ABSTRACT NUMBER: 3419 **Poster Board Number:** P213

TITLE: A Network Approach to Phosphoprotein Signaling in a Mouse Model of Gulf War Illness Using Corticosterone and Diisopropyl Fluorophosphate

AUTHORS (FIRST INITIAL, LAST NAME) AND INSTITUTIONS: J. A. Penatzer[1], J. Miller[2], N. Prince[1], L. Michalovicz[2], K. Kelly[2], J. O'Callaghan[2], and J. Boyd[1]. *[1]West Virginia University, Morgantown, WV; and [2]NIOSH, Morgantown, WV.*

KEYWORDS: Organophosphates; Neurotoxicity; Pesticides

ABSTRACT: An estimated 3 million people are exposed to organophosphates each year; however, many do not report acute effects, but report symptoms of adverse neurological effects years later, as is the case for the 250,000 veterans from the 1991 Persian Gulf War who suffer from Gulf War Illness (GWI). Our previous GWI research has focused on developing a model of GWI using organophosphate acetylcholinesterase inhibitors (OP AChEI, e.g. chemical warfare agents and pesticides) and exogenous corticosterone (CORT), to simulate high stress, in an effort to mimic several of the conditions experienced in theater and emulate the chronic neuroinflammation hypothesized to underlie GWI symptomology. In these studies, we uncovered a lack of correlation between OP AChEI-associated neuroinflammation and the levels of ACh or enzyme inhibition, suggesting that GWI and its associated neuroinflammation may result from the phosphorylation of other targets. Thus, an investigation into early phosphoprotein responses in the hippocampus and striatum was performed to better understand the signaling changes involved in this etiology. Using our validated mouse model, adult male C57BL/6J mice were exposed to CORT in the drinking water for 7 days followed by a single injection of diisopropyl fluorophosphate (DFP; 4.0 mg/kg, i.p.) on day 8. Mice were euthanized 30 min and 2 h post-injection via focused microwave irradiation. To evaluate region-specific effects, 20+ post-translationally modified protein targets were measured using multiplex ELISA (e.g., ERK1/2, GSK3, IkB-a, JNK, MEK1). To then optimize analysis of the specific data sets, a network parameter approach corresponding to radiality was used to assess the response of the phosphoprotein targets in relation to all other responses. This approach identified specific proteins (RPS6, CREB, p90RSK, and IkB-a) that were substantially activated or inhibited within the network, and is informative with regard to the mechanisms of interactions that are occurring as a result of this GWI exposure. These significant proteins suggest new potential biomolecular drivers and therapeutic targets of GWI symptomology.

ABSTRACT NUMBER: 3420 **Poster Board Number:** P215

TITLE: Cadmium-Induced Renal Toxicity through GATA Family Suppression

AUTHORS (FIRST INITIAL, LAST NAME) AND INSTITUTIONS: J. Lee, M. Tokumoto, and M. Satoh. *Aichi Gakuin University, Nagoya, Japan.*

KEYWORDS: Metals

ABSTRACT: Cadmium (Cd) can cause renal toxicity through the proximal tubular cell damage. Our previous study demonstrated that Cd changed the activities of various transcription factors in human proximal tubular HK-2 cells. Interestingly, several GATA families were included in the transcription factors whose activities were decreased by Cd treatment. GATA family has diverse roles in the proliferation of cells, development of tissues, disease regulation, oncogenic effect, and so on. However, the effect of GATA family on Cd renal toxicity has remained unclear. In this study, we examined whether

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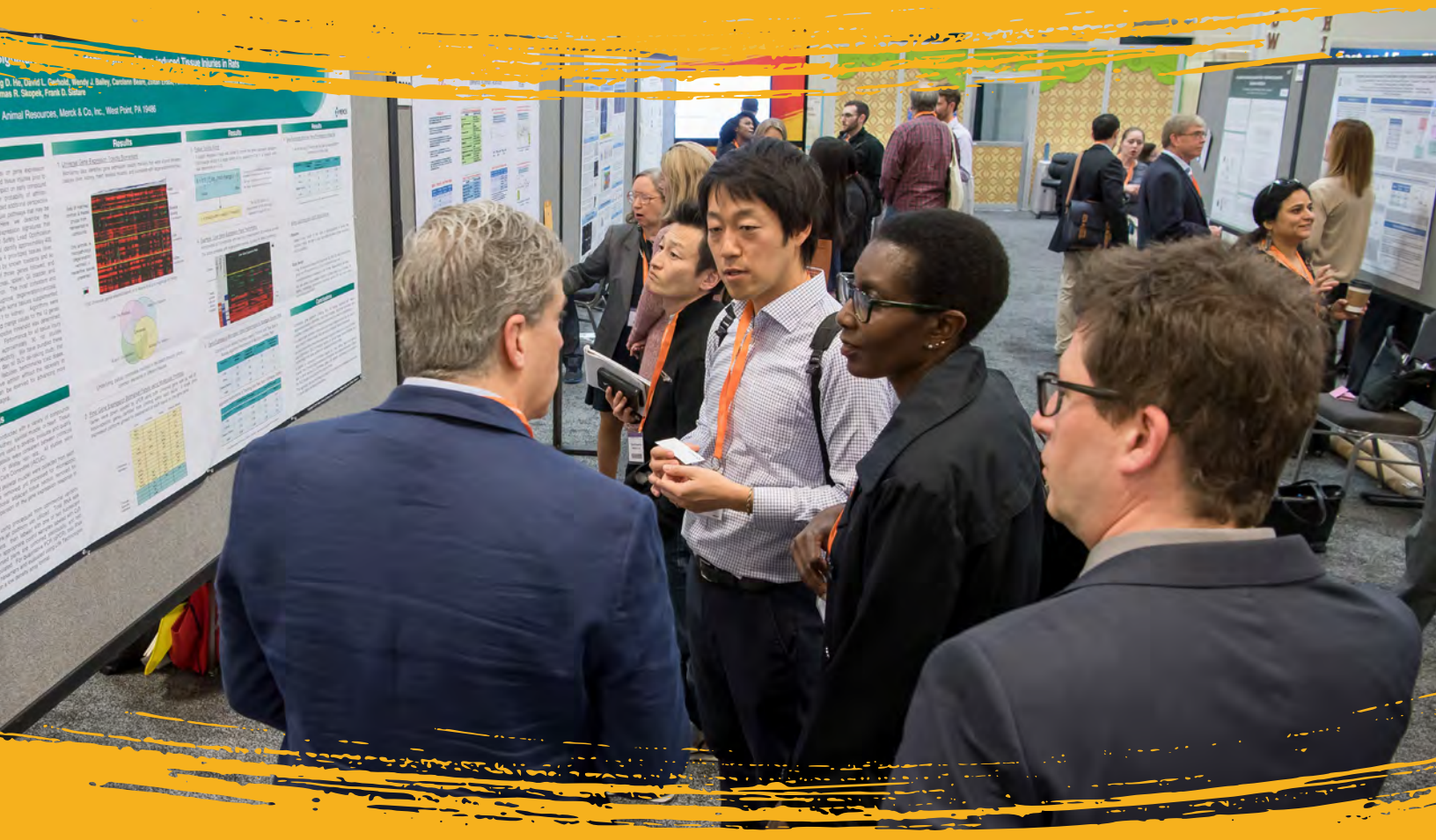

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Preface

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