Dear HOT Members,

After two years as HOT VP-Elect and VP I have the honor to take the responsibility of the HOT Presidency. I had the opportunity to be present at the meeting that created HOT in 2004 and could follow the increasing number of members and activities that HOT experienced since then. With more than 300 members, HOT is an incredible group dedicated to spread the Toxicology Science among the Iberoamerican community. Our EC for this year is a great team.

Welcome to the new Board, Ranulfo Lemus Olaide, Enrique Fuentes-Mattei, Julieta Martino, Teresa Palacios, Nilsa Rivera-Del Valle, Robert Casillas, Maria Cárdenas-González, Aline de Conti, Dania Bacardi, Alexandra Colon-Rodríguez and Yanelli Nunez. Many of them were already in the Board in previous years and new ones came, making this group a mix of experience and fresh air.

My special thanks to José Francisco Delgado and Alejandro Ramirez-Lee that will stay with us as Toxenlaces editor/co-editor helping to spread the word of HOT to the world. I have also to express my thanks to all of the previous Board members that helped me with the organization of the HOT Reception in San Antonio. A special thanks to Linval DePass that continues to work hard to get sponsors for the HOT Travel Awards and HOT Reception.

Personally, I would like to thank Robert Casillas, our Past President, without his help it would be impossible to organize that great party. HOT was built with the passion of a USA-based Hispanic group but nowadays its message is spread around Iberoamerica through our members from different nationalities and also through our Sister Organizations. This is a particular aspect of HOT that we need to increase in order to spread our proposals to the Iberoamerica community. With the SOT help the HOT Education Committee will continue to work in the organization of open access Webinars. Proposals of topics and speakers are very welcome. As in the past we will continue to work hard to support students and postdoctoral HOT members to attend national and international conferences. Also we intend to support HOT members as speakers in meetings of the Iberoamerica region.

SOT support has been of great help to achieve this goal. We intend for this year to work closely with the other Special Interest Groups through the SOT Special Interest Group Collaboration Group (SIG-CG) looking for common issues and solutions, and take advantage of their experiences to improve even more our Organization. As a member, talk to your colleagues about HOT and invite them to become a member. Working hard, new ideas, but mainly passion for Toxicology, HOT board can make much more with your help. I am used to saying that an Organization is made not only by the Board but mainly by their members. We are looking forward to hearing your voice.
2018-2019 Executive Committee

Silvia Barros, PhD
President

Ranulfo Lemus-Olalde, ScD, DABT
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Alexandra Colon-Rodriguez, PhD
Postdoctoral Representative

Ms. Yanelli Nunez
Graduate Student Representative

José F Delgado-Jiménez, BS
Toxenlaces Editor

Alejandro Ramirez Lee, PhD
Toxenlaces Editor Assistant
World Trade Center Dust Exposure: Central Nervous System and Cardiovascular Implications
By Michelle Hernández, PhD
Merck & Co., Inc.
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**WTC Introduction**

With the initial collapse of the World Trade Center (WTC) towers, approximately 500,000 people were exposed to over a million tons of debris, immediately overwhelming defensive capabilities leaving the upper- and potentially lower- respiratory airways vulnerable [1]. Over the last fifteen years, multiple groups exposed to WTC dust have been plagued by respiratory ailments similar to those affected by ambient particulate matter (PM) exposure. WTC<sub>PM</sub> characterization is highly unique in that the dust bulk is highly alkaline due 85% of its composition being made up of cement, carbon, and glass fibers (pH= 9.2-12). In terms of particle sizing, 99% of WTC particles fall between 10 and 53um [2, 3]. This imparts a unique undertaking considering most, if not all published literature on PM are based on fine (<2.5μm) and ultrafine (<100nm) fractions that are acidic. This study sought to evaluate the impact of WTC<sub>PM</sub> exposure on oronasal regions, focusing on olfaction damage and potential adverse neurologic events.

**WTC Dust Induces Markers of Neurologic Injury**

My initial studies found WTC<sub>PM</sub> exposure to induce inflammation as well as oxidative and nitrite stress outcomes in lower-whole lungs and upper respiratory- nasal and olfactory mucosal tissues in mice.

Intranasal exposure to WTC<sub>PM</sub> was found to incite markers of neurologic injury including acute edema, significant body weight and brain weight decreases, as well as increased organ specific toxicity ratios, all positively correlated to increased WTC<sub>PM</sub> dose. HO1 (an antioxidant gene), TNFα (an inflammatory gene), IBA1 (an active microglial gene), and both Amyloid Precursor Protein (App) and Tau (both neurodegenerative markers for Alz) mRNA transcripts were found to be significantly upregulated 90 days post exposure. Collectively, these data infer oxidative stress may still be occurring due to particle persistence and/or translocation to other organs including the brain, resulting in potential continued inflammation and upregulated neurodegenerative disease transcripts [4-7].

**WTC Dust Exposure Induces Olfaction Loss and Anxiety Behaviors**

In general, generic molecular studies, as well as these studies, contain copious amounts of biological data indicating that on a molecular level, significant exposure-related changes take place, without phenotypic evaluations that could prove more insightful with regards to disease and disease progression. Within the nasal passages, olfactory information is processed in olfactory epithelial cells lining the upper regions of the nasal cavity. The olfactory epithelia are innervated with olfactory receptor neurons (ORNs) responsible for transmitting olfactory information back to the CNS and are uniquely the only CNS tissue with direct links to the external world and the only CNS tissue to regenerate after being damaged [8-11]. Olfaction latency (how long it took for mice to find a buried cookie) and anxiety behavior studies were performed to investigate if WTC<sub>PM</sub> upper respiratory exposure could in fact damage olfactory sensing neurons.
Overall, WTC\textsubscript{PM} intranasal exposure alone was found to induce significant olfaction latency in mice, whether from a single exposure or from multiple smaller concentrations of exposures over the period of a few weeks. Most interestingly, when WTC\textsubscript{PM} exposure occurred during the ORN recovery period (after treatment with ORN damaging agent), olfaction latencies increased by 143.3%, suggesting ability to smell and subsequently find the cookie was directly linked to peripheral olfaction damage, as well as the inhibition of injured olfaction tissue recovery processes. Significant depressive symptoms and anxiety behaviors were noted in WTC\textsubscript{PM} exposed mice and included decreased body weight gain, increased body weight loss, less time exploring and more stationary time. WTC mental health studies have found increased incidence of depression and anxiety in numerous cohorts, with this study being the first to identify potential mental health impacts from particle exposure alone with the use of a chronic mild stress model [12-16].

**Potential Cardiovascular Implications**

Cardiovascular diseases are among the emerging health concerns from WTC\textsubscript{PM} exposure [16-18]. NO, a product of endothelial NO synthase (eNOS), is a key signaling molecule involved in vascular homeostatic processes including vascular tone and blood flow. Its involvement in anti-atherogenic activities includes anti-inflammatory, antithrombotic, anti-proliferative, as well as antioxidant affects have been vastly documented. Evidence of nitrite dysregulation was seen in WTC\textsubscript{PM} exposed mice at different time intervals post-WTC\textsubscript{PM} exposure (24hrs, 30 d, and 90 d). Inclusively, evidence of endothelial dysfunction became apparent in pharmacologic testing of vascular tone 7 days and 30 days post-exposure and was most evident in both vaso-relaxation and vaso-constrictive mechanisms.

**Summary**

Overall, the outcomes of this investigation suggest WTC\textsubscript{PM} can incite oxidative stress in olfactory mucosa and olfactory bulb tissues, promoting inflammatory markers, and ultimately allowing for a direct pathway link between upper respiratory exposure and CNS outcomes. This study suggests one of the potential mechanisms responsible for adverse upper respiratory and CNS distress may be due to antioxidant dysfunction, brought about by particle retention and translocation to other organs, with potential to alter serum NO\textsubscript{2}, oxidative stress, and inflammatory pathways of the CNS. Collectively, these data indicate WTC\textsubscript{PM} exposure alone can incite nasal, and olfactory epithelial damage, while inducing chronic stress-like parameters, highlighting dysfunctional pathways precipitating inflammatory events, and altering homeostatic balances. The tight interplay between these balances, when altered, may contribute or result in, chronically diseased physical and mental states.
References


I am Teresa Anguiano and I am proud to have served as the 2017-2018 HOT Graduate Student Representative. Throughout my tenure, I had the honor to work alongside talented and admirable individuals who also served on the HOT Executive Board this past year. I feel privileged to have borne witness to all the work that went behind the planning for our HOT events during the SOT Annual Meeting in San Antonio. If you attended the conference, you would have definitely seen how all that hard work transpired. It should be no surprise that any event HOT hosted was an immense success!

As a graduate student representative, my goal was not to simply increase HOT membership numbers, but to also offer opportunities of learning and growth to our existing student members. I encouraged graduate students to apply for our various Abstract Travel Awards and to attend our HOT Mentoring Activity, which provided a very comfortable atmosphere in which students and other trainees were able to sit and chat with a panel of experts representing academia, industry, and government divisions. It was an amazing feeling to have an overwhelming number of attendees from all over the US, Mexico, Puerto Rico, Brazil, and other South American countries.

Our organization is an ever-growing community of science and camaraderie and, although my tenure as a student representative has come to a close, I plan to remain active within our group in whichever way I am able. I would also encourage everyone to continue to renew your membership and to persistently take advantage of all the great benefits HOT has to offer.

Con mucho cariño (Com muito carinho),

Teresa Anguiano, MS
University of Pittsburgh Graduate School of Public Health
Dept. of Environmental and Occupational Health
Class of 2018
My name is Yanelli Núñez and I am a third year PhD candidate in Environmental Health Science at Columbia University. My research focuses on studying the neurotoxic effects of chronic and low-dose metal exposures, specifically, their contribution to the onset and progression of proteinopathies and neuronal degeneration in Amyotrophic lateral sclerosis (ALS). For this, I use state-of-the-art in vitro mouse neuronal models and induced pluripotent stem cell (iPSC)-derived human motor neurons.

2. What is Going On?

ALS is the most common adult-onset motor neuron (MN) disorder and is characterized by progressive paralysis due to degeneration of spinal and cortical MNs (1). 90% of ALS cases are sporadic without family history of the disease, and the rest are familial with a clear heritable pattern (2). Among familial cases, or patients with the same pathogenic genetic variant, disease onset and/or progression can differ (3). This frequent genotype-phenotype discrepancy observed among ALS patients and the predominantly sporadic nature of the disease suggest ALS is not merely genetic. Several environmental neurotoxicants, including metals, have been linked to ALS, yet a direct causal relationship remains to be demonstrated (4).

Through my research, I aim to bring insight into the potential of manganese, selenium, lead, zinc, and arsenic exposure to initiate and contribute to the progression of proteinopathies and/or motor neuron degeneration in ALS. Chronic exposure to low levels of metals through drinking water and air pollution remains extremely common within the United States and internationally (5); however, the long-term health effects of such exposures and its potential contribution to adult onset-neurodegenerative diseases, such as ALS, remains largely unknown. Thus, it is important to further our understanding on this topic in order to identify potential mechanism of neurodegeneration and new preventive and treatment avenues.

5. Tchounwou PB, Yedjou CG, Patlolla AK, Sutton DJ. Heavy metal toxicity and the environment. EXS. 2012;101:133-164. doi:10.1007/978-3-7643-8340-4_6
HOT Award Winners at SOT 2018

Congratulations!

HOT Graduate Student Travel Award
Andrés Henríquez-Coria, PhD student
Sponsored by Ingenieros Lemus de Mexico

HOT Graduate Student Travel Award
Eva Vitucci, PhD student
Sponsored by DSI and MRI Global

HOT Graduate Student Travel Award
Teresa Anguiano, PhD student
Sponsored by Maria Tort and The Pfizer Foundation Matching Gifts Programs

HOT Graduate Student Travel Award
Yazmín Godínez-Solís, PhD student
Sponsored by Ingenieros Lemus de Mexico

HOT Postdoctoral Travel Award
Maria Beatriz Camargo Monteiro Caillaud, PhD
Sponsored by HOT

Special Award Zika Virus Research
Maria Isabel Giraldo, PhD
Sponsored by HOT

Outstanding Officer Award as Toxeniacles Editor
Jose Francisco Delgado, BS
Alejandro Ramírez Lee, PhD

SOT 2018 San Antonio
★ March 11-15 ★
Dr. Guilarte was selected based on the impact impact of his work on environmental pollutants and neurological and mental diseases, and based on the outstanding commitment to developing excellence in academic environments that are inclusive, collaborative, and that advances the interest of all but in particular those of underrepresented minority faculty and students.
HOT Members and past presidents, Dr. Elena Hernandez Ramon and Dr. Pedro Del Valle, organized and chaired the Symposium “Understanding the Molecular Mechanisms of Zika Virus Reproductive and Developmental Toxicity”. The session had talks from Dr. Ricardo Rajsbaum, Dr. Jean S. Peron, Dr. Rafael Larocca, Dr. Elizabeth Mendez and Dr. Prabagran Esakky.

Considering the interest of the symposium and the number of abstracts on the area, a Platform Session titled “Zika Pathophysiology and Potential Intervention” was also organized during the SOT Annual Meeting. The platform session, supported by HOT, was chaired by Dr. Pedro Del Valle, US FDA, and Anthony M. Franchini, University of Rochester. Dr. David Pamies, Dr. Maria Giraldo, Dr. Ruben Soto Acosta, Nagela Ghabdan Zanluqui, Craolina Polonio, Lilian Oliveira, Dr. Claudia Wrzesinski and Dr. Stefanie Burleson participated as speakers on this session.
HOT MENTORING ACTIVITY

HOT successfully organized their Annual Mentoring Activity during the SOT meeting in San Antonio. The event had the theme: **Careers in Toxicology**. The event served as a workshop and aimed specifically to demonstrate the diverse opportunities that can be pursued within a career in toxicology.

The event started with the introduction of M. Sc. Teresa Anguiano, former HOT Graduate Student Representative and organizer of this activity, followed by roundtable discussions in which mentees had the opportunity to directly interact with mentors of Latino origin from a variety of sectors including industry, government and academia, to discuss the potential opportunities professionals in the Toxicology field.

If you would like to participate or support future educational events from HOT please contact Dr. Teresa Palacios (phtere@gmail.com) and Dr. Aline DeConti (aline.deconti@fda.hhs.gov), Chair and Co-Chair of education committee in HOT.
HOT Activities at SOT 2018

THANK YOU for spreading your research in toxicology around the world
HOT
Activities at SOT 2018

SOT 2018 San Antonio
★ March 11-15 ★

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If your Hispanic Organization is planning a Toxicology meeting or if you are organizing a Toxicology event intended for a primarily Hispanic audience, and want to promote it, send an email to María Cárdenas González (Councilor for Sister Organizations) at Mariana_CardenasGonzalez@hms.harvard.edu for more information for its inclusion in upcoming Toxenlaces issues.