PhD Open Days

POLYUREA DENDRIMERS: A NOVEL ANTICANCER TASK FORCE

PhD in Biotechnology and Biosciences

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Background. Cationic antimicrobial peptides (CAMPs) were shown to act as potential anticancer peptides via initial electrostatic interaction with the negatively charged cancer cell membranes. However, there are some drawbacks associated with the use of therapeutic CAMPs including their poor stability in human serum. Herein, we demonstrate the intrinsic anticancer activity of two novel core-shell polycationic dendrimers prepared from polyurea dendrimers (PURE) as an alternative to CAMPs [1].

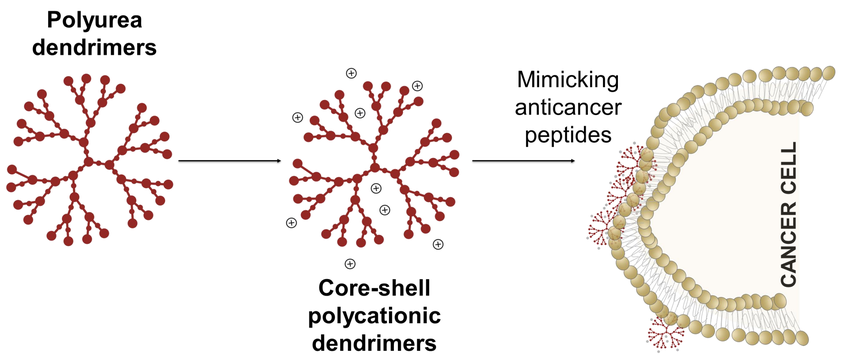

Figure 1. Global strategy of this work.

Results. To evaluate cellular toxicity (Figure 2A) we used mouse fibroblast (L929) cells as non-cancer *in vitro* model and cervical carcinoma (HeLa) cells as tumoral model. Both core-shell polycationic dendrimers shown potential against cancer cells. The cell viability assay shown selectivity for tumoral cells. The wound-healing assay (Figure 2B) reinforced these observations because L929 cells almost fully recovered from the scratch after 24hours.

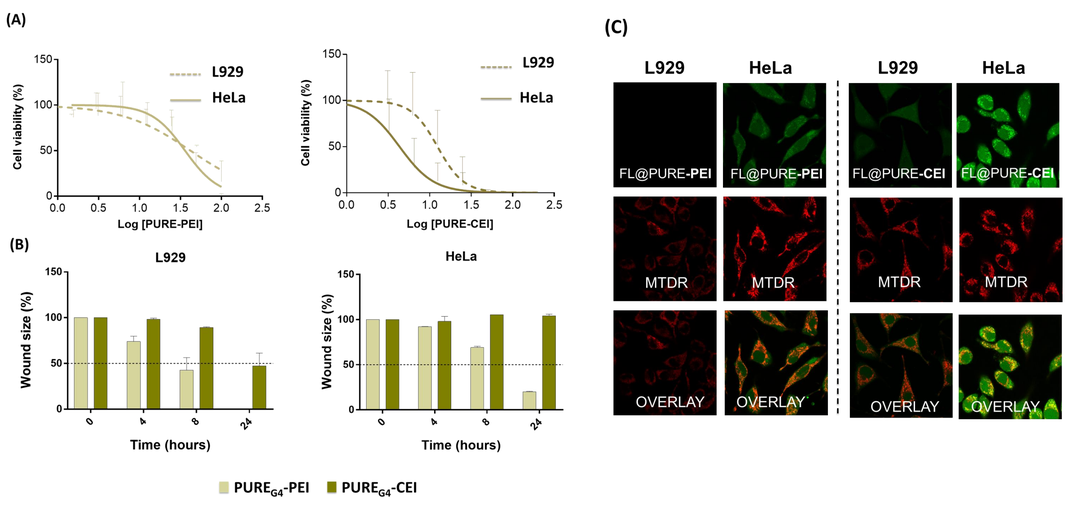

Figure 2. ***In vitro*** **potential of core-shell polycationic dendrimers**. **(A)** Cytotoxic effect of dendrimers (0-200 µM) against L929 and HeLa cells after incubation of 24hours **(B).** Wound healing assay results after treat cells with 3.125 µM for 24hours. **(C)**. Co-localization assay between Mitotracker Deep Red probe and dendrimers loaded with fluorescein.

Considering the impact on *in vitro* cancer cell model we evaluated the possible mechanism underlaying the anticancer dendrimers activity. We found that both dendrimers were localized at mitochondria level after 15min and that can interfere with mitochondrial membrane potential (Figure 2C and Figure 3). The interference with mitochondrial membrane was accessed by MitoProbe JC-1 assay. The results shown an impact on mitochondrial membrane potential ($\Delta\Psi m$) for tumoral cells. When compared with a positive control, PURE$_{G4}$-CEI seemed to be more efficient.

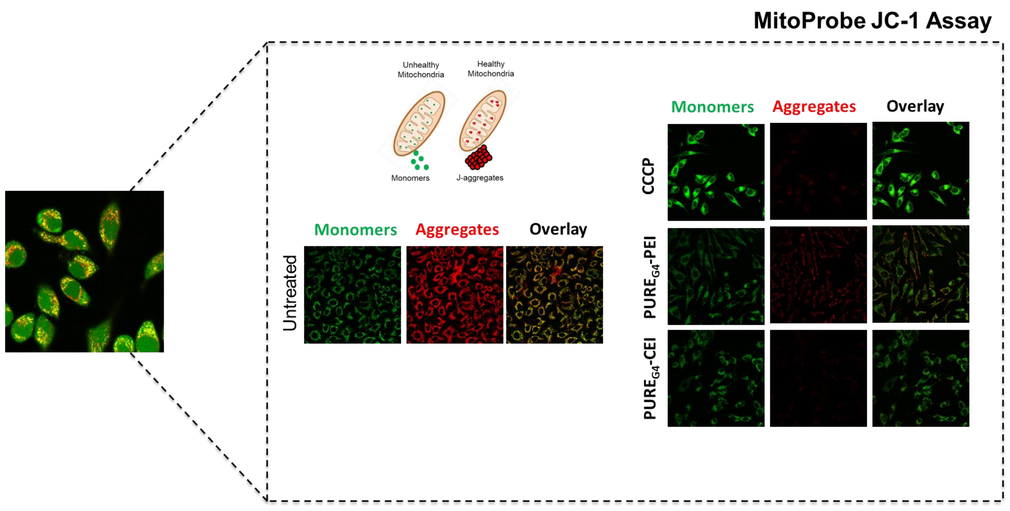

Figure 3. MitoProbe JC-1 assay for HeLa cell line. Cells were treated with core-shell polycationic dendrimers (3.125 µM) for 30 min.

Conclusion. Both dendrimers act through interactions with negatively charged surface groups, and our observations regarding the mechanism of action allow us to hypothesize that these dendrimers are possibly targeting the mitochondrial membrane.

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[1] Sandra N. Pinto *et al.*, ***Biomater. Sci.***, 2022,**10**, 5197-5207

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