

Mitochondria in pathophysiology of innate immunity in multiple sclerosis

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BACKGROUND

Recent studies suggest an important role of mitochondria in the pathophysiology of multiple sclerosis (MS), neurodegenerative and neuroinflammatory factors.

OBJECTIVES

To elaborate an approach with computational chemistry and theoretical nuclear physics methods to study mitochondria in pathophysiology of innate immunity in MS.

METHODS

Computational simulations were performed by analysing (a) activation of innate immunity and activation of autoimmune responses of acquired immunity; (b) polymorphism mitochondrial DNA changes in MS; (c) neurodegenerative and neuroinflammatory processes in MS. Computational simulations and analyses of this scientific work were elaborated with the use of software: ACD/ChemSketch, Swiss-PdbViewer, ABCpred, BepiPred-2.0, ElliPro, DEseq, GOseq, FunRich, Cytoscape, BiNGO, PepSurf, AxonDeepSeg, AxonSeg, Computer-assisted Evaluation of Myelin formation (CEM), PyMol, ICM-Browser, Visual Molecular Dynamics (VMD), Cell Illustrator, C-ImmSim, Simmune, GENESIS, NEURON, NeuronStudio and ChemDraw. The molecular docking was conducted with the tool AutoDock Vina (version 1.1.2), as implemented in the MolAr (Molecular Architecture) software. ConSurf was used for the evolutionary conservation analysis. The virtual cell based assay (VCBA) has been developed to simulate intracellular concentrations and to predict intra-mitochondrial concentrations in central nervous system (CNS).

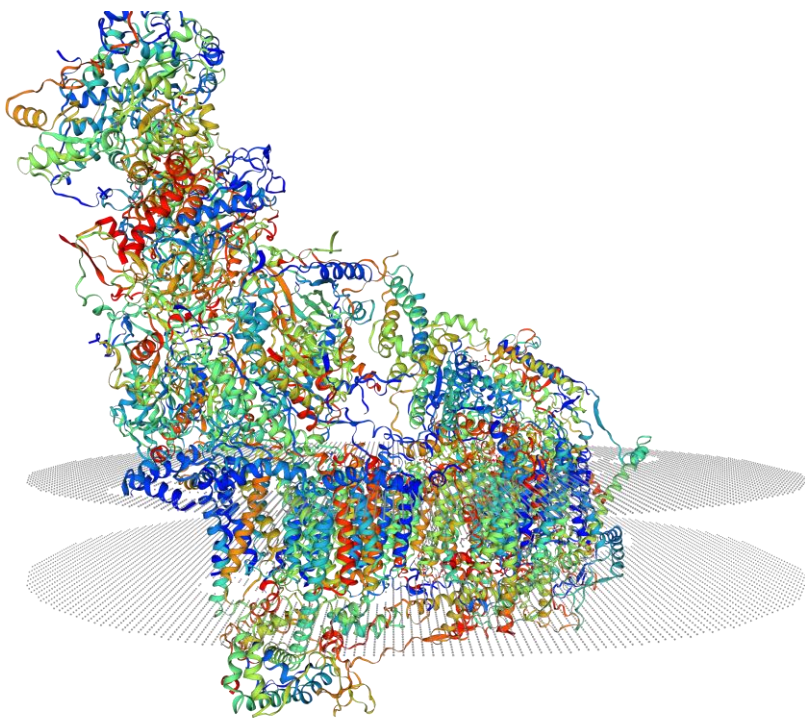


Figure I. Electron Microscopy with Theoretical Nuclear Physics:
Structure of Mitochondrial complex I.

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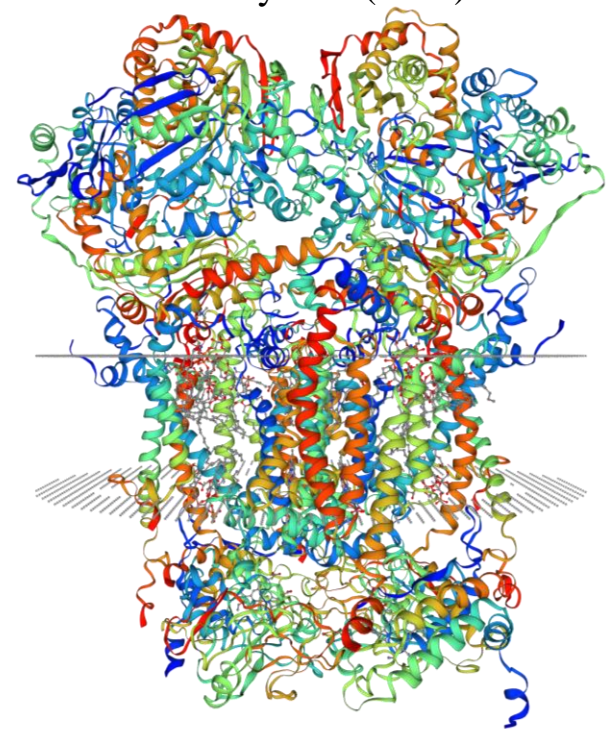


Figure II. Electron Microscopy with Theoretical Nuclear Physics:
Structure of Mitochondrial complex III.

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RESULTS

This work suggests that structural and functional changes in N-acetyl aspartate, heme oxygenase 1, nuclear factor erythroid 2-related factor 2, mtHSP70 and LONP1 can trigger deficient neuroimmune responses. This research suggests that mtDNA deletions in the subunits of complex IV and disturbances in chemical bonds in complex I and III activities can induce active and chronic lesions in CNS by processes of inflammation, demyelination and neurodegeneration. Changes in conformation of OXPHOS and proteins 4 and 5 can induce deficits in the functions of PGC-1 α , stimulating the formation of a favorable environment for inflammation.

CONCLUSIONS

Understanding the role of mitochondria in pathophysiology of innate immunity should help guide future research into MS therapeutics.