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Enhancing natural killer cytotoxicity by miR-486-5p in hepatocellular carcinoma

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Insulin-like Growth Factor-1 Receptor (IGF-1R) activation is a hallmark in Hepato-Cellular Carcinoma (HCC), stimulating several mitogenic signaling pathways most importantly PI3K/Akt/mTOR pathway. As an essential cornerstone of the innate immune system, Natural Killer (NK) cells are recognized as the first native defender against HCC. Interestingly, NK cells are among the immune cells with the highest level of IGF-1R and it was also reported to have a prominent role in NK cell differentiation. NK cells are known to be activated by the activating receptor, NKG2D, mediating its cytotoxicity mainly through perforins release. IGF-1R expression was found to be regulated by several miRNAs. However, miR-486-5p has never been investigated in HCC. So, the aim of this study was to control the HCC tumor progression through the direct impact of miR-486-5p on NK cells as well as their target hepatocytes in an immunotherapeutic approach. Huh7 cells were cultured and NK cells were isolated from 27 HCC patients. Both cell types were transfected by miR-486-5p using lipofection. Total RNA was extracted and quantified using qRT-PCR. Viability and proliferation analysis were performed using MTT and BrdU assays. miR-486-5p showed significant down regulation of both IGF-1R and its down-stream oncoprotein mTOR in Huh7 cells and consequently, Huh-7 cellular viability and proliferation were repressed. Upon ectopic expression of miR-486-5p in NK cells of HCC patients both NKG2D and perforins expression were significantly elevated. However, a significant down-regulation of IGF-1R and mTOR were observed. In conclusion, it was shown that miR-486-5p has a dual role in enhancing NK cell cytotoxicity and harnessing the tumor progression of its target hepatocyte mainly through tuning essential members of IGF-axis.

Biography

Rana Ahmed Youness has completed her MSc degree from German University in Cairo (GUC) under the supervision of Professor Dr Ahmed Ihab Abdelaziz, Founder of the Molecular Pathology Research Group (MPRG).

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