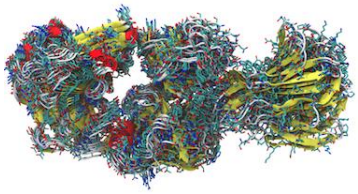

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Computational insights on the biorecognition process of myelin oligodendrocyte glycoprotein by antibodies in demyelinating and neurodegenerative diseases

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Abstract:

Biorecognition process support several events in the mechanism of demyelinating and neurodegenerative diseases, especially multiple sclerosis and neuromyelitis, in which autoantibodies bind self-components of the central nervous system as autoantigens. Those autoantibodies target some proteins as the myelin oligodendrocyte glycoprotein (MOG), a well-known myelin biomolecule. In this work, MOG recognition by a specific experimental anti-MOG molecule was detailed by combining computational modeling, molecular dynamics (MD), steered molecular dynamics (SMD), and atomic force microscopy (AFM). The structure of the analyzed antigen-antibody complex consisted of the MOG external domain and the anti-MOG crystallographic information from the Protein Data Bank (PDB ID 1PKQ). A 200 ns MD simulation data highlighted a major contribution of complementarity-determinant region (CDR) loops in the anti-MOG and MOG external domain complex formation. In the MOG structure, thirteen residues were identified as the antigen-antibody interaction anchors, from which five of them were included in the region of the renowned peptide MOG_{92-106} (ASP102, HIS103, SER104, TYR105, and GLN106). In consideration of this, an analysis of antigen-antibody interaction forces was performed focusing on MOG_{92-106} using SMD and AFM. Obtained data revealed a remarkable consonance between computational and experimental data, presenting force values of 765 pN and 780 pN for SMD and AFM, respectively. All the AFM experiments, as well as the measured antigen-antibody binding, were proved by the surface plasmon resonance method. Hybrid methods combining computational modeling and simulation with experimental measurements presented a strong potential to support demyelinating and neurodegenerative diseases investigation, especially during the planning and pre-clinical steps of research, directly contributing to financial and animal usage reduction.

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