# ENERGETICS OF PEPTID E TRANSPORT THROUGH THE MEMBRANE.

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Non-assisted transport of peptides across the membrane is involved on a delivery. A non-assisted peptide crossing event is ordinarily driven by the free-energy variation of partitioning the peptide between water/lipids phases. In this contribution, we estimate the free-energy cost of such process using full atomistic free-energy molecular dynamics (MD) simulations. We consider the transport of the canonical loop (CTKIPPQC) of a serine protease inhibitor (BTCI) through a fully-hydrated di-oleyl-phospatidyl-choline (DOPC) lipid bilayer. We find that the peptide transport is opposed by a dominant free-energy barrier (>30KT) at the lipid-head-group region, suggesting the formation of a peptide-contained pore on the membrane surface as the rate-limiting step of the reaction process. Overall, our results point to molecular details participating on the mechanism of non-assisted transport and provide new insights for further rational design of compounds that could facilitate the lipid transportation by BTCI-like peptides.

Supported by: CNPq and FINATEC
Acknowledgments: Thanks to Dr. João Alexandre from LNLS for technical support.