SELECTED ORAL COMMUNICATION - Extracellular matrix signature activates epithelial-to-mesenchymal transition determining gastric cancer progression

Francesco Albano[1,2,3], Sabino Russi[1], Simona Laurino[1], Pellegrino Mazzone[3], Giuseppina Di Paola[3], Pietro Zoppoli[4], Elena Amendola[2,5], Chiara Balzamo[2], Alessandro Sgambato[6,7], Rocco Galasso[7], Geppino Falco[1,2,3*] and Giovanni Calice[1]

[1] Laboratory of Preclinical and Translational Research, Centro di Riferimento Oncologico della Basilicata (IRCCS-CROB), Rionero in Vulture (PZ), Italy

[2] Dipartimento di Biologia, Università "Federico II", Napoli, Italy

[3] Biogem S.c.a.r.l., Istituto di Biologia e Genetica Molecolare, Via Camporeale, Ariano Irpino, Italy

[4] Dipartimento di Medicina Molecolare e Biotecnologie Mediche, Università "Federico II", Napoli, Italy

[5] Istituto per l'Endocrinologia e l'Oncologia Sperimentale "Gaetano Salvatore", IEOS-CNR Via S. Pansini 5, 80131, Napoli, Italy

[6] Dipartimento di Medicina e Chirurgia Traslazionale, Università Cattolica del Sacro Cuore, Roma

[7] Scientific Direction, Centro di Riferimento Oncologico della Basilicata (IRCCS-CROB), Rionero in Vulture (PZ), Italy

Background and aim

Gastric Cancer (GC) is an aggressive malignancy characterized by a great cellular and molecular heterogeneity. Pathological progression of the intestinal-type GC (iGC) is well described, with cancer cells that starts to invade through the stomach (Stage I) until they metastasize to distant organs (Stage IV) conducing to bad prognosis. In this work we compared gene expression profiles of Stage IV *versus* Stage I iGC patients to isolate molecular players governing the metastatic process. Furthermore, we generate a new biological model useful to study molecular signaling of metastasis, or to test candidate drugs to use in late iGC stages.

Methods

We implemented a robust workspace of gene expression profiling data and their respective associated clinical information. This workspace was composed of two collections: the first included 719 iGC samples generated by assembling seven different datasets, while the second included 281 non-neoplastic samples as controls. Next, we performed functional enrichment analysis comparing Stage IV vs Stage I patients. Finally, we translated *in silico* results, by reproducing *in vitro* a model to shape some of the events occurring during Stage I to IV GC progression.

Results

We identified a specific signature composed by 6 genes (APOD, COL1A2, FSTL1, GEM, LUM, SPARC), strongly related to extracellular matrix (ECM) organization and to Epithelial-to-Mesenchymal transition (EMT). We reproduced a minimum microenvironment from the signature, using it to grow GC tumor cells and, finally, we demonstrated that this microenvironment was able to induce them to invade through the ECM by activating EMT.

Conclusion

We detailed the molecular and cellular progression characterizing iGC progression from Stage I to Stage IV. Our analysis identified a new gene signature for Stage I patients that is strongly associated with the progression to Stage IV. Our findings could be useful for the management of Stage I patients and to suggest a closest follow-up and/or alternative therapeutic strategy to restrain disease progression. Furthermore, our experimental model could be useful for the dissection of the molecular signaling beneath the metastatic spread of cancer cells.