Hydrophobic effects in membrane sensing peptides for small Extracellular Vesicle isolation and analysis

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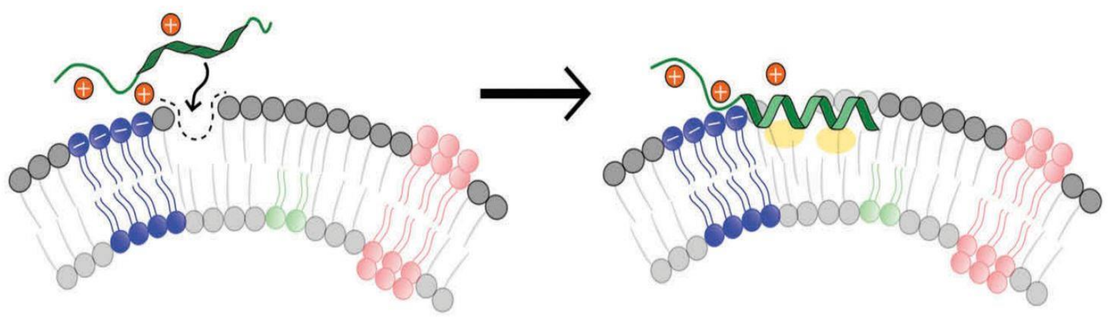
Highlights :

- Our recent work has identified a class of membrane-sensing peptides, RPPGFSPFR (BK), derived from Bradykinin protein as a novel class of molecular ligands for integrated small EV isolation and analysis[1];
- We investigate the role of such hydrophobic amino acids on the membrane recognition efficiency for both exosome-mimicking liposomes[2] and fluorescent EVs.

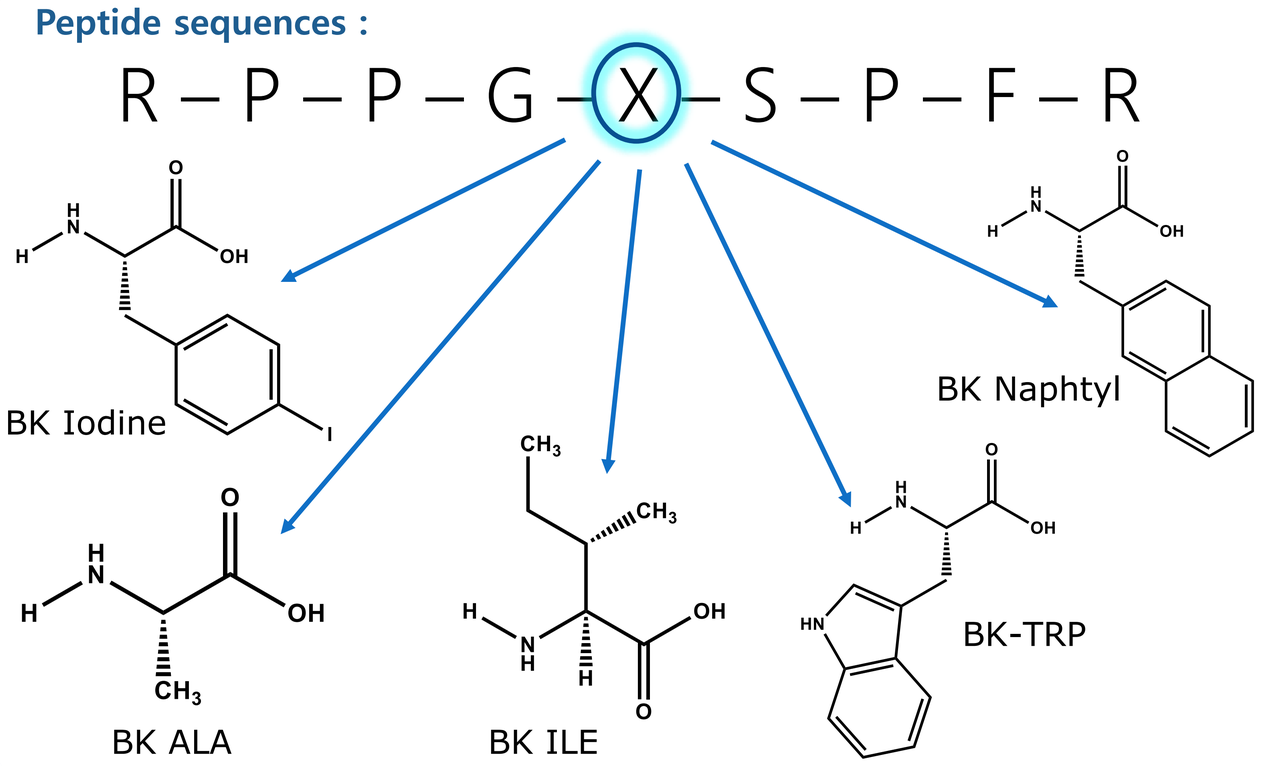
Mechanism of Binding :



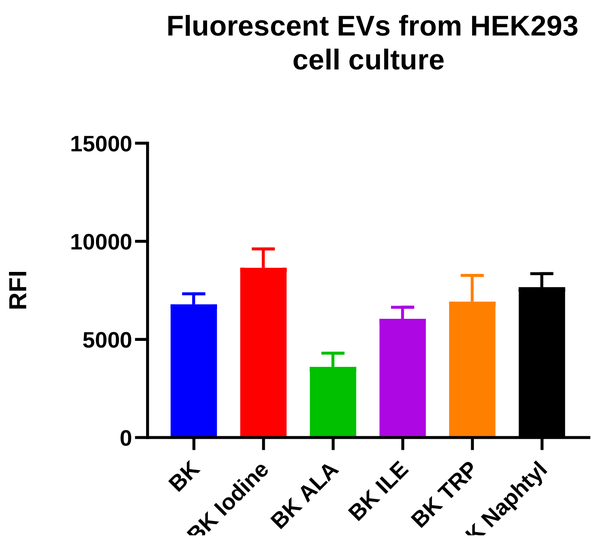
Amphipathic peptides

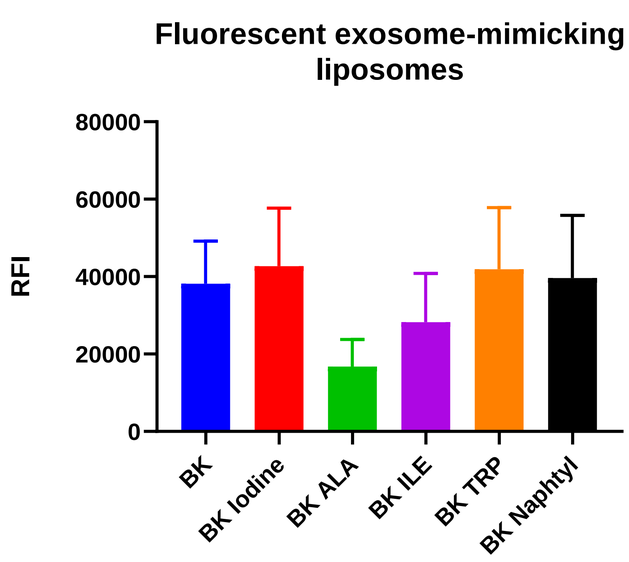
The early events of membrane recognition and binding are based on complementary electrostatic interactions between the peptide/protein effector domain and the phospholipids on the outer membrane leaflet, that subsequently can lead to the insertion of the sensing effector into the membrane defects that characterize highly curved membranes[1].

Peptide sequences :

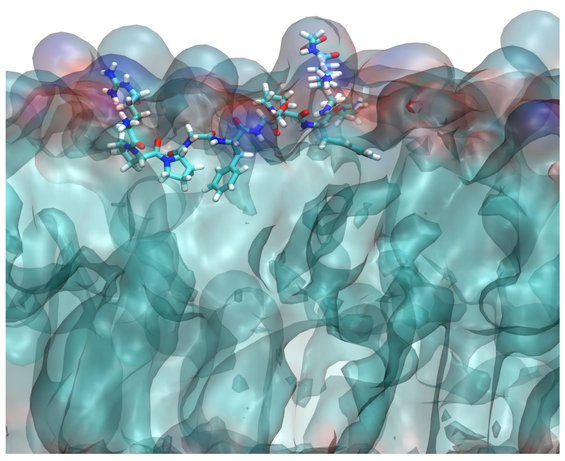


Results and Discussion :

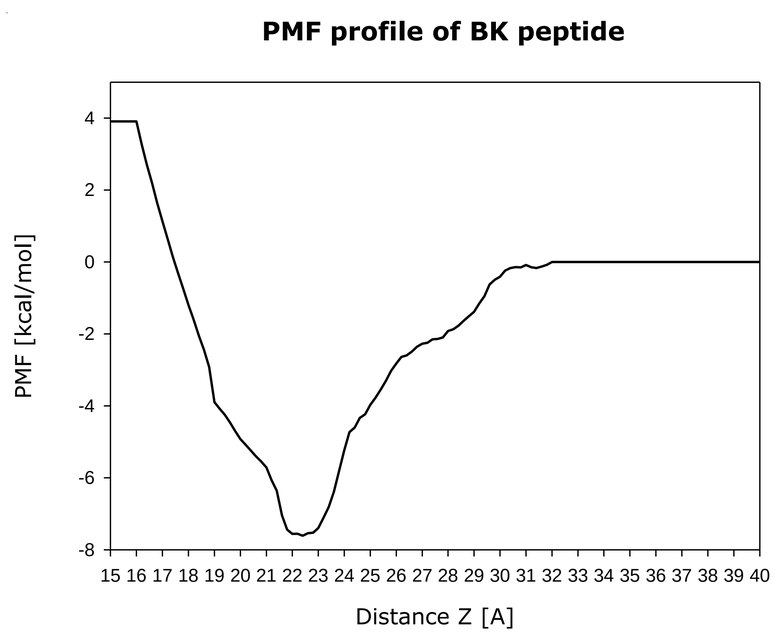




These graphs show how the mono-selective substitution of phenylalanine with residues with different degree of hydrophobicity influence the membrane recognition efficiency.
In particular, the introduction of an Iodine atom and the substitution with another aromatic residue enhance the affinity for both EVs and liposomes. In contrast, an aliphatic hydrophobicity, BK ILE and BK ALA, decrease the ability of binding.



In the binding mode in DOPC/SM/Chol/DOPS/DOPE membrane, BK peptide interacts with the membrane surface through its phenylalanine residues, which have their side chains oriented toward the phospholipids heads.
The free-energy profile shows a lowest energy minimum at Z = 22.4 Å demonstrating the peptide interaction with the phospholipids polar heads.



Conclusions and Future Perspectives :

- ✓ We here showed how the hydrophobic component of peptide sequence play an important role in membrane sensing;
- ✓ The same profile of binding for both types of particles demonstrated the possibility to use synthetic liposomes as model for biological extracellular vesicles;
- ✓ These results represent a step forward in the development of a new generation of membrane-sensing peptides for EV isolation and analysis.

References:

[1] Gori, A. et al. Membrane-binding peptides for extracellular vesicles on-chip analysis. J. Extracell. Vesicles 9, (2020).

[2] Lu, M. et al. Comparison of exosome-mimicking liposomes with conventional liposomes for intracellular delivery of siRNA. Int. J. Pharm. 550, 100–113 (2018).

Acknowledgments

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