Data S1.

Competing endogenous (ce)RNA transcripts can crosstalk by competing for common micro (mi)RNAs, with miRNA response elements (MREs) as the foundation of this interaction (1). These RNA transcripts have been termed as competing endogenous RNAs-ceRNAs (2). Any RNA transcript with MREs may act as ceRNAs, and ceRNAs include pseudogene transcripts, long non-coding RNAs, circular RNAs and mRNAs, these transcripts can compete for the same MREs to regulate them mutually. To identify potential target of mi, the target/microRNAs is predicted with home-made miRNA target prediction software based on TargetScan 7.2 (http://www.targetscan.org/vert_71/) & miRanda (http://www.microrna.org/) (3-7).

Through merging the common targeted miRNAs, ceRNA networks were constructed. There are three conditions that must exist for ceRNA network to occur (1): i) The relative concentration of the ceRNAs and their microRNAs is important; ii) the effectiveness of a ceRNA depends on the number of microRNAs that it can 'sponge'; iii) not all of the MREs on ceRNAs are equal. So, ceRNA-pairs relations required further filtering.

Besides, as a measure of the number of common miRNAs, a hypergeometric test can be performed performed for each ceRNA pair separately, which was defined by four parameters: i) N is the total number of miRNAs used to predict targets; ii) K is the number of miRNAs that interact with the chosen gene of interest; iii) n is the number of miRNAs that interact with the candidate ceRNA of the chosen gene; and iv) is the common miRNA number between the two genes (8). The test calculates the P-value by using the following formula:

$$P = \sum_{i=c}^{\min(K,n)} \frac{\binom{K}{i}\binom{N-K}{n-i}}{\binom{N}{n}}$$

References

1. Salmena L, Poliseno L, Tay Y, Kats L and Pandolfi PP: A ceRNA hypothesis: The Rosetta stone of a hidden RNA language? Cell 146: 353-358, 2011.
2. Phelps M, Coss C, Wang H and Cook M; Reproducibility Project: Cancer Biology; Reproducibility Project Cancer Biology: Registered report: Coding-independent regulation of the tumor suppressor PTEN by competing endogenous mRNAs. Elife 5: e12470, 2016.
3. Huang M, Zhong Z, Lv M, Shu J, Tian Q and Chen J: Comprehensive analysis of differentially expressed profiles of lncRNAs and circRNAs with associated co-expression and ceRNA networks in bladder Carcin. Oncotarget 7: 47186-47200, 2016.
4. Friedman RC, Farh KH, Burge CB and Bartel DP: Most mammalian mRNAs are conserved targets of microRNAs. Genome Res 19: 92-105, 2009.
5. Garcia DM, Baek D, Shin C, Bell GW, Grimson A and Bartel DP: Weak seed-pairing stability and high target-site abundance decrease the proficiency of lsy-6 and other microRNAs. Nat Struct Mol Biol 18: 1139-1146, 2011.
6. Grimson A, Farh KH, Johnston WK, Garrett-Engele P and Bartel DP: MicroRNA targeting specificity in mammals: Determinants beyond seed pairing. Mol Cell 27: 91-105, 2007.
7. Enright A, John B, Gaul U, Tuschl T, Chris S and Mark SC: MicroRNA targets in Drosophila. Genome Biol 5: R1, 2003.
8. Li JH, Liu S, Zhou H, Qu LH and Yang JH: starBase v2.0: Decoding miRNA-ceRNA, miRNA-ncRNA and protein-RNA interaction networks from large-scale CLIP-Seq data. Nucleic Acids Res 42 (Database Issue): D92-D97, 2014.