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Editorial

Advancing the Role of Neuroimmunity and Genetic Susceptibility in Gulf War Illness

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Gulf War Illness (GWI) is a chronic multi-symptom disorder affecting as many as 30% of veterans of the 1991 Gulf War. Over the past 30 years since the war ended, an increasing body of research has accumulated on the pathobiology of this disorder. Overall, most evidence is suggestive of in-theater neurotoxicant exposures as a major underlying cause of chronic health symptoms [1]. As reflected in the titles of the two Special Issues, neuroimmune mechanisms are thought to be the primary targets of the neurotoxicant exposures that instigate the multiple symptoms modulated by underlying genetic susceptibility. Much has been learned about potential molecular targets of the disease, but a broad array of validated biomarkers of GWI are needed before the efficacy of treatments can be fully realized. Multiple animal models are now being utilized to elucidate the molecular mechanisms of GWI and evaluate potential therapeutics. The neuroimmune (i.e., brain-immune) mediators implicated in both animal studies and clinical assessments of ill veterans are suggestive of neuroinflammatory responses that likely underlie the symptoms of GWI. Recent PET imaging of neuroinflammatory responses in ill GW veterans further affirms the likely neuroimmune basis of GWI [2], emphasizing the need to expand neuroimaging analyses of GW veterans. To that end, several of the papers in the two issues demonstrate novel approaches to human brain image analyses [3,4]. The diverse imaging methodologies presented in these studies represent comprehensive approaches to achieving an in-depth understanding of brain structures/cell types affected in GWI, devising and implementing appropriate treatments. This includes using common data elements across the field [5].

A strong role for genetic susceptibility was also reinforced by findings presented in the two issues, both with respect to ill veterans (e.g., PON1 variants, immune genetic variants) [6,7] but also in novel genetic strains of mice exposed to GW-relevant neurotoxicants [8]. Among Gulf War veterans that served in the same unit, some returned ill while others did not. If genetics underlies this susceptibility, identifying the affected gene products offers hope for restoring function through genetic interventions in the future [9].

The incidence and severity of GWI may be affected by factors outside of nervous system targets that are not necessarily involved in genetic susceptibility. For example, in the first issue, the potential role of the gut microbiome in GWI was demonstrated, raising the possibility of modulating the illness through diet and selected antimicrobial therapies [10,11]. Potential objective biomarkers of GWI were identified based on blood-based central nervous system autoantibodies [12]. In addition, sex differences in CNS autoantibodies were identified in the second issue, suggesting that men and women veterans may benefit from different therapeutic strategies [13]. Finally, the following were introduced to the field with samples and data freely available to GWI researchers: a much-needed brain tissue biorepository [14], and a biorepository of existing and newly obtained biospecimens, brain imaging, and corresponding demographics, health symptom surveys and neurotoxicant exposure histories [15].

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