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Transmembrane peptide-loaded ionic liquid nanocarriers targeting ErbB2-positive cancer

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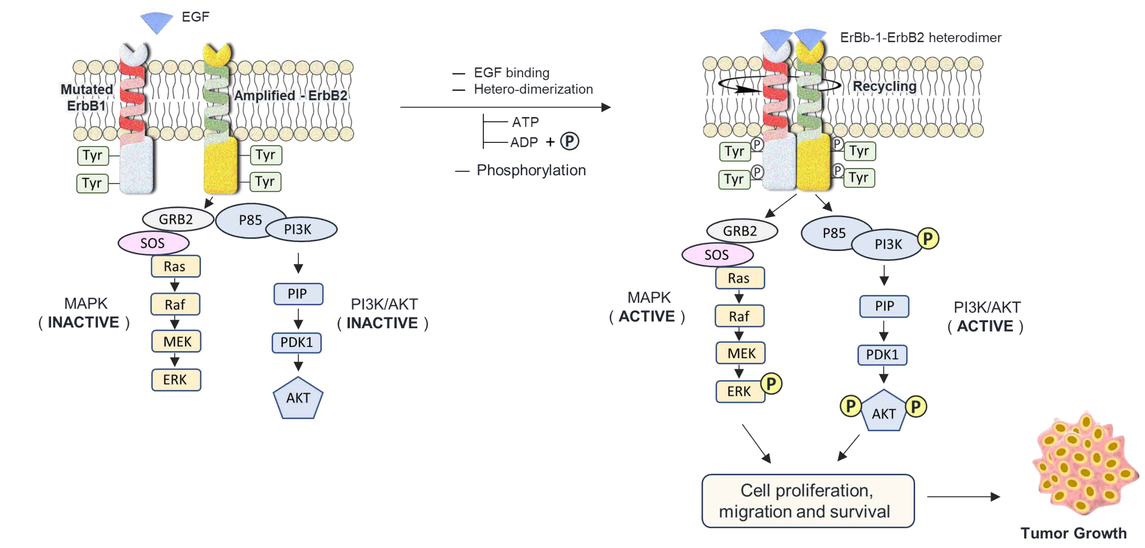
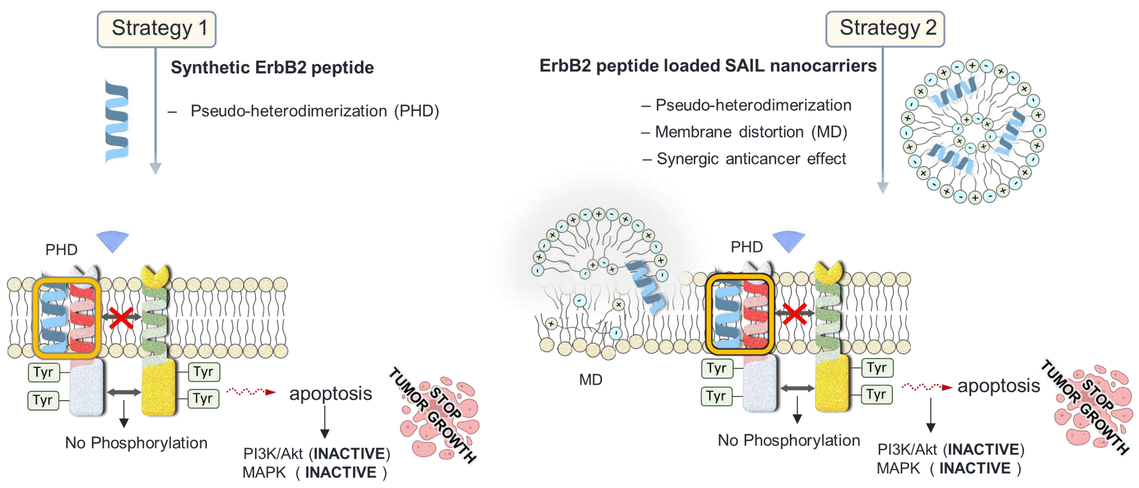
Peptide and Nanocarrier formulation

Project concept

Illustration of general tumor growth mechanism due to amplified ErbB2



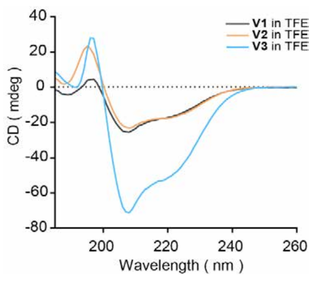
This work — Inhibiting cancer using synergic effect of ErbB2 peptide-loaded ionic-liquid nanocarriers



Peptides for the study

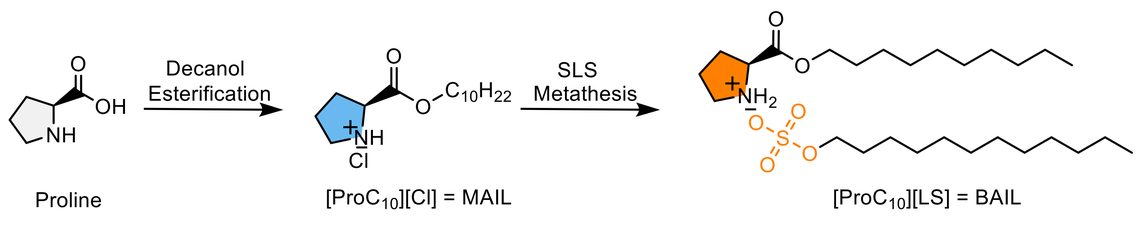
Peptide variant	Representation of amino acids sequence	Experimental Mw[(a)] [g/mole]	ppm	t_R[(b)] [min]
ErbB2_TM		-	-	-
V1	Solubilizing tag	984.3067	12.6	4.7
V2	Dye – Solubilizing tag	1103.6897	19.4	4.6
V3	Dye – Spacer – Solubilizing tag	1186.6244	485	4.8

(a) Mass peaks detected as $[M+3H]^{3+}$. (b) Retention time (t_R) based on LC-UV 214 nm detection.

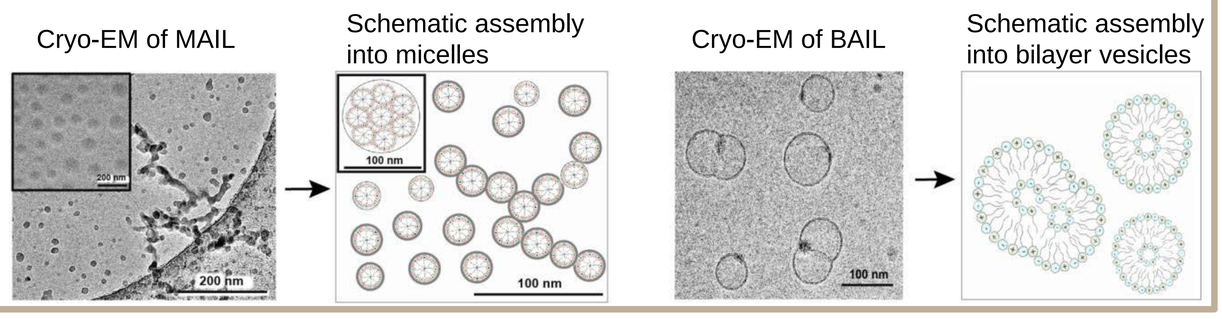


TM peptides synthesized via SPPS and characterized using LC-MS displayed α-helical structures

Ionic Liquid-based Nanocarriers



Self-assembly of MAIL and BAIL in aqueous buffer solution

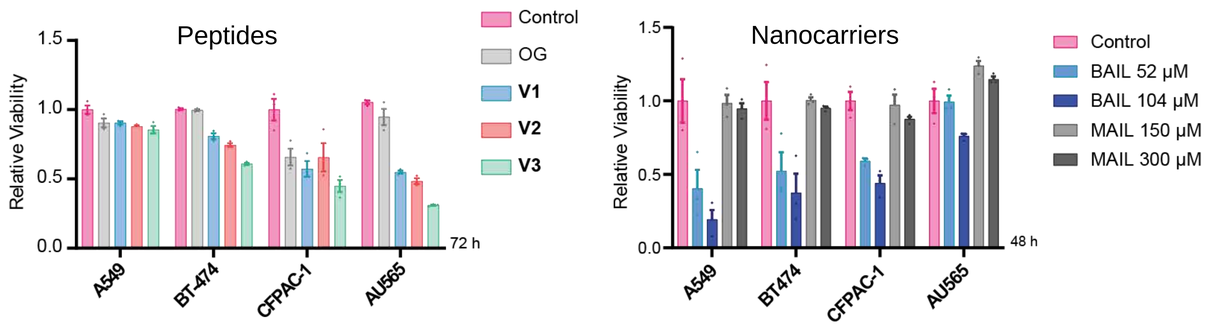


Anti-cancer activity

Effect on cancer cells viability

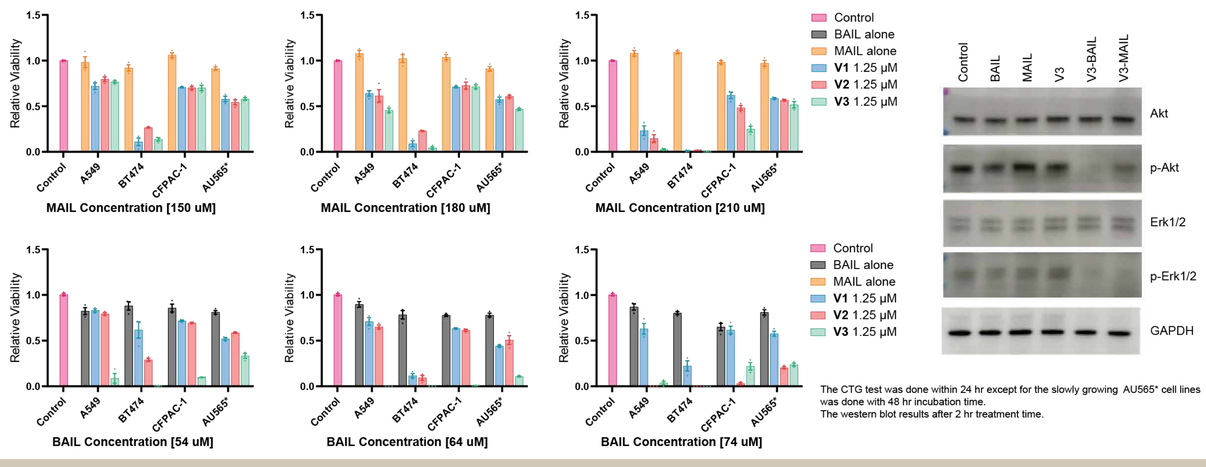
Cell line	Cancer type	Molecular Subtype	ERBB2 expression (RNA)	ERBB2 CRISPER Effect
BT-474	Breast	HER2 overexpressed	10.5	N/A
AU565	Breast	HER2 overexpressed	11.6	-1.09
A549	Lung	-	4.2	-0.78
CFPAC-1	Pancreatic	-	5.7	-0.87

- Cancer cells with varying ErbB2 protein expression levels
- CellTiter-Glo assay
- TM peptides were cytotoxic at low micromolar concentrations (1.25 µM)
- Cytotoxic nanocarriers at CMC



Synergetic effect of nanocarriers on ErbB2 positive cancer cells

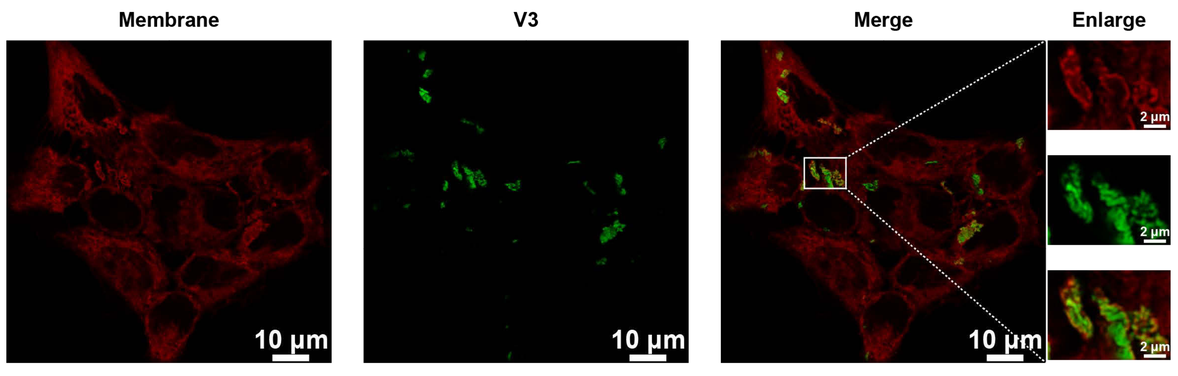
- TM peptides were incorporated into nanocarriers via reverse phase evaporation technique
- Substantial reduction in viabilities in all cell lines with a dose-dependent effect
- TM peptide-nanocarrier suppressed both the ErbB2 MAPK and PI3K/Akt intracellular pathways (Western blot)
- Synergistic anticancer activity of TM peptides in combination with MAIL or BAIL nanocarrier



The CTG test was done within 24 hr except for the slowly growing AU565* cell lines was done with 48 hr incubation time.
The western blot results after 2 hr treatment time.

Localization of nanocarriers in cancer cell lines

TM peptide **V3** showed membrane localization following 24 h incubation with stained BT474 cells



Conclusion

- New approach for synthesis and characterization of a series of transmembrane domain-derived hydrophobic peptides
- Design of novel surface-active ionic liquids nanocarriers
- Novel strategy for targeting ErbB2 receptors in cancer by combining transmembrane peptide and nanocarriers

Acknowledgment

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