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Emerging nano and microtechnologies in prostate cancer research: New tools for diagnosis & biomarkers discovery

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The acini of the prostate gland are the basic 3D structures constituting the secretory epithelium and are organized as tree-like structures. Key events during tumor progression in glandular organs, such as the prostate, include the disruption of apical polarity, 3D organization and the progressive transformation of acini into spheroids. Therefore, the analysis of acinar cell polarity and branching morphogenesis is critical to study the progression of epithelial tumors and to assess epithelial development [1]. However, even the mechanisms regulating the development of normal acini and ductal structures are poorly understood. To address this issue and develop a deeper understanding of acini and ductal morphogenesis, we utilize a range of microsystems that include microfluidics, 3D scaffolds and single cell encapsulation [3] as new nano- and microstructured tools to investigate new 3D cell models which better mimic the physiological context of the prostatic tissue and the tumor. A particularly important technique for our work is a novel lens-free imaging system coupled with holographic 3D image reconstruction. That system has enabled us to (i) discriminate differentiated acini from prostatic tumor-like spheroids, and (ii) assess the dynamics of cellular interactions in a 3D network [2]. To analyse dynamic cellular processes, confocal videomicroscopy is very effective at observing cellular and sub-cellular level but, because of the small field of view, it misses the whole picture where the environment predominates. With lens-free imaging, we could track in real-time the collective dynamics of cell-cell communication during epithelial tubulogenesis. The large field of view gives access to the representative cooperation between cells that collectively change their environment. Lens-free imaging can be extended to biomedical and drug screening applications to evaluate anti-cancer drugs and new biomarkers. In the context of the controversial issue of PSA (Prostatic Specific Antigen), we took advantage of our recent technological innovations using 96 image sensors for parallel lens-free imaging to perform RNAi-based high content screening in 3D cell cultures of prostate cells. Our development of new analysis methods based on the quantification of cell migration processes could constitute a novel approach to the problems of understanding glandular changes during carcinogenesis in the prostate. Importantly, as general tools for the fight against cancer, these technologies are able to be extended to any secretory epithelium as well as to large scale screening for drug discovery or toxicology studies in organ-like models.

Biography

Nathalie Picollet-D'hahan, (46, PhD in biophysics and pharmacology) is senior project manager at the CEA Grenoble (France) since 2002. After post-doctoral training in electrophysiology (CEA, 1997-2000), followed by the creation of a start-up, she has obtained in 2002 a permanent position at the CEA and was in charge to initiate new projects in cell-on-chip devices. Since 2009, she is the head of the "3D group" within BIOMICS laboratory. Involved in 2D/3D cell biology and Cancer research, she has experience in managing multidisciplinary research projects, supervising PhD/post-doctorate students and teaching. She organized international workshop and has acquired a visibility in the field of 3D cell culture (8 publications, 3 best-posters prices at international congresses, invited conferences, patents).

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