In recent years, the importance of the tumor microenvironment in the development of the tumors has been demonstrated. Proliferation, progression and resistance to tumor drugs do not depend exclusively on the autonomous properties of the tumor cells themselves, but are also deeply influenced by the local microenvironment. In the tumor microenvironment, cancer-associated fibroblasts (CAFs) are one of the most abundant and active stromal cell types. Recent advances suggest that exosomes are critical mediators of cellular communication in the tumor microenvironment, generating an active carcinogenic microenvironment that promotes tumor growth, stimulates angiogenesis, activates stromal fibroblasts, modifies the extracellular matrix, promotes the premetastatic niche, suppresses the immune response and favors resistance to treatments. In our study, two fibroblast-related signatures have been evaluated in a large tumor series of patients with colon cancer (N=1273). First signature is related with high CAFs component in the tumor (CT signature), and the second one is related with target
genes deregulated in recipient cells by CAFs-derived exosomes (CEx signature). A 39.7% of patients were classified as high risk using the CT signature, and a 39.8% using CEx signature. A high concordance of risk classification of patients was detected between both signatures ($p<0.001$). Moreover, both signatures were associated with a shorter overall survival ($p=4.9E-17$ and $p=3.0E-13$ to CT and CEx signature, respectively). A synergy of both signatures was observed, showing a stronger association with overall survival, mainly in the CMS4 group. In conclusion, our results suggest that CAFs in tumors may deregulate specific target genes in recipient cells by exosomes. Thus, tumors with high CAF proportion would have a higher deregulation of these target genes. Our signature of both events (CAF component and deregulated target genes) could be indicative of an active and protumorigenic microenvironment and it be used as prognostic biomarker.