Materials in medicine: from tissue engineering to drug delivery

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BACKGROUND

Dr. Susana Rocha is currently a post-doctoral researcher in the Group of Prof. Johan Hofkens, from the Molecular Imaging and Photonics division of KU Leuven in Belgium. She has been appointed a tenure track position, starting from October of 2019.
After finishing the Chemistry degree in the Technical University of Lisbon (Portugal), Dr. Rocha started a PhD on single molecule fluorescence microscopy, under the supervision of Prof. Johan Hofkens (KU Leuven). During this period, she has become an expert in single particle tracking and super-resolution fluorescence microscopy. After obtaining her doctoral degree in 2014, Dr. Rocha continued developing advance microscopy based approaches to unravel biological questions. In 2017, she perform a research stay in the group of Prof. Paul Kouwer (Radboud University, Nijmegen, The Netherlands), where she became familiar with novel biomimetic polymers.
The current interests of Dr. Susana Rocha lie on the relation between the mechanical and structural properties of extracellular matrices and (cancer) cell behaviour, 3D multi-cellular structures and nano-particle based drug delivery systems.

ABSTRACT

The rapid development of molecular biology techniques and DNA sequencing have resulted in a surge in research activities in the genome and proteome, and their respective roles in development and function of organisms and cells. However, it is now clear that DNA-encoded information alone cannot explain all cellular behavior: the dynamic interactions between a cell and its microenvironment play a crucial role. This microenvironment includes not only other neighboring cells and biochemical molecules, but also the extracellular matrix (ECM) and the forces applied to the system.
In a research laboratory, cells are embedded in polymeric hydrogels to investigate the effect of mechanical properties on cell behaviour. Currently, most 3D cell models use natural ECM components (like collagen and fibrin), complex ECM mixtures (like Matrigel®) or traditional artificial hydrogels (like polyethylene glycol, PEG, and polyacrylamide, PA). Obviously, the natural ECM hydrogels provide a more biomimetic cellular microenvironment, but it is difficult to independently control critical parameters, such as the (nonlinear) mechanical properties, pore size and porosity. In contrast, synthetic matrices exhibit reproducible and tunable mechanical properties, which can be readily tailored and modified.
In our group we are developing new microscopic approaches to investigate both the structure and mechanics of biomimetic hydrogels at the nano- and micrometre scale. As a model system, we use polyiscyanopeptide gels, a new synthetic material that mimics the mechanical aspects of natural gels. Fluorescence microscopy has shown that these gels present a highly heterogeneous network, with pores reaching a few micrometers in size (data analyzed using a 3D segmentation algorithm). In order to retrieve the rheological parameters at a subcellular level, we are establishing 2-point micro-rheology experiments in a multi-plane wide field microscope (developed in our group).
Another research line currently ongoing is the use of polymer to improve the targeting and efficiency of drug delivery systems. Over the last years, mesoporous silica nanoparticles (MSNPs) became highly popular drug nanocarriers in cancer therapy because they offer many advantages such as high drug loading capacity, easy surface functionalization and high biocompatibility. A full understanding of their behavior inside the tumor is vital knowledge for their further translation towards the clinic. Unfortunately, nanoparticle uptake and efficacy studies often remain at the single cell level. We investigate the permeability of MSNPs into 3D cell assemblies called organoids, directly originating from cancer patient's biopsies. These ''tumoroids'' recapitulate key features of the real tumor and therefore serve as a near-physiological model to study the behavior of drug delivery systems. We aim to test the uptake, permeability and diffusion of MSNPs with different polymer coatings, in patient-derived tumaroids. Preliminary results suggest that the biochemical and mechanical properties of the ECM affect the particle uptake and consequently the specificity of functionalized nano carriers.