Comparative Simulation Studies of Native and Single Site Mutant Human Beta-Defensin-1 Peptides

Supplementary Material

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TABLES

Table SM1: Details of MD simulations including: PDB codes, mutation sites, trajectory lengths, and the number of simulation runs for all the systems. Monomers and dimers were used in equilibrium simulations at $T = 300$ K; heating simulations (from $T_{in} = 300$ K to $T_{fin} = 500$ K) were carried out only for the monomeric species.

System	PDB code	Mutation site	Equilibrium Simulations	Heating Simulations
WT monomer	1IJV	-	30 ns (3 runs)	10 ns
WT monomer [§]	1IJV	-	25 ns (3 runs) [§]	-
Mut1 monomer	2NLB	Asn4Ala	30 ns (3 runs)	10 ns
Mut2 monomer	2NLP	Gln24Glu	30 ns (3 runs)	10 ns
Mut3 monomer	2NLQ	Lys31Ala	30 ns (3 runs)	10 ns
WT dimer	1IJV	-	30 ns (3 runs)	-
Mut1 dimer	1IJV [*]	Asn4Ala	30 ns (3 runs)	-
Mut2 dimer	1IJV [*]	Gln24Glu	30 ns (3 runs)	-
Mut3 dimer	1IJV [*]	Lys31Ala	30 ns (3 runs)	-

[§]GROMACS simulations: three runs (a, b, and c) were performed using three different force fields (see, also, Fig. SI3).

^{*}Due to the absence of mutant dimers in the PDB, 1IJV (WT) dimers were mutated at the reported mutation site (see main text).

Fig. SM1: The root-mean-square fluctuations (RMSF) for the monomers of native HBD-1 peptide (WT) (panel (a)), and Mut3 (panel (b)) obtained from averaging over three equilibrium simulation runs at room temperature $T = 300$ K (WT; dots and Mut3; diamonds), and from heating simulations at increasing temperature (from $T_{in} = 300$ K to $T_{fin} = 500$ K: WT; squares and Mut3; triangles). In panel (a), the RMSF curve for heating simulation is below the RMSF curve for WT, whereas in panel (b) the RMSF curve for heating simulation of Mut3 lies above the RMSF curve for equilibrium simulations.

Fig. SM2: Panels (a) and (b): The total solvent accessible surface area (SASA) versus time for the monomers of native HBD-1 peptide (WT) (panel (a)) and Mut2 (panel (b)). Panels (c) and (d): The time dependence of the end-to-end distance for the monomers of WT (panel (c)) and Mut2 (panel (d)). Plots were obtained from 30 ns equilibrium simulation runs at $T = 300$ K (average of three trajectories; black curves), and from heating simulations at increasing temperature (from $T_{in} = 300$ K to $T_{fin} = 500$ K; green curves). Equilibrium simulations curves were truncated at 10 ns due to only minor differences observed beyond that point.

Fig. SM3: Time evolution of the secondary structure propensity for the α -helical portion (residues 2-7) of the native HBD-1 peptide (WT) monomer from equilibrium simulations at $T = 300$ K using the GROMACS software package applying GROMOS force field and twin range cutoff (panel (a)), GROMOS and Particle Mesh Ewald (PME) summation method (panel (b)), and OPLS AA force field and PME (panel (c)). Minor π -helix occurrence was observed when compared to simulation results obtained using the NAMD package applying CHARMM force field (Fig. 2 in the main text). In panel (a), the arrow at 22.5 ns indicates the point when α -helix became unstructured. Color denotation is presented in the graph.