Effects of tryptophan residue fluorination on streptavidin stability and biotin-streptavidin interactions via molecular dynamics simulations.

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Streszczenie

Due to its highly specific and very strong binding, the (strept)avidin-biotin system forms the basis for numerous applications in the life sciences: immunoassays, DNA detection systems, affinity chromatography, etc. Fine-tuning of the ligand binding abilities of this system might provide new technologies with relevance to nanoscale research. Here, we report our computational investigations on wild type (WT) and modified streptavidin (SAV), assessing the impact of fluorination of tryptophan residues on biotin binding ability. Complexes of biotin with four SAV protein variants (WT-SAV, 4fW-SAV, 5fW-SAV and 6fW-SAV) were studied. We found that protein stability and folding are predicted to be weakly affected by fluorination. The host protein binding pocket decreases its ability to form numerous hydrogen bonds to biotin in the case of the 4fW-SAV variant. Conversely, the 5fW-SAV mutant is predicted to have an even more stable ligand-host hydrogen bonding network than WT-SAV. Thermodynamic perturbation investigations predict a decrease in biotin binding free energy from 3.0 to 6.5 kcal/mol per tetrameric host, with the 5fW-SAV mutant being least affected. Overall, the computational findings indicate that 6fW-SAV and, especially, 5fW-SAV to be promising variants of streptavidin for potential modifiable picomolar binding of the biotin ligand family.

Adres publiczny

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