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Efficacy of therapeutic nanoformulations in a collagen-based three-dimensional colorectal cancer *in vitro* model

Victor Lopez Davila
University College London, UK

Background: Colorectal cancer therapy shows very low response rates leaving room for improvement. In this work we approach the problem from two points of view: loading the MEK inhibitor AZD6244 in organic nanoparticles to improve its delivery to colorectal cancer cells and testing these nanoformulations in a collagen-based 3D *in vitro* model of cancer to mimic physiological conditions.

Methods: AZD6244-containing GCPQ micelles and DOPE/DC-cholesterol liposomes were fabricated using sonication and extrusion methods respectively. These formulations were tested together with the free drug in HCT116 cell monolayers and a collagen-based 3D cancer model to determine differences in efficacy between both models. Fluorescent nanoparticles were used to determine their ability to penetrate the scaffold and reach its core.

Results: Drug delivered in nanocarriers proved to inhibit proliferation in monolayers much more efficiently than on its own. Conversely, nanocarriers were significantly less effective in 3D compared to monolayers. Penetration studies revealed that this phenomenon was most likely due to the inability of the nanoparticles to overcome physical barriers in the 3D model. Surprisingly, the free drug was more effective in 3D than in 2D while cells tend to be more sensitive to therapeutic agents in monolayers.

Conclusions: These results highlight the need to include 3D *in vitro* testing during drug development prior to *in vivo* testing particularly in the case of nanoformulations.

Biography

Victor Lopez Davila is a PhD Candidate at University College London (UK) in the field of Nanomedicine and Tissue Engineering. He completed his MSc in Nanomedicine in Cranfield University (UK) and his BSc in Biotechnology in Lleida University (Spain) in 2011. He also works part time as a Biobank Technician for Tissue Access for Patient's Benefit (TAPB).

victor.lopez-davila.11@ucl.ac.uk

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