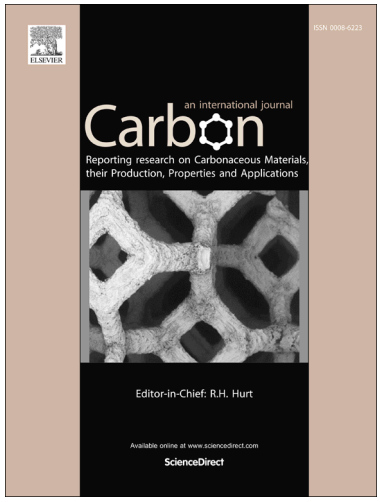

Photoluminescent Carbon Nanotubes Interrogate the Permeability of Multicellular Tumor Spheroids

Prakrit V. Jena, Yosi Shamay, Janki Shah, Daniel Roxbury, Navid Paknejad, Daniel Heller

PII: S0008-6223(15)30143-3
DOI: http://dx.doi.org/10.1016/j.carbon.2015.08.024
Reference: CARBON 10189

To appear in: *Carbon*

Received Date: 16 June 2015
Revised Date: 4 August 2015
Accepted Date: 9 August 2015

Please cite this article as: Jena, P.V., Shamay, Y., Shah, J., Roxbury, D., Paknejad, N., Heller, D., Photoluminescent Carbon Nanotubes Interrogate the Permeability of Multicellular Tumor Spheroids, *Carbon* (2015), doi: http://dx.doi.org/10.1016/j.carbon.2015.08.024

Photoluminescent Carbon Nanotubes Interrogate the Permeability of Multicellular Tumor Spheroids

Prakrit V. Jena[†1], Yosi Shamay[†1], Janki Shah[1], Daniel Roxbury[1], Navid Paknejad[1], Daniel Heller[1,2*]

[1]Memorial Sloan Kettering Cancer Center, New York, NY 10065

[2]Weill Cornell Medical College, New York, NY 10065

†Contributed equally to this work

*Corresponding author. E-mail: hellerd@mskcc.org (Daniel Heller)

Abstract:

Nanotechnology has been extensively used in both fundamental research and in the clinic for cancer drug delivery and imaging. Nanoparticles that show promise in two-dimensional cell culture systems often fail in more complex environments, possibly due to the lack of penetration in dense, three-dimensional structures. Multicellular tumor spheroids are an emerging model system to investigate interactions of nanoparticles with 3D *in vitro* cell culture. Using the intrinsic near-infrared emission of semiconducting carbon nanotubes to optically reconstruct their localization within a three-dimensional volume, we resolved the relative permeability of two different multicellular tumor spheroids. Nanotube photoluminescence revealed that nanotubes rapidly internalized into MCF-7 breast cancer cell-derived spheroids, whereas they exhibited little penetration into spheroids derived from SK-136, a cell line that we developed from murine liver cancer. Characterization of the spheroids by electron microscopy and immunohistochemistry revealed large differences in the extracellular matrix and interstitial spacing, which correlated directly with nanotube penetration. This platform portends a new approach to characterize the permeability of living multicellular environments.

1. Introduction

The use of nanotechnology for cancer drug delivery aims to increase tumor drug concentration while avoiding healthy tissues in order to improve anti-tumor efficacy and reduce dose-limiting toxicities [1, 2]. Although nanomedicines remain promising, with rapid advancement on multiple fronts including nanoparticle formulation, targeting specificity, and multifunctional abilities,