Analysis of helix to coil transitions in human serum albumin

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V. Paboineu[I], V. Khrustalev[I], A. Stazharau[I], T. Khrustaleva[II]

[I]Belarusian State Medical University, Minsk, Belarus, [II]Institute of Physiology of the National Academy of Science of Belarus, Biochemistry Group of MDL, Minsk, Belarus

Human serum albumin has quite intriguing distribution of amino acid residues and combinations of hydrophobic and hydrophilic residues (in pentapeptides) among structurally stable (remaining in all 104 analyzed 3D-structures) and structurally instable fragments of its alpha helices (that may turn to random coil at least in one of them). According to the alpha-helical pattern of PentaFOLD algorithm (chemres.bsmu.by), both stable and instable alpha helices are predicted with approximately the same success: 57.5% of helices, 16.4% of beta sheet and 26.1% of random coil vs. 52.28%, 4.6%, and 43.15%, respectively. Unexpectedly, beta-structural pattern of PentaFOLD algorithm predicted 54.3% of residues in structurally stable fragments of alpha helices as beta sheet, while just 29.0% of residues from structurally instable alpha helices, where 44.4% were predicted as random coil. Stable alpha helices are significantly enriched by both amino acid residues and their combinations prone to form beta sheet (34.0% vs. 22.8%, $P< 0.05$; 38.6% vs. 22.8%, $P< 0.05$, respectively) relatively to structurally instable alpha helices. Residues from structurally stable fragments of alpha helices show significantly lower average value of surface accessibility calculated by DSSP (https://www3.cmbi.umcn.nl/xssp/) compared to fragments of alpha helices prone to change their conformation to random coil ($33.5\pm5.0\%$ vs. $50.46\pm4.8\%$, $P< 0.05$). Indeed, the usages of strong beta sheet formers are much higher in stable than in structurally instable fragments of alpha helices (Val: $10.6\pm0.8\%$ vs. $5.9\pm0.4\%$; Phe: $7.3\pm0.6\%$ vs. $4.6\pm0.3\%$; Thr: $6.0\pm0.5\%$ vs. $3.8\pm0.2\%$). Alpha-helical hydrophobic buried core of HSA incorporates significant number of residues known to be strong beta-formers. In contrast, fragments of alpha helices on a surface of that protein are protected from alpha to beta transitions by the decreased usage beta-formers, but they are prone to helix to coil transitions.