Wireless electrostimulation nanomaterials platform for cancer treatment

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Controlled drug delivery systems are key to develop new cancer treatment strategies, as cancer is the leading cause of death in many developed countries. The use of controlled drug delivery systems allows to provide a localized therapy and avoiding systemic toxic effects, as lower amounts of drug administration would be required. A wireless electrostimulation system was developed for the treatment of breast and prostate cancer composed of two components: poly(3,4-ethylenedioxythiophene) (PEDOT) nanoparticles (NPs) loaded with anticancer drug curcumin (CUR), encapsulated in biodegradable coaxial poly(glycerol sebacate)/poly(caprolactone) (PGS/PCL) fibers. Both NPs and fibers were fully characterized. The PEDOT NPs allowed the controlled delivery of CUR using specific applied potentials. The coaxial fibers were employed to control the systemic release of the PEDOT NPs, depending on lipolytic activity. A controlled release of CUR from NPs was achieved by electrostimulation, achieving 79% of CUR released at an electrical potential of -1.5 V. Biodegradation of the fibers was assessed using lipase, resulting in a sustained release of NPs. Wireless electrostimulation of PC-3 cancer cells using CUR/PEDOT NPs was successfully performed, resulting in 67% decrease in cancer cell viability, caused by the controlled release of CUR from the PEDOT NPs. We have successfully produced PGS/PCL coaxial fibers, with embedded electroresponsive PEDOT NPs, which were loaded with the anticancer drug CUR. PC-3 and MCF7 cancer cell lines internalized CUR/PEDOT NPs in 24h, with no perceived cell death or alterations in cell morphology in the absence of electrical stimulation. Most importantly, wireless electrostimulation of cancer cells using CUR/PEDOT NPs was successfully performed, resulting in a very significant decrease in cancer cell viability, caused by the controlled release of CUR from CUR/PEDOT NPs. Overall, our results show the potential of using wireless electrostimulation of drug-loaded NPs for cancer treatment, using safe voltages for the human body, and ensuring the delivery of the anticancer drug in a highly controlled way. Additionally, our results highlight the potential of using FDA approved materials to create a transdermal implant that would act as a reservoir of the NPs to be delivered in a sustained manner to the patient. This work is financed by national funds from FCT - Fundação para a Ciência e a Tecnologia, I.P., with dedicated funds from the project eOnco (2022.07252.PTDC) and the PhD scholarship (SFRH/BD/145057/2019) and in the scope of the project Belive (PTDC/EMD-EMD/30828/2017), iBB (UIDB/04565/2020 and UIDP/04565/2020), i4HB (LA/P/0140/2020), and project BioMaterARISES (EXPL/CTM-CTM/0995/2021).

Figures

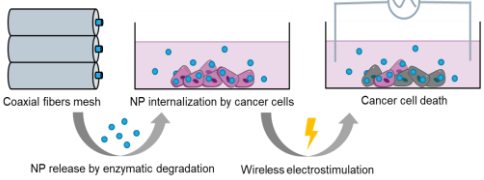

Figure 1: Schematic representation of controlled release of CUR/PEDOT NPs from PGS/PCL fibers through lipolytic enzymatic activity, followed by NP internalization by cancer cells and subsequent wireless electrostimulation to promote cancer cells death.

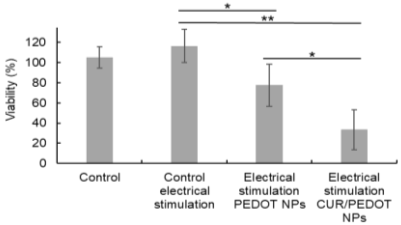

Figure 2: Viability of PC-3 cells after 24 h incubation in culture medium supplemented with 50 µg/mL of either PEDOT NPs or CUR/PEDOT NPs under wireless electrical stimulation and respective controls, n=3. *p-value<0.05;**p-value<0.01