UNCOVERING MOLECULAR INTERPLAYS OF THE EFFECT OF THE HEPTAPEPTIDE ANGIOTENSIN-(1-7) IN A549 LUNG TUMOR CELLS: HOW MIRNAS GETS INVOLVED

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To uncover mechanisms that control gene expression several researches are focused on understanding the regulatory function of non-coding RNA on the fine-tuning of cellular homeostasis. Considering tumoral diseases there has been extensively studies on molecular mechanisms aiming the development of new therapies and microRNAs (miRNAs) has been considered a hot spot of investigation. In more recently years, the hepatetide Angiotensin-(1-7) [(Ang-(1-7)] was described as a potential element that inhibits tumor growth and angiogenesis. Interesting, this peptide was initially characterized by its physiological function in cardio-renal systems and this new mechanism of the Ang-(1-7) on cellular homeostasis should be more investigated. In this study, using A549 (ATCC® CCL-185™) a human lung cancer cell line, we aimed to investigate the modulatory effect of the heptapeptide on cellular physiology and in the expression pattern of 776 microRNAs (miRNAs) and mRNAs in PCR arrays. For that, 1.5 x 10⁴ cells were grown up to 90% confluence in the presence or absence of 10⁻⁷M of the heptapeptide. Cellular growth was investigated in wound healing assays, miRCURY LNA™ Universal RT microRNA PCR Array (Exiquon) was performed and also regular qRT-PCR evaluate the pattern of gene expression. The analyses demonstrated a reduction cellular growth and migratory rates in cultures treated with the Ang-(1-7). In addition, the expression pattern of miRNA appointed the hsa-miR 140-5p, hsa-99b-3p, -34b-5p as overexpressed molecules and hsa-miR-636 and -495-3p as down-regulated miRNAs that have potential target sites at the 3’-UTR of mRNAs of proteins correlated to the adhesion process. Preliminary qRT-PCR analyses have been reinforcing the potential connection between the above miRNAs and the investigated messengers RNAs. The functional validation of such miRNAs will bring some insights in the adhesion mechanisms that are modulate by the Ang-(1-7), that could be useful in the development of future therapies. Studies are currently been processed!

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