EBioMedicine 2 (2015) 1854–1855

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.ebiomedicine.com

Commentary

Organic Pollutants and Telomere Length: A New Facet of Carcinogenesis

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ARTICLE INFO

Article history:
Received 25 November 2015
Accepted 25 November 2015
Available online 26 November 2015

Persistent organic pollutants (POPs) are a class of lipid-soluble compounds known to affect risks of many human diseases (Petriello et al., 2014). These toxins have been used in a variety of industrial applications and are resistant to environmental degradation, resulting in their bioaccumulation in humans and many animal species in the food chain (Beyer & Biziuk, 2009). Most POPs are known endocrine disruptors, and individual pollutants can cause other biological effects that include the formation of reactive oxygen species and DNA adducts, and immunotoxicity (Lauby-Secretan et al., 2013). Due to their persistence, bioaccumulation, and negative health effects most classes of POPs including polychlorinated biphenyls (PCBs), dioxins, and dioxin-like compounds have been banned in countries around the world. Despite this, their persistence and bioaccumulation mean that these chemicals continue to generate a host of increased health risks for outcomes that include fetal abnormalities, reproductive health, cancers (with some POPs classified as group 1 carcinogens by The International Agency for Research on Cancer), cardiovascular disease, obesity, and diabetes (Petriello et al., 2014).

Telomeres are tandem repeats at the ends of each chromosome, and play a major role in cellular senescence and protecting genomic stability. They are also thought to play a role in human aging and disease, especially in most cancers, but the exact nature of this role remains unclear (Barrett et al., 2015). There is, however, at least some evidence that longer leukocyte telomere length (LTL) is associated with an increased risk of cancer over the short term (Hou et al., 2015). Hijacking telomere maintenance mechanisms is believed to be necessary for cell immortalization prior to cancer development (Hou et al., 2015). Not only would this be necessary to ensure sustained cancer cell proliferation over time, but longer telomere length would prolong cellular survival, resulting in an increased likelihood of cells accumulating mutations necessary for neoplastic transformation (Noy, 2009).

Little research has been done to link these two subjects in humans, but two studies have identified associations between PCBs and LTL (Mitro et al., 2015; Shin et al., 2010). In this issue of EBiomedicine, Scinicariello and Buser expand these results and identify associations between serum levels of multiple specific classes of POPs (including PCBs) and greater telomere length in blood leukocytes (Scinicariello & Buser, 2015). Using cross-sectional data on 2431 participants collected as part of the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2002 they find that both dioxin-like and non-dioxin-like PCBs are associated with greater LTL, and that these associations increase in a dose-responsive manner. Similar associations were found for other classes of POPs and for specific compounds and PCB congeners. These relationships were independent of the normal age-related attrition of LTL, and gender-specific reactions ruled out in stratified analyses. These findings across a variety of chemicals suggest a novel new mechanism of action for PCBs and other POPs, potentially explaining a new link between these chemicals and cancers. In addition, the fact that LTL measurements were derived from easily accessible blood samples suggests the possibility of using them as a biomarker of exposure to these toxic and ubiquitous chemicals. Finally, determining exactly how POPs cause LTL to lengthen may provide insight into the mechanisms by which cancer cells do the same, leading to new and targeted treatments potentially effective across the majority of human cancers.

This study adds to the growing body of research showing a link between environmental exposures and LTL (Barrett et al., 2015), and suggests that POPs may be able to activate telomerase or other telomere-elongating mechanisms. Activation of telomerase is a critical, early event in carcinogenesis for the majority of cancer types. Once telomere elongation has been hijacked by cancer cells, they will be able to overcome cellular senescence and apoptosis, and will have better survival. Changes in LTL are believed to be a reflection of these in situ processes (Hou et al., 2015). Questions remain about the exact mechanism by which POPs induce longer telomeres, and the temporal sequence of the relationship, both of which will need to be answered before this observed relationship can be exploited clinically. Other important confounders such as various nutrient intakes and body fat will need to be ruled out as well, and POP-induced LTL changes will need to be evaluated for their effects on human disease.

DOI of original article: http://dx.doi.org/10.1016/j.ebiom.2015.11.028.
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http://dx.doi.org/10.1016/j.ebiom.2015.11.046

Cross-sectional and prospective studies of telomeres have identified inconsistent relationships between LTL and cancer, with authors identifying both longer and shorter telomeres as predisposing to cancer risk, frequently across different cancers (Hou et al., 2012). This is another question that will need to be answered to assess the relationships between POPs, LTL, and cancer. While NHANES includes self-reported data on prior cancer diagnoses, which was explored in this study, the number of available cancer cases is relatively small, and lacks detailed clinical information (e.g., histology) that would be relevant to this area of research and available through inclusion of formal medical records. Nonetheless finding significant, dose-dependent changes in LTL associated with so many different types of POPs demonstrates that this is a promising area of research. Future prospective, longitudinal studies incorporating detailed data on medical history, lifestyle, and environmental exposures will help completely elucidate the causal mechanisms involved in the complex and dynamic relationship between carcinogens and LTL.

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