

**Title: Multilayered transcriptional crosstalks are sustained by cooperating micro-societies in human colorectal cancer**

**Abstract:**

Alterations in the balance of mRNA and microRNA (miRNA) expression profiles contribute to the onset and development of colorectal cancer. The regulatory functions of individual miRNA-gene pairs are widely acknowledged, even if group effects are largely unexplored. Interactions between mRNA-miRNA and miRNA-miRNA expression profiles, measured from matched specimens of human colorectal cancer tissues and adjacent non-tumorous mucosa, were summarized by a hypernetwork-based model, which highlighted the propensity of several miRNAs to aggregate into tight micro-assemblies. Some of these miRNAs resulted to modulate several genes, which in turn participate to fulfill a set of significantly enriched cancer-enhancer and cancer-protection biological processes, still being under the control of miR-145, a cell cycle and MAPK signaling cascade master regulator. Thus, miR-145 came up as a potent upstream regulator of a complex RNA-RNA crosstalk, and to mechanistically coordinate several signaling pathways and regulatory circuits that - when deranged - contribute to the colorectal carcinogenesis.