

HIV1 TAT PEPTIDE TRANSLOCATION IN GIANT UNILAMELLAR VESICLES

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ABSTRACT

Cell penetrating peptides like the HIV1 TAT peptide are able to translocate across cell membranes and to carry molecular cargoes into the cellular interior [1; 2]. For most of these peptides the biophysical mechanism of the membrane translocation is still unknown. We analyzed HIV1 TAT peptide binding, migration within and translocation across biological model membranes. We generated giant unilamellar vesicles (GUVs), and characterized the mobility of fluorescently labeled lipids within liquid-ordered and liquid-disordered lipid phases by single molecule tracking. The interaction of fluorescently labeled TAT peptides with the respective GUVs was examined in salt-free and physiological solutions. In salt-free solution TAT efficiently bind to anionic GUVs, and less marked to neutral GUVs. In a physiological NaCl solution TAT binding was completely abrogated, but the peptides were equilibrating across the GUV membrane by passive translocation. Single molecule tracking revealed that HIV1 TAT peptides in salt-free solution move on the GUV surface faster than fluorescent lipid analoga and independent of the phase state of the membrane. This indicated that the TAT peptides were not incorporated into but rather floating on the membrane. In the presence of salt no peptides could be detected on the membrane even at increased imaging rate, pointing an extremely fast translocation process not involving pore formation. We suggest that the charge compensation of the cationic TAT peptides in physiological solution enhances its solubility in the lipid bilayer thus allowing fast passive permeation of the membrane.

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