Exogenous Plant miRNAs have a cross-Kingdom regulatory roles in the human metabolism

MiRNA play significant roles in the modulation of several physiological and pathological processes such as organism development, ageing and cancer. Recent studies have demonstrated that particular plant/food-derived miRNAs are accumulate in sera, tissues, and feces.

The ITB-Bari research group, in collaboration with CNR-IBIOM, is involved in studies investigating if exogenous plant miRNA could act as functional analogues of human miRNAs binding human genes in a sequence-specific manner to regulate their post-transcription expression.

To this aim, we developed a bioinformatic platform, composed by various bioinformatic pipelines and a data warehouse as backend, to understand the molecular mechanisms underlying the interaction between plant miRNA and human genes through an \textit{in-silico} approach.

Surprisingly, the result of this study showed that 3,172 plant miRNAs could, under specific conditions, mimic the effects of 1,606 human miRNAs.

The functional and gene network analyses results on these 1,606 human miRNAs, allowed us to select seven edible plant miRNA analogous of 20 human miRNAs involved in the regulation of cell cycle, cancer suppression and apoptosis.

These seven plant miRNAs were tested by transfection experiments in HCT116 colon-rectal cell lines to evaluate their effect on cell proliferation, gene expression and on the capacity to bind in a sequence-specific manner human genes.

The results of our analyses demonstrated a significant decrease in proliferation of transfected cells, and 446 genes differentially expressed after 72h from transfection.

Finally, we demonstrated that two, out of seven plant miRNAs, used in the experiment (mtr-miR-5754, and gma-miR4995) bind in a sequence specific manner MALAT1 and NEAT1, two long non-coding RNA genes, downregulated in transfected HCT116 cells line.

MALAT1 and NEAT1 are “\textit{key regulators}” that are often upregulated in many types of cancer and other human diseases.

In conclusion, these results demonstrate that plant exogenous miRNAs can have a regulatory effect in human by targeting both protein and non-coding mRNAs. These results open the way to broader applications of miRNAs as functional effectors in human health and disease, nutrigenomics and ageing.

References:


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