Effects of change-of-function mutations on helical propensity in the intrinsically disordered τ1-core activation domain of the Glucocorticoid receptor.

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In recent years the physiological role of unstructured regions in proteins has been proven. The intrinsically disordered proteins (IDPs) hold important functions at cellular level, such as regulation of transcription and translation, signal pathways and self-assembly of macromolecular units in active complexes. The lack of compact 3D-structure or folding upon binding to their targets is related to the specific role of the unstructured regions. The Glucocorticoid receptor (GR) belongs to a family of ligand-inducible nuclear receptors. Two of its domains (τ1 and τ2) have shown a conserved activity after they have been removed from the receptor entity[1]. The disordered core region of the τ1-domain consists of 58-amino-acids. It carries most of the activity and has shown a helical propensity in hydrophobic solvent conditions (TFE). We have investigated the effect of change-of-function point mutations in the τ1-core transactivation domain in GR on the helical propensity using an *in silico* model system. For our goal we used CHARMM simulation package[2] with Charmm36ff to perform molecular dynamics simulations at different temperature regimes.

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