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In search for the peptide/protein ligands of human serum albumin able to affect its interaction with amyloid β peptide

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Motivation and Aim: Human serum albumin (HSA) is the most abundant protein in blood, comprising ca 60 % of its total protein content. HSA is a depot for amyloid β peptide (Aβ), one of the key factors in progression of Alzheimer's disease (AD). An imbalance between production and excretion of Aβ in AD patients leads to Aβ accumulation in the brain and formation of noxious amyloid oligomers/plaques. A promising approach to AD prevention is to reduce free Aβ concentration by directed stimulation of the HSA-Aβ interaction.
Methods and Algorithms: In this study, we systematically searched for the peptide/protein HSA ligands able to affect Aβ interaction with HSA. The bioinformatic analysis of DrugBank, BioGRID and IntAct databases, as well as Alzforum online resource gave rise to a panel of 11 peptides and 34 proteins, potentially able to modulate the HSA-Aβ interaction. As the candidate selection criteria, we used the values of molecular weight, subcellular location and strong association with AD, according to DisGeNET database and Open Targets Platform. The algorithm for search of the potential candidates and their in-depth analysis was implemented using the high-level programming language Python.
Results: The resulting protein candidates include apolipoprotein E, apolipoprotein C-III, cystatin-C, S100A8, serotransferrin, and others. The lead peptide candidates comprise vancomycin, enalapril, semaglutide, octreotide.
Conclusion: The most promising candidates are subject to experimental validation regarding their effect on the HSA-Aβ interaction. They serve as a basis for further development of the first-in-class medications for prevention of AD onset.
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