

## Auto-inflammation is a Diaeventontological Trigger in Neuropsychiatric disorders

Daniel J. Guerra

VerEvMed, USA



### Abstract

Single biochemical or cellular events cannot be expected to explain complex neuropsychiatric disease and, while animal models are indispensable for pharmacotherapy and pharmaceutical discovery, they will not fully apprehend these human disorders. Clinical studies have the advantage of authentic examination of human neuropsychiatric pathology, but they cannot holistically arrive at sound theories or practice for surmounting these debilitating diseases, even when precise molecular tools are employed. This is because 'Systems' approaches such as the standard OMIX platforms or cell Sorting/Screening from biological specimens fail to imagine the three-dimensional architectonics of Genetic Environmental and Neuroimmunoepigenetic phenomena as event ontologies through time. A paradigm shift is necessary to approach and indeed engage neuropsychiatric disease. A Diaeventontological method is therefore proposed. It starts with a dialectic approach that transcends dogma and conventional principles while preserving truths via coherence and foundational ascendancy by isolating and verifying premises that can be used to generate sound epistemological arguments. This is sequentially followed by the generation of hypotheses via the deductive method by implementing careful hermeneutical analysis of both cross-sectional and cohort-based published research. Once theses/ antitheses / syntheses have been proposed according to a justification of truth qualia that better explains the necessary and sufficient relational competency of rational foundational concepts, temporally centered experimentation using human subjects allow for a comprehension of biochemical interactions as a vectorial dynamic flux within cells/tissues/organs and entire organisms that recognize these as processes having three phases: Initiation, Extension and Termination. A case in point are T lymphocytes that react in the intact human dynamic event ontology to respond to the environment, maintain cellular and physiological health and to prepare for future change that includes nutrition, neurological imprinting, disease and aging. T lymphocyte lineages and associated biochemical communication are modified via changes in the epigenome as well as canonical inducible and repressible gene expression and membrane recombination. Synergy between IL-12 and IL-18 for the induction of IFN- $\gamma$  production and subsequent involvement of the heterodimeric IL-12 receptor leads to STAT4 phosphorylation after recruitment of the kinases Tyk2 and JAK2. STAT4 then transactivates IFN- $\gamma$  transcription and upon binding of IL-18 to its receptors there is activation of the MAPK pathway downstream leading to the stabilization of IFN- $\gamma$  mRNA and enhanced IFN- $\gamma$  secretion by NK cells. Secreted IFN- $\gamma$  also activates B cells to mature to IgG producing plasma cells from germinal centers thus inducing a potential autoimmune disease when initial antigen presentation involved host metabolites. IL-12- co-activation of STAT1 and STAT4 mediates histone modification, with a sequentially expanding T follicular helper -Th1-like cells activation and recruitment. When these biochemical and cellular pathologies align in specific CNS nuclei, an autoimmune neuropsychiatric event may result. These T and B cell mediated cytokine and intracellular signaling phenomena will be discussed against a general framework leading to better experimental design and hypothesis driven ontological research in human auto-immune associated neuropsychiatric disease.



### Biography

Daniel J. Guerra, Ph.D., Co-Founder and Chief Scientific Officer of VerEvMed ([www.verevmed.com](http://www.verevmed.com)). DEGREES EARNED: PhD 1984: Biochemistry and Physiology-Plant Science, Utah State University; MS 1981: Plant Biochemistry, University of Arkansas; BS 1978: Agriculture, Agronomy, University of Illinois. Dr. Guerra has been a university professor of biochemistry and molecular genetics for 3 decades. He has also been an active research scientist working primarily on lipid metabolism and neuroscience with strong interests in gene expression, epigenetics and immunology. Currently, Dr. Guerra is the co-founder and CSO of VerEvMed, a biomedical consultancy company that specializes in the examination and verification of the published research literature for the purpose of making this information available to a wider audience of health professionals, institutions, students, and interested lay people.

### Publication

- Guerra, Daniel. (2011). The Molecular Genetics of Autism Spectrum Disorders: Genomic Mechanisms, Neuroimmunopathology, and Clinical Implications. Autism research and treatment. 2011. 398636. 10.1155/2011/398636.
- Guerra, Daniel & Colonnello, Valentina & Panksepp, Jaak. (2011). The neurobiology of RAGE and anger & psychiatric implications with a focus on depression.
- Hauvermale, Amber & Kuner, J. & Rosenzweig, B. & Guerra, Daniel & Diltz, S. & Metz, J.G.. (2006). Schizochytrium sp. ATCC 20888 type I fatty acid synthase gene, complete cds.
- Hauvermale, Amber & Kuner, J & Rosenzweig, B & Guerra, Daniel & Diltz, S & Metz, J. (2006). Fatty acid production in Schizochytrium sp.: Involvement of a poly-unsaturated fatty acid synthase and a type I fatty acid synthase. Lipids. 41. 739-47. 10.1007/s11745-006-5025-6.
- Schnurr, JA & Guerra, Daniel. (2000). The CaMV-35S promoter is sensitive to shortened photoperiod in transgenic tobacco. Plant Cell Reports. 19. 279-282. 10.1007/s002990050012.

[10<sup>th</sup> Global Summit on Neuroscience and Neuroimmunology](#) | Paris | February 19-20, 2020

**Citation:** Daniel J. Guerra, Auto-inflammation is a Diaeventontological Trigger in Neuropsychiatric disorders, Neuroimmunology 2020, Paris, February 19-20, 2020, PP. 31