Introduction
The Fas receptor is a representative death receptor, and the Fas-Associated Protein with Death Domain (FADD) is a crucial adapter protein needed to support the Fas receptor’s activity. The Fas-FADD interactions constitute an important signaling pathway that ultimately induces apoptosis or programmed cell death in biological systems. Using a computational approach, the present poster explores certain essential structural aspects of the Fas-FADD death domains and their interfacial interactions.

Results and Discussion

Structure of the Fas DD and FADD DD
- 1DFD is the solution based NMR structure of closed Fas DD. It is predicted that α5 and α6 are the possible FADD binding regions in Fas (Figure 2A).
- The DD of FADD is described in 1E3Y. 1E3Y has six α-helices connected by short loops (Figure 2B).

Insight into FAS DD–FADD DD Interactions
- For the FAS–FADD death domain, we use pdb file 3EZQ. Our present structural studies are mostly centered on Chains A (residues 223–337) and B (residues 93–191), which represent the FAS DD and FADD DD respectively.

Structural Analyses of the Individual Protein Chains and Protein Complex using Molecular Dynamics Simulation
- From the MD simulation we assume that the Fas–FADD pair complex is more stable (all atom RMSD max value 2.37 Å) than the individual species of Fas DD or FADD DD (Figure 4A).
- The number of hydrogen bonds with the water molecules experiences a minor net increase indicating more compact nature of the complex with respect to those of the individual protein chains (Figure 4C).
- The SASA values of individual Fas chain and Fas residues in 3EZQ pair complex are comparable. Nonetheless, the FADD individual species has more exposed residues compared to the corresponding case of the FADD residues within the Fas–FADD pair complex (Figure 4D-F).
- Similar to Fas DD and FADD DD, the total, potential and van der Waals energies of Fas–FADD pair complex are temporally steady (Figure 4G-I).

Methods
- 1DFD and 1E3Y are used as structural representatives of Fas and FADD DD.
- The Fas–FADD pair complex of 3EZQ (chains A and B) is used for the MD simulation.
- Nanoscale Molecular Dynamics (NAMD) and Visual Molecular Dynamics (VMD) programs have been used.

Summary and Outlook
- The Fas–FADD pair complex (3EZQ; Chain A and B) is more stable than the individual Fas (1FAD) or FADD (1E3Y) protein chains.
- The structure of the protein complex is somewhat more compact than those of the individual proteins (Fig. 5c).
- FADD is more stable than Fas as an individual protein and also in a protein complex (Fig. 5a, b).
- The total energy of the Fas–FADD pair complex has a comparatively lower value indicating the stable nature of the complex.

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Reference