

## Extramural papers of the month

By Nancy Lamontagne

- [Elevated numbers of copy number variants linked with autism](#)
- [How dietary omega-3s reduce tumor growth](#)
- [Air pollution associated with increased risk for serious birth defects](#)
- [Text mining improves chemical-gene-disease curation](#)

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

### Elevated numbers of copy number variants linked with autism

New results from the NIEHS-funded Childhood Autism Risks from Genetics and Environment (CHARGE) study show that children with autism had significantly more DNA deletions or duplications, known as copy number variants (CNV), than those with typical development. The researchers propose that a greater number of CNVs, especially those caused by duplication, could predispose people to autism.

The researchers examined data from 516 children with autism or typical development from the CHARGE study. The frequency of CNVs was significantly higher in the children with autism than for children with normal development. This remained true even after removal of rare and likely pathogenic events, showing that the CNVs consisted of more common variants not exclusively found in children with autism. The level of personal and social skills negatively correlated (Spearman's  $r = -0.13$ ,  $P = 0.034$ ) with duplication CNV load for the affected children. Communication ( $P = 0.048$ ) and socialization ( $P = 0.022$ ) scores showed the strongest associations.

The researchers say that finding an overall increase in genetic change in children with autism heightens the need to understand the basis of this variation. Although scientists know that environmental factors can affect the stability of the genome, the researchers note that it is not known if the increased CNVs found in the children with autism result from environmental exposures, nutrition, medical factors, lifestyle, genetic susceptibility, or combinations of many elements together.

*Citation:* Girirajan S, Johnson RL, Tassone F, Balciuniene J, Katiyar N, Fox K, Baker C, Srikanth A, Yeoh KH, Khoo SJ, Nauth TB, Hansen R, Ritchie M, Hertz-Picciotto I, Eichler EE, Pessah IN, Selleck SB. (<http://www.ncbi.nlm.nih.gov/pubmed/23535821>) 2013. Global increases in both common and rare copy number load associated with autism. *Hum Mol Genet*; doi:10.1093/hmg/ddt136 [Online 27 March 2013].

### How dietary omega-3s reduce tumor growth

NIEHS grantees report a key mechanism by which dietary omega-3 fatty acids could reduce tumor growth and spread of cancer. The studies suggest that combining dietary omega-3 with some anti-cancer drugs could effectively treat cancers, while reducing potential side effects.

Cell and mouse experiments showed that epoxy docosapentaenoic acids (EDPs), which are metabolites of the omega-3 fatty acid docosahexaenoic acid, inhibit tumor growth and metastasis, by blocking the formation of new blood vessels. Administering a low-dose epoxide hydrolase inhibitor, along with EDPs, stabilized the EDPs in circulating blood, leading to approximately 70 percent inhibition of primary tumor growth and metastasis. The anti-cancer drugs sorafenib and regorafenib are FDA-approved kinase inhibitors that also inhibit epoxide hydrolase, and the researchers say that EDPs could provide a new way to block blood vessel growth, while reducing side effects in cancer patients.

The researchers also found that a metabolite of the arachidonic acid omega-6 fatty acid had the opposite effect of EDP, slightly increasing blood vessel growth and tumor progression in mice. This increase in blood vessel growth encourages wound healing and tissue repair.

*Citation:* Zhang G, Panigrahy D, Mahakian LM, Yang J, Liu JY, Stephen Lee KS, Wettersten HI, Ulu A, Hu X, Tam S, Hwang SH, Ingham ES, Kieran MW, Weiss RH, Ferrara KW, Hammock BD. (<http://www.ncbi.nlm.nih.gov/pubmed/23553837>) 2013. Epoxy metabolites of docosahexaenoic acid (DHA) inhibit angiogenesis, tumor growth, and metastasis. *Proc Natl Acad Sci U S A* 110(16):6530-6535.

### Air pollution associated with increased risk for serious birth defects

Women in the San Joaquin Valley of California, who were exposed to the highest levels of carbon monoxide, nitrogen oxide, or nitrogen dioxide during their first eight weeks of pregnancy, were more likely to have a baby with spina bifida or anencephaly

neural tube defects than women with the lowest exposure, according to an NIEHS-supported study. These results add evidence of a link between air pollution exposure and some birth defects.

The researchers used data from the California Center of the National Birth Defects Prevention Study, and the NIEHS-funded Children's Health and Air Pollution Study, to investigate whether air pollution in the San Joaquin Valley of California is associated with risks of five types of birth defects. After controlling for factors, such as maternal race/ethnicity, education, and multivitamin use, the researchers observed increased odds of spina bifida or anencephaly neural tube defects in the babies of women who experienced the highest levels of carbon monoxide, nitrogen oxide, or nitrogen dioxide exposure during their first eight weeks of pregnancy. Ozone exposure was associated with decreased odds of neural tube defects.

The adjusted odds ratio was 1.9 (95 percent confidence interval: 1.1, 3.2) for neural tube defects among those with the highest quartile of carbon monoxide exposure compared with those with the lowest exposure. Nitrogen oxide exposure showed similar effects with the highest quartile of nitrogen oxide exposure associated with neural tube defects (adjusted odds ratio = 1.8, 95 percent confidence interval: 1.1, 2.8), and the adjusted odds ratio for the highest quartile of nitrogen dioxide exposure was 1.7 (95 percent confidence interval: 1.1, 2.7).

*Citation: Padula AM, Tager IB, Carmichael SL, Hammond SK, Lurmann F, Shaw GM. (<http://www.ncbi.nlm.nih.gov/pubmed/23538941>) 2013. The association of ambient air pollution and traffic exposures with selected congenital anomalies in the San Joaquin Valley of California. *Am J Epidemiol* 177(10):1074-1085.*

## Text mining improves chemical-gene-disease curation

NIEHS grantees report that text mining can help rank more relevant scientific research for inclusion in the [Comparative Toxicogenomics Database](http://ctdbase.org/) (CTD). The CTD is a public resource that provides information on chemical-gene, chemical-disease, and gene-disease interactions that are manually curated from scientific articles.

The researchers used a text-mining approach that assigns each article a document relevancy score, with a high score indicating that the article is more likely relevant for the CTD. They tested this approach on 14,904 articles, covering seven heavy metals, and found that integrating text mining with their current system of manual curation helped prioritize more relevant articles, increasing productivity by 27 percent and novel data content by 100 percent.

*Citation: Davis AP, Wieggers TC, Johnson RJ, Lay JM, Lennon-Hopkins K, Saraceni-Richards C, Sciaky D, Murphy CG, Mattingly CJ. (<http://www.ncbi.nlm.nih.gov/pubmed/?term=Text+Mining+Effectively+Scores+and+Ranks+the+Literature+for+Improving+Chemical-Gene-Disease+Curation+at+the+Comparative+Toxicogenomics+Database>) 2013. Text mining effectively scores and ranks the literature for improving chemical-gene-disease curation at the Comparative Toxicogenomics Database. *PLoSOne* 8(4):e58201.*

(Nancy Lamontagne is a science writer with MDB Inc., a contractor for the NIEHS Division of Extramural Research and Training.)

---

The Environmental Factor is produced monthly by the [National Institute of Environmental Health Sciences \(NIEHS\)](http://www.niehs.nih.gov/) (<http://www.niehs.nih.gov/>), Office of Communications and Public Liaison. The content is not copyrighted, and it can be reprinted without permission. If you use parts of Environmental Factor in your publication, we ask that you provide us with a copy for our records. We welcome your [comments and suggestions](#). ([bruskec@niehs.nih.gov](mailto:bruskec@niehs.nih.gov))

This page URL: NIEHS website: <http://www.niehs.nih.gov/>  
Email the Web Manager at [webmanager@niehs.nih.gov](mailto:webmanager@niehs.nih.gov)