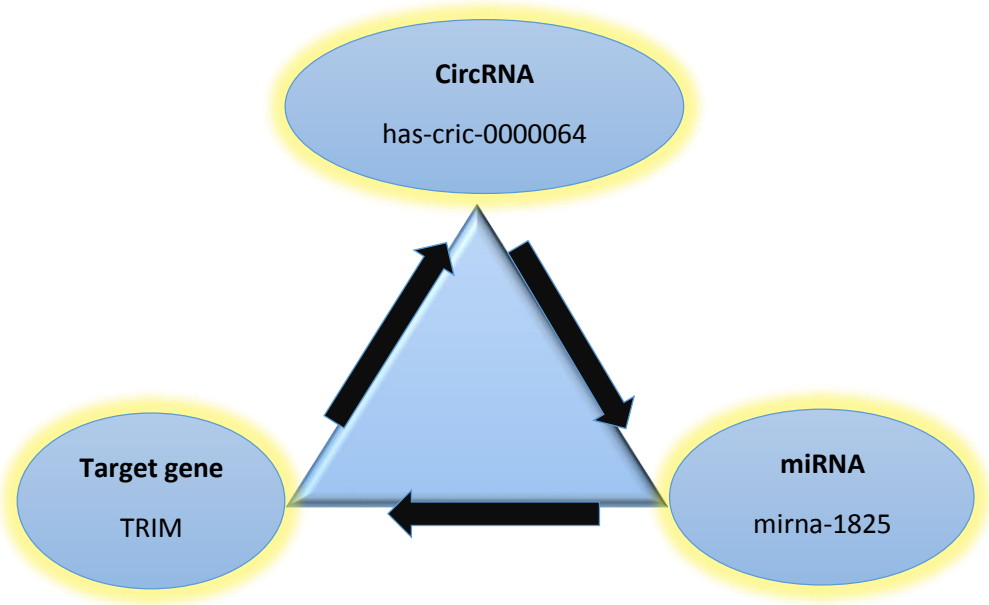
What is the role of ceRNA?



Given the intricate interplay among the diverse RNA species, our team this year will disseminate its proposal: being a modification for last year's with the application of the "Crispr gene-editing tool".

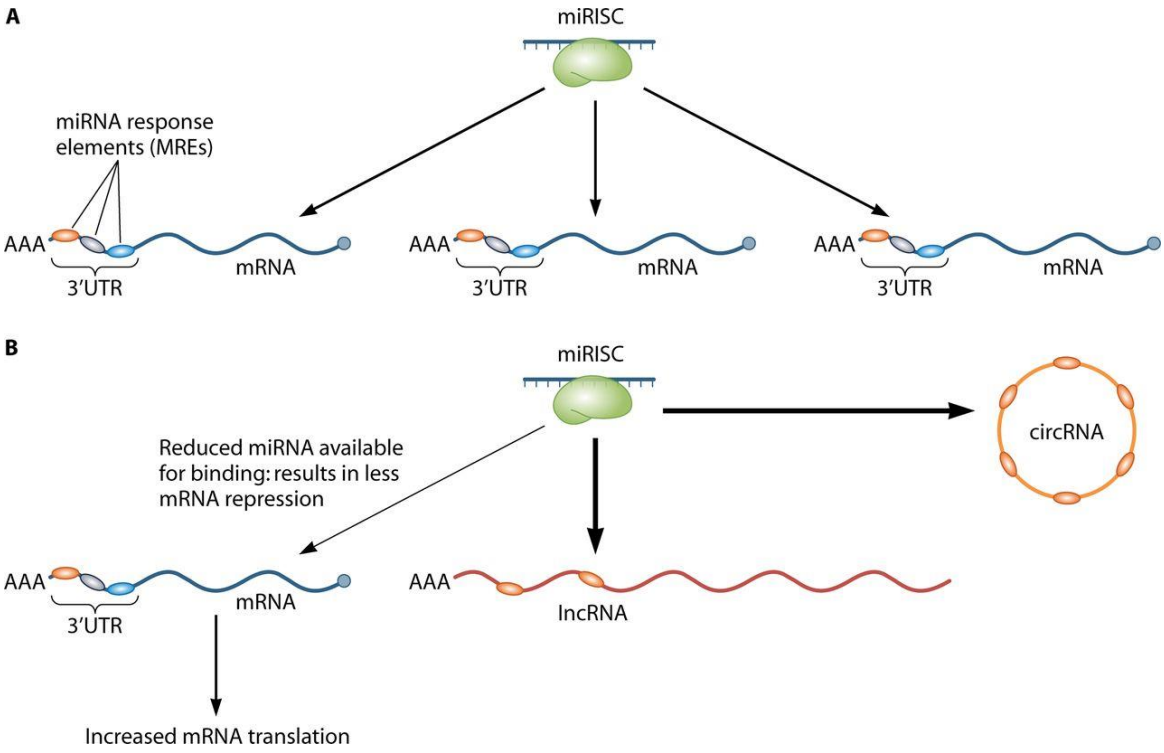
Well what is the story? And how does the deregulation affect cancer cell growth?

RNA transcripts, like the long non-coding RNA and circular RNA, act as competing endogenous RNAs (ceRNAs) or natural microRNA sponges — they communicate with and co-regulate each other by competing for binding to shared microRNAs, a family of small non-coding RNAs that are important post-transcriptional regulators of gene expression. Such competing endogenous RNAs (ceRNAs) regulate the distribution of miRNA molecules on their targets and thereby impose an additional level of post-transcriptional regulation. On the same note, this regulation is scientifically effective way in manipulating critical roles in both normal physiology and tumorigenesis. *(As shown in the below figure)*

Therefore, Competitive endogenous RNAs (ceRNAs) act as molecular sponges for a microRNA through their miRNA binding sites (also referred to as miRNA response elements, MRE), thereby de-repressing all target genes of the respective miRNA family.

miRNAs were revealed to repress their target genes via binding imperfectly to miRNA response elements (MREs) on the 3 ′ untranslated regions (3 ′ -UTRs) of target RNA transcripts and causing to reduced expression of their target proteins either by mRNA breakdown or translational repression. Because each miRNA could target hundreds of genes and, vice versa, each gene can be targeted by many miRNAs; such molecules are critically mentioned in the fine-tuned regulation of gene expression. RNAs functioning as in this course are named ceRNA. Some coding RNAs, pseudogenes, ncRNAs, and **circular RNAs** could work as ceRNAs. CeRNAs having common MREs can compete for binding of miRNA. They delineate a concealed RNA B jargon: a network of interactions of different RNA types that regulate gene expression. It was suggested that these ceRNAs can talk to each other via their ability to compete for binding of miRNA. **This cross-talk produces comprehensive cis - and Trans -orga- nizing communication across all the transcriptome.**

Moreover, ceRNA networks further depend on the subcellular dispersion and tissue particularity of RNAs and miRNAs found in a specific cell type at a specific. The concentration of miRNAs is an important factor for ceRNA activity. If there are a less number of miRNAs than their targets, the ceRNA activity is reduced as the targets will remain largely unrepressed. Also, if there are more miRNAs as compared to their targets, there would have been no cross- regulation due to almost a universal repression of the targets



Then, why ceRNA in Hepatocellular carcinoma?

Hepatocellular carcinoma (HCC) is originally the fifth most common cancer worldwide and the third cause of cancer mortality. The Eastern and South-Asia, Middle and Western Africa are considered to be of high incidence rate. In Egypt, HCC is one of the health problems facing the health authorities. Egypt is the sixth largest country in the middle east and Arab world, it is the Third largest country in Africa, it is the fifteenth most populous nation in the world about 90 million inhabitants. According to a study published by El-Zayadi et al: they reported almost 2 folds increase in HCC among chronic liver disease patients over a decade. Also, according to Ibrahim et al, HCC is the first most common cancer in males and second most common cancer in females.

Given this high prevalence of a disease-statistics, we followed the lead of Ji-hang Yuan et al, through the ceRNA world, who demonstrated that lncRNA-ATB acts as a key regulator of TGF-β signaling pathways and

revealed roles of TGF-β in regulating long noncoding RNAs. The findings of this study have significant implications regarding our understanding of HCC metastasis pathogenesis. As direct targets of lncRNA-ATB, miR-200-ZEB and IL-11 mediated the role of lncRNA-ATB in local invasion and distant colonization, respectively. Similarly, Zhang J et al showed the lncRNA expression patterns and a complex ceRNA network in HCC, and identified a complex cancer specific ceRNA network, which includes 14 lncRNAs and 17 miRNAs in HCC

What is next?

Via our bioinformatics analysis, we led through into a long process of dry lab work, deciding a suitable and effectively tested regulatory pathway to do our hypothesis. Our modeled ceRNA contained, as provided in the figure, the circular RNA (has-cric-0000064) competing for shared microRna (mir-1825) and sequestrate it within the cell as they have MREs(microRNA sponge); lastly deregulating our target gene (TRIM) And yes! A sophisticated and effective molecular level control.

What is our aim for a ceRNA

1- To analyze circRNA and disease databases to select significantly relevant circRNA for HCC

2- To analyze circRNA-miRNA interaction databases to retrieve competing endogenous RNA specific for HCC

3- To characterize the expression of cirRNA-associated ceRNA genes in HepG2 cell line to evaluate their role in pathogenesis of HCC

4- To compare between the efficacy of knocking in of circular RNA using synthetic circuits and crisper techniques

References

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