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Dysregulation of apoptosis-regulating miRNA by curcumin sensitizes kidney cancer cells to TRAIL induced apoptosis

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Renal cancer is the ninth most common cancer in the world. In 2012 there were 337,860 newly diagnosed renal cancer cases worldwide, with 121,629 cases in Europe alone. In 2013, the number of deaths in the USA due to renal cancer was 13,680 out of 65,150 total cancer deaths (21%) cancer cases. Renal cell carcinoma (RCC) is the most common type of kidney cancer in adults, responsible for approximately 95% of cases. The tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), is a trimeric ligand, which binds to death receptors. Upon incorporation with DR4 (TRAIL-R1) and/or DR5 (TRAIL-R2), it activates the death inducing signaling cascade (DISC) in which fas associated death domain (FADD) recruits and activates the initiator procaspase 8 to active caspase 8, which in turn, amplifies the death signal by cleaving and activating many caspases including procaspase 3. Micro-RNAs (miRNAs) are a class of a highly conserved, small (~19-25 nucleotides) non protein-coding RNA. They silence gene expression by the induction of mRNA degradation or translational inhibition. Following the exposure of cancerous human renal cells (ACHN) to 25 μ M curcumin for 24h, an miRNA screening test was performed for an estimated number of 84 apoptosis-regulating miRNA. The results revealed that let-7C was significantly upregulated. Several bio-informatic tools were used to identify let-7C gene targets. The results of the search revealed that genes regulating cell cycle phases and those controlling tumor metabolism are the primary targets of let-7C. Inhibition of let-7C using antagomirs was associated with the abrogation of curcumin effects on cell cycle and cancer cell metabolism.

Biography

Ismael Obaidi is currently a final year PhD Student at the Conway Institute, School of Biomolecular and Biomedical Sciences, UCD, Ireland. He is also a Pharmacist, and has an MSc in Pharmacology and Toxicology, from the School of Medicine, University of Babylon, Iraq. He has more than eight published papers/abstracts. He is currently a Member of the International Cell Death Society.

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