GLUCOSE OXIDASE VIRUS-BASED NANOREACTORS FOR SMART BREAST CANCER THERAPY

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Introducción. Breast cancer is the most common malignant tumor disease and the leading cause of female mortality. The evolution of nanomaterials science opens the opportunity to improve traditional cancer therapies, enhancing therapy efficiency and reducing side effects. This work encapsulated glucose oxidase in VLPs from Brome Mosaic Virus (BMV). The catalytic properties of the resulted nanoreactors were analyzed, and their effect on tumor cell lines was determined. The potential of GOx-based enzymatic nanoreactors for targeted breast cancer therapy is discussed.

Metodología. Herein, protein cages conceived as enzymatic nanoreactors were designed and produced using virus-like nanoparticles (VLPs) and glucose oxidase enzyme (GOx). The GOx enzyme was encapsulated into the BMV capsid (VLP-GOx) by self-assembly method and the resulting enzymatic nanoreactors were coated with human serum albumin (VLP-GOx@HSA) for breast tumor cell targeting. We hypothesized that once the GOx catalytic activity arrives inside tumor media, it would generate hypoxia, starvation, oxidative stress, and kill the breast tumor cells. Therefore, the effect of the synthesized GOx nanoreactors on breast tumor cell lines was studied *in vitro*.

Resultados. Both nanoreactor preparations VLP-GOx and VLP-GOx@HSA showed to be highly cytotoxic for breast tumor cell cultures. Cytotoxicity for human embryonic kidney as healthy model was also found. The monitoring of nanoreactors treatement on triple negative breast cancer cells showed an evident production of oxygen by the catalase antioxidant enzyme induced by the high production of hydrogen peroxide from GOx activity.

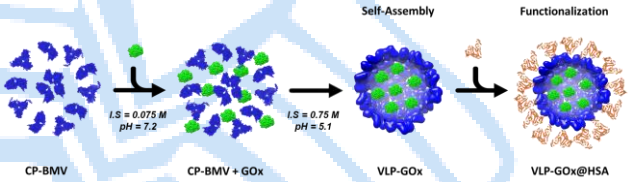

Fig. 1. Schematic representation of VLP GOx-nanoreactors self-assembly encapsulation and HSA functionalization.

Tabla 1. Se pueden insertar Tablas. El título va con letra Arial 8, centrado y arriba. De preferencia evitar el sombreado por renglón.

Preparation	Hydrodymanic diameter (nm)	V_{max} (U/g protein)	K_M (mM)
Free GOx	12.2 ±4.1	237,985	27.8
VLP-GOx	28.8 ±7.9	1,208	34.6
VLP-GOx@HSA	29.7 ±8.9	106	70.4

Conclusiones. The nanoreactors containing GOx activity are fully suitable for cytotoxicity generation in tumor cells. The HSA functionalization of the VLP-GOx nanoreactors could result in a prevailing strategy to improve selective cancer targeting. The GOx containing enzymatic nanoreactors seems to be an interesting alternative to improve the current cancer therapy. *In vivo* and clinical studies are envisaged to reinforce the effectiveness of this treatment strategy..

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