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Expression of miR-148a, miR-152 and miR-21 and genetic interactions network in uterine leiomyosarcoma cells

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MiRNAs are endogenous non-coding RNAs that modulates the gene expression at the posttranscriptional level, inhibiting protein synthesis. Oncomirs can regulate oncogenes or tumor suppressor genes and exert functional effects on cell signaling pathways leading to tumor development. To date, ten studies have been performed on the role of the expression profile of these molecules in uterine mesenchymal tumors. So, this study aimed to evaluate the expression profile of 84 miRNAs and their gene network in immortalized cells of myometrium (PCS-460-011), uterine leiomyoma (T HESCs CRL-4003) and uterine leiomyosarcoma (SK-UT-1 HTB-114). Cell lines were cultured in specific medium and conditions (ATCC recommendations) and used for miRNA extraction. Quantitative Real Time – PCR was performed using the MIHS-109ZA-Qiagen 96 wells plate; all data were normalized using SNORD61 and SNORD68 and analyzed by ??Ct method. In silico analysis were performed with the mirtarbase.mbc.nctu.edu.tw software to identify the genetic interactions network strongly related to tumorigenesis. Values were calculated based on a student's t-test; statistical significance was set at $p < 0.05$. Among a total of 84 oncomirs evaluated in uterine tumor cells, miR-148a-3p showed a significant overexpression in ULMS compared to MM cells ($p < 0.0001$). This oncomir strongly modulates the transcription of BCL2 gene, which is correlated with ULMS development. We found a significant underexpression of miR-152-3p ($p < 0.0001$) and miR-21-5p ($p < 0.0001$) in ULMS compared to MM cell line. In ULM cells, our results showed an inverse expression profile of miR-152-3p ($p < 0.005$) and miR-21-5p ($p < 0.0001$) compared to ULMS, using as reference MM cells. The miR-152-3p seems to interact with IGF1R gene. Moreover, the miR-21-5p showed strong interactions with six relevant genes for cell cycle progression, apoptosis, cellular transformation, growth factors and tumor suppression (BCL2, PTEN, ERBB2, MYC, VEGFR and VEGFA), besides a weak interaction with TP53. Our preliminary data suggest that the altered expression of miR-148a-3p, miR-152-3p and miR-21-5p in ULMS possibly influences the major cell signaling pathways, leading to changes in target-gene expression profiles.

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