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Microenvironment Rheology Modulates the Effect of the Anticancer Peptide CIGB300 on 3D Head and Neck Tumoroids

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Abstract

3D cell systems for in vitro experimental studies are able to mimic the in vivo efficacy of drugs before they are tested on animals. However, many studies are still needed in order to mimic the physiological environment with 3D cell-growth systems. The mechano-physical properties of the microenvironment are relevant for the invasiveness of cancer cells and for their drug resistance. In this study, 3D tumoroids of human oral squamous cell carcinoma (OSCC) CAL27 cells of different stiffnesses were produced using a tunable PEG–silk fibroin hydrogel (PSF), and the antitumor activity of the peptide CIGB300, an anticancer therapeutic peptide, with respect to these 3D tumoroid models was assessed. Furthermore, spectroscopic studies on the CIGB300 peptide are reported regarding its structure, stability, aggregation and diffusion properties. For the first time, the diffusion of the peptide CIGB300 in tunable silk fibroin hydrogels of different stiffnesses is investigated over time via fluorescence spectroscopy as a potential tool in drug-screening using hydrogel-based 3D tumoroids.

Keywords: anticancer peptides; spheroids; hydrogels; stiffness; CAL27; 3D cell culture systems

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1. Introduction

3D cell culture systems are suitable tools for significantly enhancing our insight into the effects of the microenvironment on cancer cells' invasiveness and responses to mechano-physical cues and pharmacological treatments [1–5]. Recently, a valid alternative to simple spheroids obtainable through commercial *kits*, in which the cell density and rheology of the spheroid are not tunable, was presented: the use of cellular microsphere systems produced by photopolymerizable semi-synthetic hydrogels [6–9]. This strategy allows one to vary the chemical and mechano-physical properties of the system and thus assess different