ABSTRACT:
Myelin is the lipid-rich multilamellar membrane that ensheathes axons in the central nervous system and facilitates the efficient conduction of nerve impulses. Multiple sclerosis (MS) is a disease characterized by demyelination, and remains enigmatic since its first clinical identification in the mid 19th century - we do not know its cause, nor is there any cure. Our group has focussed on an essential structural component of CNS myelin - myelin basic protein (MBP) - in order to try to understand how MS develops. We apply a bevy of complementary biochemical, biophysical, and cell biological approaches in order to elucidate MBP's structure-function relationships in detail. Our work has been guided in part by the realisation that a third of eukaryotic proteins, including MBP, are intrinsically disordered. We are beginning to appreciate that MBP is structurally dynamic, and plays a multitude of roles as programmed by a combinatorial "molecular barcode" of post-translational modifications. The emerging picture of MBP centrality in myelin provides us with a new framework to examine potential triggers of MS. An intriguing new hypothesis published last year by Rubenstein suggests that MS is a consequence of our Western diet, arising due to dramatic changes in agricultural practise in Napoleonic Europe.


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