Genetic background and metabolic phenotype in cancer: impact of the mutation in *FGFR3* in bladder cancer *in vitro* models

Giacomo Ducci [1,2], Giorgia Ciufolini [3], Giulia Gigliotti [1,2], Daniele Benedetti[1,2], Alessia Ruggiero [1], Valentina Pasquale [1,2], Gloria Campioni [1,2], Simone Ponzetto [1,2], Bruno Galuzzi [4], Daniel Cicero [3], Greta Petrella [3], Marco Vanoni [1,2], and Elena Sacco [1,2]

E-mail: giacomo.ducci@unimib.it

[1] Department of Biotechnology and Biosciences, University of Milano-Bicocca, Piazza della Scienza 2, 20126 Milan

[2] SYSBIO-ISBE-IT-Candidate National Node of Italy for ISBE, Research Infrastructure for Systems Biology Europe, 20126 Milan, Italy

[3] Department of Chemical Science and Technology, University of Rome "Tor Vergata", 00133 Rome, Italy [4] Institute of Molecular Bioimaging and Physiology, National Research Council, Segrate, Milan, Italy

Keywords: bladder cancer, metabolism, high-content analysis, omic data, computational analysis

Abstract:
Bladder cancer (BC) is one of the most common malignancies worldwide. Therefore, identifying new markers contributing to patients' stratification is crucial to direct them to more effective and less toxic targeted treatments, improve prognosis, and avoid relapses[1]. Energy metabolism reprogramming is an established cancer hallmark, and altered metabolic pathways can represent attractive clinical targets exploitable in new therapeutic strategies[2].

Here we exploited a systems metabolomic approach to characterize a panel of six BC cell lines at different stages and grades, considering the presence of mutations in *FGFR3* currently used as a marker to distinguish luminal and basal tumors. Specifically, we integrated morpho-functional features (e.g. cell proliferation, cell migration, etc.) and metabolic features (metabolic fluxes by exometabolomics and Seahorse technology[3], and redox homeostasis) with computational analysis. Results showed that *FGFR3* mutation correlates with a metabolic shift toward a more respiratory metabolic phenotype. Moreover, using a mathematical model of metabolism[4,5] on a BC cell line dataset from the literature, we extended the analysis to a larger number of cell lines, confirming what we observed experimentally in our cell line panel.

These findings support the *FGFR3* oncogene contribution in driving the metabolic rearrangements in bladder cancer cells, which could be considered for future development of therapeutic strategies directed against metabolic targets for precision medicine[6].

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