposure to air pollution produces harmful brain changes in mice, including brain enlargement that is also seen in humans with autism and schizophrenia.

Exposure to air pollution has been linked with neurological and behavioral health effects in children and adults. To explore the biology involved, the researchers exposed mice to levels of ultrafine particles similar to what people might experience in mid-sized U.S. cities during rush hour. For two weeks after birth, the mice were exposed to four hours of polluted air a day, for two four-day periods.

The researchers examined the brains of one group of mice 24 hours after the final pollution exposure. All showed inflammation throughout the brain and had lateral brain ventricles two to three times larger than normal. As seen in autism and schizophrenia, the changes occurred predominately in males. The white matter normally surrounding the ventricles wasn't fully developed, which the researchers attributed to damage from inflammation. The ventricles likely expanded to fill the space normally occupied by the white matter. The changes were also observed in mice examined 40 and 270 days after exposure, indicating that damage was permanent. The exposed mice performed poorly in tests of short-term memory, learning ability, and impulsivity. Brains of mice in all three groups also showed higher levels of the neurotransmitter glutamate, which is elevated in people with autism and schizophrenia.

Citation: Allen JL, Liu X, Pelkowski S, Palmer B, Conrad K, Oberdorster G, Weston D, Mayer-Proschel M, Cory-Slechta DA.
(<http://www.ncbi.nlm.nih.gov/pubmed/24901756>)

2014. Early postnatal exposure to ultrafine particulate matter air pollution: persistent ventriculomegaly, neurochemical disruption, and glial activation preferentially in male mice. *Environ Health Perspect*; doi:10.1289/ehp.1307984 [Online 5 June 2014].

Enhancing vesicular packaging may offer new therapeutic target for Parkinson's

NIEHS grantees report that mice genetically engineered to overexpress a protein involved in packaging the neurotransmitter dopamine showed higher levels of dopamine neurotransmission and were protected from a neurotoxin that causes permanent symptoms of Parkinson's disease. The findings point to a possible new therapeutic target for Parkinson's, which is associated with the loss of dopamine-producing neurons.

Vesicular monoamine transporter 2 (VMAT2) is a protein that packages dopamine and other monoamine neurotransmitters into vesicles for later release by neurons. Recent research has shown that VMAT2 function is impaired in people with Parkinson's. To learn more about the potential benefits of increasing VMAT2 function, the researchers generated transgenic mice with increased levels of the protein.

The VMAT2-overexpressing mice exhibited a twofold increase in vesicular transport, which increased dopamine release 84 percent. The mice also showed improved outcomes for anxiety and depressive behaviors, increased movement, and protection from the effects of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). MPTP causes permanent symptoms of Parkinson's and is used to study the disease in animal models. Overall, the work suggests that enhanced vesicular function can be sustained over time and, thus, interventions that target vesicular function might be beneficial to Parkinson's, as well as other disorders that involve storage and release of dopamine, serotonin, or norepinephrine neurotransmitters.

Citation: Lohr KM, Bernstein AI, Stout KA, Dunn AR, Lazo CR, Alter SP, Wang M, Li Y, Fan X, Hess EJ, Yi H, Vecchio LM, Goldstein DS, Guillot TS,

Salahpour A, Miller GW.

(<http://www.ncbi.nlm.nih.gov/pubmed/24979780>)

2014. Increased vesicular monoamine transporter enhances dopamine release and opposes Parkinson disease-related neurodegeneration in vivo. *Proc Natl Acad Sci U S A* 111(27):9977-9982.

Potential treatment for mustard gas skin exposure

A new study, funded in part by NIEHS, demonstrates the potential of an antioxidant metalloporphyrin in treating skin lesions caused by 2-chloroethyl ethyl sulfide (CEES). CEES is similar in structure to sulfur mustard gas, a chemical warfare agent, and is used to study toxic effects of the gas. The findings show the antioxidant's potential as a medical countermeasure against skin effects from exposure to chemical warfare agents.

Since previous studies showed that oxidative stress plays a role in skin injuries caused by CEES, the researchers tested the ability of the antioxidant Mn(II) tetrakis(N,N'-diethylimidazolium-2-yl)porphyrin, known as AEOL 10150, to treat skin effects of CEES exposure. Mouse skin exposed to CEES and then treated with AEOL 10150 showed more than 50 percent ($p < 0.05$) reversal of increases in skin bi-fold and epidermal thickness and in myeloperoxidase activity - all markers of CEES-induced skin injury - as well as decreased DNA oxidation.

Treating cultured mouse epidermal cells and human skin cells with AEOL 10150 (50micrometers) one hour after CEES exposure brought about significant ($p < 0.05$) reversal of decreases in both cell viability and DNA synthesis induced by CEES. The researchers also measured reactive oxygen species in the cytoplasm and mitochondria, finding that the treatment improved CEES-induced oxidative stress in both cell lines.

Citation: Tewari-Singh N, Inturi S, Jain AK, Agarwal C, Orlicky DJ, White CW, Agarwal R, Day BJ.

(<http://www.ncbi.nlm.nih.gov/pubmed/24815113>)

2014. Catalytic antioxidant AEOL 10150 treatment ameliorates sulfur mustard analog 2-chloroethyl ethyl sulfide-associated cutaneous toxic effects. *Free Radic Biol Med* 72:285-295. (*BJ Day is a consultant for and holds equity in Aeolus Pharmaceuticals, which is developing metalloporphyrins as potential therapeutic agents.*)

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