

LETTER to the EDITOR

Coaxing Cancer Pro-Apoptotic: An Approach Blending Therapeutic miRNAs and Dietary Phytochemicals*Asian Pac J Cancer Prev*, 15 (13), 5499-5500**Dear Editor**

The present letter is latest analysis on pro-apoptotic therapy through combination of therapeutic miRNA and dietary phytochemical as improved method for the treatment of cancer as a current therapeutic approaches. RNA, being the rudiment of biological life, has purportedly unveiled mysterious framework on microRNAs in the last 25 years. Within the macrocosm genomic studies, these molecules plunged from a mere “background noise” to over-sizing roles in carcinogenesis. These miRNAs pre-eminently dictate to abate mRNA stability, often mediating inflammation, cell cycle modulation, stress response, differentiation and apoptosis commission. At all events, an errant miRNA will contravene vital protein progression, eventuating cancer instigation (Ahmad et al, 2013). Consequently, a closer scrutiny in establishing therapeutic agents relative to diverse miRNA production routes and their associating complex regulatory networks seems imperative in debilitating cancer emanation (Mollaie et al., 2013; Orang et al., 2014).

A latter study entitled “MicroRNA goes nuclear” upsurge evidence signifying mature miRNAs aggregated in cellular compartments. Albeit conventional miRNAs, (be it canonical or non- canonical) regulate gene expression through post-transcriptional events in cytoplasm, these miRNA variants with corresponding Ago proteins get conveyed back into nucleus with the aid of Importin 8. The miRNA-Ago complex sequentially targets the chromosomal DNA promoter or promoter derived nascent cognate transcript, dispatching gene activation (Hung and Li, 2012). When access count of miR-21 was disclosed in cell nucleus, one’s speculation on nucleus fraction to be contaminated by cytoplasm remnants becomes inevitable. Intriguingly, the relocation of cytoplasm-assembled miRNA into the cell was substantiated with the discovery of hexanucleotide 3’ terminal motif (AGUGUU). The presence of this terminal motif not only to be indicative of miR-29b and miR-29a, yet further guides its nuclear importation (Tang and Zen, 2011).

In like manner, a study conducted by Barry and colleagues contributes a new insight into other cellular compartment. Mitochondria, the energetic function provider of cells have roles in regulating cytosolic calcium, initiating intrinsic apoptosis pathway, along with heme and steroid synthesis. Recent reports denote the accounts of two pre-mature (pre-mir-302a and pre-let-7b) and one mature miRNA (miR-365) in human mitochondria.

Bioinformatic analyses corroborated mitochondrial DNA sequences to be highly complement with target sites found on miRNA, conducting facts that acquaints miRNA and mitochondrial DNA together. The derivation of these mitochondrial miRNA to compel RNA silencing in mitochondria of cancer cells is yet to determined (Barry et al., 2011).

The use of therapeutic agent to combat cancer is ephemeral while the study to apprehend underlying mechanisms of carcinogenesis is often perpetual. Evasion of apoptosis is the key performance held culpable for cancer cell propagation and dissemination. The nucleus, cytoplasm and mitochondria may have consolidating role to induce apoptosis in cancer cells, given the credential that miRNA manifest in these areas. The miRNA recognized as master of oncogenes or tumor suppressors were anticipated as hope. Resultantly, the birth of therapeutic miRNA is prominence to specifically target aberrant miRNA to manoeuvre pro-apoptotic operation in cancer cells. Studies are channelled to gain complete target validation by miRNA based therapeutic plus their involvement in pharmacological drug delivery (Bader et al., 2011). In spite of miRNA based therapy setting off as potential modulators in cancer treatment, hurdles remain lingering as with the choice of delivery system and the type of cancers, though gradual improvements are establishing (Wu et al., 2013).

Per contra, dietary phytochemical render as a field with great diversity in offering active anticancer ingredients such as; paclitaxel, etoposide and teniposide, vinca alkaloids, vinblastine, vincristine, and camptothecin derivatives. Histone deacetylase inhibitor, LAQ824 and curcumin have demonstrated to alter miRNA expression in cancer cells by promoting apoptosis (Moiseeva et al., 2007; Sun et al., 2008). Interestingly, curcumin spared normal cells from cytotoxicity effects while facilitating apoptosis in cancer cells (Syng-Ai, 2004). In this occasion, curcumin is designated to selectively respond to promote pro-apoptotic in tumorigenic cells by incidental cellular bio mechanism alteration which may target one or more miRNA in favour.

Therapeutic miRNA collaborated dietary phytochemical may be postulated as improved combination method to trigger pro-apoptotic in cancer cells hence minimizing adverse effects on normal cells. In future, exploration of viewing miRNA as therapeutic entities with combination of plant photochemicals as great source of pro-apoptotic should serve as general insight into targeting perturbed

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miRNAs in the nucleus, cytoplasm and mitochondria of
cells.

References

- Ahmad J, Hasnain SE, Siddiqui MA, et al (2013). MicroRNA in carcinogenesis and cancer diagnostics: a new paradigm. *Indian J Med Res*, **137**, 680-94.
- Bader AG, Brown D, Stoudemire J, Lamners P (2011). Developing therapeutic microRNAs for cancer. *Gene Ther*, **18**, 1121-26.
- Barrey E, Auret GS, Bonnamy B, et al (2011). Pre-microRNA and mature microRNA in human mitochondria. *PLoS ONE*, **6**, 20220.
- Hung V, Li L-C (2012). MiRNA goes nuclear. *RNA Biology*, **9**, 269-73.
- Moiseeva EP, Almeida GM, Jones GD, Manson MM (2007). Extended treatment with physiologic concentrations of dietary phytochemicals results in altered gene expression, reduced growth, and apoptosis of cancer cells. *Mol Cancer Ther*, **6**, 3071-9.
- Mollaie HR, Monavari SH, Arabzadeh SA, et al (2013). RNAi and miRNA in viral infections and cancers. *Asian Pac J Cancer Prev*, **14**, 7045-56.
- Orang AV, Safaralizadeh R, Hosseinpour Feizi MA (2014). Insights into the diverse roles of miR-205 in human cancers. *Asian Pac J Cancer Prev*, **15**, 77-83.
- Sun M, Estov Z, Ji Y, et al (2008). Curcumin (diferuloylmethane) alters the expression profiles of microRNAs in human pancreatic cancer cells. *Mol Cancer Ther*, **7**, 464-73.
- Syng-Ai C, Kumari AL, Khar A (2004). Effect of curcumin on normal and tumor cells: role of glutathione and bcl-2. *Mol Cancer Ther*, **3**, 1101-8.
- Tang R, Zen K (2011). Gold glitters everywhere: nucleus microRNA and their function. *Front Biol*, **6**, 69-75.
- Wu Y, Crawford M, Mao Y, et al (2013). Therapeutic delivery of microRNA-29b by cationic lipoplexes for lung cancer. *Mol Ther Nucleic Acids*, **2**, 84.

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