NANOSECOND MOLECULAR DYNAMICS OF HIV PROTEASE- INHIBITOR COMPLEXES:INSIGHTS INTO THE DIFFERENTIAL BINDING POTENCY OF DIASTEREOISOMERES

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The inhibitory potency of four nanomolar diastereomeric inhibitors of HIV-1 protease [1] was studied by molecular dynamics simulations and MM-GBSA/PBSA analysis. As a starting point we used the crystal structures of protease-inhibitor complexes [2, 3]. Having added hydrogens, we surrounded the complexes with a box of explicit water molecules and added counterions to neutralize the box. Using AMBER 7 program package [4], we minimized, heated and equilibrated the system after which we ran 2-nanosecond-long production dynamics. Periodic boundary conditions were used and long-range electrostatics was treated by particle mesh Ewald (PME) technique.

An analysis of the molecular dynamical trajectories was performed and their quality assessed. The protease-inhibitor binding energies were calculated with MM-GBSA/PBSA approach. The effect of the length of the simulation, method to calculate solvation energy, and other factors upon the results was determined.

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FULL CHARACTERIZATION OF NATURAL KILLER CELL MEMBRANE MICRODOMAINS

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Natural killer (NK) cells are cytotoxic effector lymphocytes, which do not express antigen-specific cell surface receptors. NK receptors that mediate signals leading to the initiation or supression of natural cytotoxicity processes are poorly characterized. Moreover, these receptors may associate with other co-stimulating molecules and adaptor proteins, which transduce the signal from the receptor to the cell. Such complexes may be observed as biochemically distinct parts of plasmatic membranes and are commonly referred to micro domains or glycosphingolipid enriched microdomains (GEMs). They are enriched in GPI-anchored and acetylated proteins and in cholesterol and glycosphingolipids. It is believed that they may aid in signal transduction as well as in trafficking through the secretory and endocytic pathways and in cell to cell interaction.

In this study we focused on membrane microdomains from rat NK leukaemia cell line (RNK-16). For detailed characterization we used a shotgun strategy based on microcapillary HPLC - tandem mass spectrometry. Aditionally, we applied techniques of native electrophoresis for detailed mapping of protein complexes present in the GEMs. We have identified a large number of proteins (e.g. gp-42, CD2, LAT, CD161, CD44 or g-proteins in GEM and tubuline in non-GEM fractions).

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HIGH AFFINITY LIGANDS FOR HUMAN LYMPHOCYTE RECEPTOR CD69

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CD69 is one of very important activating receptors expressed on the surface of human lymphocytes. This molecule exists as a homodimer, each of its subunits being terminated with the globular domain related to the C-type lectin family. Although the crystal structure of this domain has been recently solved [1], its potential ligands and the function of the whole receptor remain unclear. In our labo-