

Elongation of the C-terminal domain of an anti-amyloid β single-chain variable fragment increases its thermodynamic stability and decreases its aggregation tendency

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Abbreviations used: AD, Alzheimer's disease; CD, circular dichroism; FTIR, Fourier-transformed infrared spectroscopy; scFv, single chain variable Fragment; WL, worm-like.

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aligned sequence were filtered to discard false results. The PDB code of the sequence with the highest score coincident in the search of both domains was selected among a total of 24 candidates. The crystal structure of a scFv antibody against the SARS-spike protein-receptor binding-domain (with PDB code: 2GHW-B), matching the alignment with a 70% identity (94% similarity) and E-value $2e-84$, was selected to construct a 3D model for the scFv-h3D6 using MODELLER 9v2.³⁸ Five possible conformations were initially constructed for the V_H and V_L domains. Although the linker region is the same in both scFv molecules, (Gly₄Ser)₃, a defined diffraction pattern in the template structure (2GHW-B) could not be obtained because of the linker's high degree of flexibility, and the coordinates for the model were calculated using the loop-refinement and energy minimization approach (MODELLER 9v2³⁸). Ten different structures matched the five initial models for the domains and the best conformation with minimum energy was selected using the criterion of knowledge-based potentials of ProSa2003.³⁹

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