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10th World Summit on IMMUNOLOGY AND IMMUNOTHERAPY

August 30-31 2022 | Webinar

Immune dysregulation in PTSD: Interrelation between central and peripheral tissues

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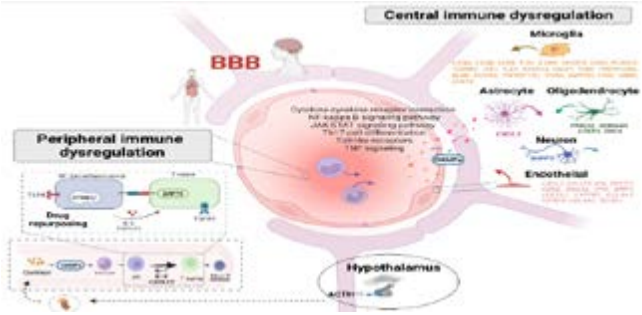
Abstract

Statement of the Problem: Posttraumatic stress disorder (PTSD) developed by some individuals after experiencing a traumatic event reaches a prevalence between 6-10% in general population and ~35% in individuals with high lifetime exposure to trauma (e.g., combat veterans). The biological mechanisms that may explain the resilience or vulnerability to develop PTSD among exposed individuals to trauma remain poorly understood. Growing evidence have highlighted the role of inflammatory markers in development and maintenance of PTSD such as an increasing of interleukins and C-reactive protein (CRP) levels in serum samples of individuals with PTSD and a dysregulated secretion of cytokines, chemokine's and growth factors by cerebral microglia. However, the potential interplay between the central and peripheral immune system, as well as the biological mechanisms underlying this dysregulation remains poorly understood. Methodology & Theoretical Orientation: We reviewed the role of the inflammatory system in PTSD across tissue and species, with a particular focus on the genomics, transcriptomics, epigenomics, and proteomics domains. Findings: our integrative multi-omics analysis across the central and peripheral systems in both human and animal models revealed 84 convergent immune-related genes significantly enriched (FDR <0.05) in pathways such as cytokine-cytokine receptor interaction, NF-kappa B signaling, Toll-like receptor signaling, JAK-STAT signaling and Th17 cell differentiation pathways. Further, we found that ~50% of convergent genes were enriched for cell type markers in the brain including microglial, endothelial, oligodendrocytes, and astrocyte and neuron cells. Taken together, these findings support interplay between the central and peripheral systems that orchestrate a systemic immune dysregulation in PTSD. We also identified drug targets for genes involved in Toll-like receptor signaling pathway, Th17 cell differentiation, and cytokine-cytokine receptor interaction. Conclusion & Significance: Substantial evidence supports an important role of a systemic immune dysregulation in the etiology of PTSD, opening new avenues of drug development for treatment interventions. We propose the existence of common regulatory markers able to cross BBB, impact the expression of those 84 convergent genes and orchestrate systemic inflammation in PTSD through important immunological pathways.



Biography

Diana L Nunez Rios has an MSc in human genetic and completed her PhD in the Universidad de Los Andes in Bogotá, Colombia. During her PhD, she assessed rare CNVs (copy number variants) and rare de novo single nucleotide variants in the etiology of autism spectrum disorder. Dr Nunez joined to Montalvo-Ortiz Lab to investigate epigenetic mechanisms related with post-traumatic stress disorder in postmortem brain samples.

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