

# Circulating cancer stem cell progeny: correlation with 'niche' cancer stem cells and monitoring of anticancer drug treatment in Non Small Cell Lung Carcinoma

N. Malara<sup>1,2</sup>, V. Trunzo<sup>2</sup>, F. Givigliano<sup>3</sup>, S. Aprigliano<sup>1,2</sup>, C. Raso<sup>4</sup>, M. Gliozzi<sup>2,5</sup>, A. Marchese<sup>3</sup>, V. Mollace<sup>2,5</sup>.

<sup>1</sup>Bionem Laboratories, Department of Experimental and Clinical Medicine, Salvatore Venuta Campus, University 'Magna Graecia' of Catanzaro (Italy)

<sup>2</sup>Interregional Research Centre for Food Safety and Health (IRC-FSH). Department of Health Science, University 'Magna Graecia' of Catanzaro (Italy)

<sup>3</sup>Thoracic Surgery, Cancer Centre of Excellence Tommaso Campanella Foundation, University 'Magna Graecia' of Catanzaro, (Italy)

<sup>4</sup>Systems Biology, University College of Dublin, Belfield, Republic of Ireland

<sup>5</sup>Centro del farmaco - IRCCS San Raffaele Pisana, Rome, Italy.

High degree of cellular heterogeneity which characterizes cancer cell populations and their cross talk during cancer development represented to date a severe limitation to an unique and efficient approach for monitoring cancer sensitivity to antitumor treatments. In fact, this 'cross-cells puzzle' has been studied by means of a global survey approach which underestimated this aspect. **Purpose:** to evaluate the responses to anticancer treatments of circulating cancer stem cell progenies (CSCs) and 'niche' stem cells deriving from patients suffering from non small cell lung cancer (NSCLC). **Procedures:** 21 untreated patients recently diagnosed for NSCLC were used, and multiple tissue fragments were collected to individuate the area enriched in stem cells. Phenotype analysis was performed to evaluate cancer stem cells, differentiated epithelial and stromal and immune counterparts. In these experimental settings, short-time human cultures were developed, cancer progeny was isolated and in vitro expanded and proliferation and chemo-sensibility assays were performed by means of specific biomarkers. **Findings:** stem cell niche was localized proximal to conducting airway region with significant correlation between  $\alpha 1$  integrin expression and disease-progression. Chemo sensibility test through check of proliferation-profile and apoptosis-fraction performed on in-vitro-cellular-model including Transit-Amplifying cellular subset showed clear correlation with cancer progression. In addition, CSCs showed and high degree of apoptotic response to incubation with adriablastin and taxotere, an effect which correlated with the response found in patients undergoing NSCLC. **Conclusions:** Our data suggest that this innovative approach allowed, for the first time, identification of chemo-sensitive populations among tumor CSCs which correlates with stem cells located into airway region undergoing NSCLC. Toxicological characterization of primary short-term cultures and the individuation of personalized IC50 offers a significant opportunity for the development of customized anticancer interventions.