Conformational changes upon phosphorylation of proline rich region of tau(210-240) peptide using molecular dynamic simulation

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The conformational dynamics of intrinsically disordered proteins (IDPs) regulated by post-translational modifications (PTMs) such as phosphorylation is challenging to elucidate. A well-known IDP Tau is found hyper-phosphorylated in Alzheimer's disease (AD) in humans [1]. The proline-rich motif of tau(210-240) peptide directly interacts with proteins such as BIN1, 14-3-3 etc. Microsecond time scale, all atoms molecular dynamic (MD) simulation studies have been performed for apo and four phosphorylated (212^{P}Thr, 217^{P}Thr, 231^{P}Thr, 235^{P}Ser) tau(210-240) peptide using three different temperature variants (278K, 298K and 310K) and two different force field parameters (AMBER99SB-ILDN and CHARMM36m) with TIP4PD water model as these force fields parameters combine with water model worked the better for IDPs found from our group previous studies [2, 3]. These four-phosphorylations cause increase in compactness of the peptide. The binding of associated proteins like BIN1 with tau may alter by the strong salt bridges, forming nearby lysine and arginine due to the phosphorylation [4]. Phosphorylation induces a strong structural transition, with tau(210-240) favouring a bent conformation. The MD simulation results were verified using NMR experimental parameters like chemical shift and ^{3}J-coupling. The experimental part has been carried out by our collaborator Prof. Isabelle Landrieu.

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