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DEC 14, 2021 – 1:30 PM
AULA C, LITA Segrate

THYROID CANCER CELLS AND FIBROBLASTS INTERPLAY: *IN VITRO* MODELING FOR DRUG SCREENING

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Thyroid cancer (TC) is the most common endocrine tumor. Although TCs are usually well differentiated, therapy resistance and disease recurrence is high, with local and distant metastasis.
Similar to other epithelial tumors, TC present a certain degree of intratumor heterogeneity, with the coexistence of different TC cells subpopulation in specific microenvironmental niches. Anyway, little it is still known about TC niches biology and their role in therapy resistance and disease recurrence. This is principally due to the scarcity of reliable preclinical models effectively reproducing the tumor microenvironment.
Among the different components of tumor microenvironment, the extracellular matrix (ECM) plays a fundamental role in TC biology. Indeed, retrospective studies showed that the presence of a tumoral interstitial fibrosis and desmoplastic stromal reaction, two processes characterized by alterations in ECM composition, correlate with increased local and distant metastatization. Moreover, one of the most common genetic driver of TC, BRAFV600E, is known to induce fibroblasts activation and ECM remodeling.
Despite these strong indications of the fundamental role of ECM modifications in TC biology, little it is still known about its biology and its role in therapy resistance.
The aim of the current project is the development of a simple but effective in vitro model for studying the influence of TC cells and fibroblast interplay on the ECM composition and how this influences the response to anticancer therapy. In particular, the first aim is to characterize how factors secreted by cancer cells with different genetic background influence fibroblasts and ECM properties. In this model, fibroblast are plated onto gelatin-coated dishes and grown in media conditioned by different TC cells and supplemented with ascorbic acid to allow matrix deposition. After two weeks, the ECM can be decellularized and either collected for further analysis or used as a substrate for TC cells cultivation and treatment. The results show that TC cells with different genetic background can induce a different degree of fibroblast activation and ECM deposition. Moreover, the different ECMs significantly influence the growth rate, migration abilities and therapy resistance of TC cells.

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