

# Characterization of pancreatic ductal adenocarcinoma cells in a 3D-cell culture model: focus on epithelial-to-mesenchymal transition

Nicoletta Gagliano<sup>1</sup> - Giuseppe Celesti<sup>2</sup> - Lorenza Tacchini<sup>1</sup> - Marco Rasile<sup>3</sup> - Vincenzo Conte<sup>1</sup> - Patrizia Procacci<sup>1</sup>

<sup>1</sup> Università degli Studi di Milano, Department of Biomedical Sciences for Health, Milano, Italia - <sup>2</sup> Humanitas Clinical and Research Center, Department of Gastroenterology, Rozzano, Milano, Italia - <sup>3</sup> Università degli Studi di Milano, Department of Medical Biotechnology and Translational Medicine, Rozzano, Milano, Italia

Three-dimensional (3D) cell cultures provides a key to the information encoded in the tissue architecture, therefore mimicking the functions of living tissues [1]. Considered the key role of epithelial-to-mesenchymal transition (EMT) in carcinoma progression [2], we aimed at analyzing the effect of the 3D-arrangement on the expression of some key markers of EMT in pancreatic adenocarcinoma (PDAC) cells cultured in either 2D-monolayers or in 3D-spheroids by morphological and molecular methods. HPAF-II, HPAC, and PL45 cell ultrastructure was analyzed by transmission electron microscopy. The main EMT markers E-cadherin,  $\beta$ -catenin, N-cadherin, collagen type I (COL-I), vimentin,  $\alpha$ -smooth muscle actin ( $\alpha$ SMA), Snail, Slug, Twist, Zeb1 and Zeb2 were evaluated by confocal microscopy and molecular methods. Moreover, the expression of cytokeratins was characterized in PDAC cells grown in 2D-monolayers and 3D-spheroids to better understand PDAC cell behaviour. We show important differences in the phenotype of PDAC cells grown in 3D-spheroids or in 2D-monolayers, especially providing additional correlative evidence of EMT marker expression in PDAC cells and contributing to a clarification of the role of EMT in PDAC progression. Considered as a whole, our results suggest that a 3D cell culture model could provide deeper insight into the understanding of the biology of PDAC.

## References

- [1] Hirschhaeuser F, Menne H, Dittfeld C, West J, Mueller-Klieser W, Kunz-Schughart LA. Multicellular tumor spheroids: an underestimated tool is catching up again. *J Biotechnol.* 2010;148:3-15.
- [2] Thiery JP, Sleeman JP. Complex networks orchestrate epithelial-mesenchymal transitions. *Nat Rev Mol Cell Biol.* 2006;7:131-42.

## Key words

Epithelial-to-mesenchymal transition; pancreatic adenocarcinoma; spheroids; E-cadherin.