Extramural papers of the month

By Nancy Lamontagne

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BPA linked with endometriosis

An NIEHS grantee and colleagues reported that higher urinary BPA levels are associated with increased risk of nonovarian pelvic endometriosis. Endometriosis is an estrogen-driven and often painful condition in which tissue that normally lines the uterus grows in other locations in the body.

Previous studies of BPA and endometriosis have shown inconsistent results and had various limitations, including small sample size. For the new study, the researchers used data from the Women's Risk of Endometriosis study, which is a population-based, case-control study of endometriosis, conducted among females enrolled in a large health care system. They compared urinary BPA levels in 143 women with surgically confirmed endometriosis, and 287 randomly selected study participants without endometriosis.

The investigators observed statistically significant positive associations between urinary BPA concentrations and nonovarian pelvic endometriosis (second versus lowest quartile: OR 3.0; 95% CI: 1.2, 7.3; third versus lowest quartile: OR 3.0; 95% CI: 1.1, 7.6). There was no statistically significant association between total urinary BPA concentration and endometriosis, overall, or ovarian endometriosis. The researchers say that the association between urinary BPA concentration and nonovarian pelvic endometriosis suggests that BPA may affect normal structural changes of hormonally responsive endometrial tissue during the menstrual cycle, promoting establishment and persistence of refluxed endometrial tissue in people with nonovarian pelvic endometriosis.

Citation: Upson K, Sathyanarayana S, De Roos AJ, Koch HM, Scholes D, Holt VL *(http://www.ncbi.nlm.nih.gov/pubmed/25205760)* . 2014. A population-based case-control study of urinary bisphenol A concentrations and risk of endometriosis. Hum Reprod 29(11):2457-2464.

Uranium exposure linked with lupus

Researchers, funded in part by NIEHS, report a link between uranium exposure and systemic lupus erythematosus in people living near a former uranium processing facility. The study offers insight into the types of environmental exposures that may contribute to lupus.

The researchers studied the Fernald Community Cohort, which consists of people who lived near a uranium ore processing plant in Fernald, Ohio, while it was operating. The Fernald Community Cohort was monitored for 18 years, providing an ideal group for studying environmental exposures to uranium. The study included 4,187 people with background uranium exposure, 1,273 with moderate exposure, and 2,756 with higher exposure. Anyone who worked at the plant was excluded.

The investigators found a nearly four-fold increase in odds of lupus in people with the highest levels of uranium exposure (OR 3.92, 95% CI 1.131-13.588, p = 0.031) compared to people with minimal exposure. Twelve of the 25 systemic lupus erythematosus cases identified came from the higher exposure group. The researchers say that the relationship between high uranium exposure and lupus may come from possible autoimmune, estrogenic, or epigenetic effects of uranium, acquired mutations, or an unidentified accompanying exposure.

Citation: Lu-Fritts PY, Kottyan LC, James JA, Xie C, Buckholz JM, Pinney SM, Harley JB *(http://www.ncbi.nlm.nih.gov/pubmed/25103365)* . 2014. Systemic lupus erythematosus is associated with uranium exposure in a community living near a uranium processing plant: a nested case-control study. Arthritis Rheumatol; doi:10.1002/art.38786 [Online 7 August 2014].

Predicting placement of epigenetic modifications

An NIEHS grantee and colleagues have developed a way to predict which DNA sequences are likely to contain epigenetic modifications. Scientists could use this information to edit these sequences, which would reveal more about how these sections of DNA regulate epigenetic modifications that control gene expression.

Epigenetic modifications change how genes are expressed ,without changing the DNA code. These alterations include histone modifications and DNA methylation, and they play critical roles in development, disease, and other biological processes. By comparing DNA sequences with and without epigenetic modifications, the researchers identified specific sequences that are recognized by the DNA-binding proteins that specify exactly where other enzymes make epigenetic modifications. The researchers call their new analysis approach Epigram, and have made it and the DNA sequences they identified openly available to other scientists online
(http://wanglab.ucsd.edu/star/epigram/)
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The scientists said their study provides the first catalog of DNA sequences that could be used to guide epigenome editing, which might one day link variations in DNA sequence with epigenomic effects that lead to disease.

Citation: Whitaker JW, Chen Z, Wang W
(http://www.ncbi.nlm.nih.gov/pubmed/25240437)
. 2014. Predicting the human epigenome from DNA motifs. Nat Methods; doi:10.1038/nmeth.3065 [Online 21 September 2014].

Environment stronger than genetics for eosinophilic esophagitis

Researchers have found that the environment plays more of a role than genetics in eosinophilic esophagitis, a severe, chronic allergic inflammatory disease that renders people unable to eat a wide variety of foods. A better understanding of the risk factors for this disease could lead to better strategies for prevention and management, and possibly identify modifiable environmental risk factors.

Although evidence suggests that eosinophilic esophagitis involves both genetic and environmental factors, scientists did not know the extent of the relative contribution. To study gene and environment contributions, the researchers used a cohort of families at the Cincinnati Center for Eosinophilic Disorders at Cincinnati Children's Hospital Medical Center. They also established a new separate cohort with histologically confirmed eosinophilic esophagitis in at least one twin or triplet.

The researchers found that 2.4 percent of siblings and 1.8 percent of first-degree relatives of patients with eosinophilic esophagitis also had the disease. Brothers, fathers, and males were more likely to have the disease than sisters, mothers, or females. Twins had 20 to 40 percent increased risk of the disease, depending upon whether they were identical or fraternal. Both the family and twin analyses supported a genetic contribution to eosinophilic esophagitis risk. Analysis of the twin cohort revealed genetic heritability contributed 14.5 percent of the variability, while environmental factors were responsible for 81 percent. These findings show that much of the familial clustering seen with this disease is due to a shared environment.

Citation: Alexander ES, Martin LJ, Collins MH, Kottyan LC, Sucharew H, He H, Mukkada VA, Succop PA, Abonia JP, Foote H, Eby MD, Grotjan TM, Greenler AJ, Dellon ES, Demain JG, Furuta GT, Gurian LE, Harley JB, Hopp RJ, Kagalwalla A, Kaul A, Nadeau KC, Noel RJ, Putnam PE, von Tiehl KF, Rothenberg ME
(http://www.ncbi.nlm.nih.gov/pubmed/25258143)
. 2014. Twin and family studies reveal strong environmental and weaker genetic cues explaining heritability of eosinophilic esophagitis. J Allergy Clin Immunol; doi:10.1016/j.jaci.2014.07.021 [Online 22 September 2014].

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The Environmental Factor is produced monthly by the National Institute of Environmental Health Sciences (NIEHS)
(http://www.niehs.nih.gov/)
, Office of Communications and Public Liaison. We welcome your comments and suggestions.
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