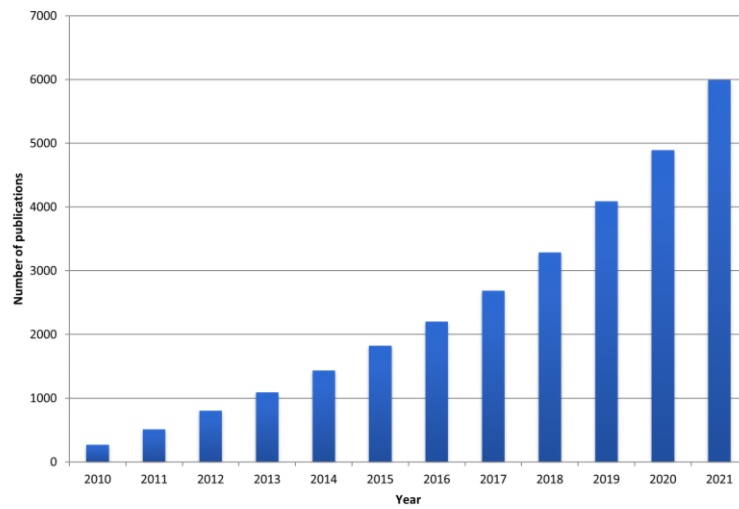


## Supplementary Figure



**Supplementary Fig. 1. Number of ceRNA-related publications across 2010-2021.** The figure shows the number of articles published by year obtained by querying the NCBI PubMed database with the specific keywords: "competing endogenous RNA", "ceRNA", "sponge", "competing triplets" or "RNA-RNA crosstalk".

## Supplementary Tables

**Supplementary Table 1.** Summary of statistics-based methods.

<b>Name, Year</b>	<b>Method</b>	<b>Data type</b>	<b>Database</b>	<b>Cases of study</b>
Hermes, 2011 [1]	Mutual information and conditional mutual information	Expression data, miRNA-target interaction data	TCGA	Glioblastoma multiforme
Zhou et al., 2014 [2]	Pair-wise correlation	Expression data, miRNA-target interaction data	GEO, TCGA, miRanda	Breast invasive carcinoma
Paci et al., 2014 [3]	Sensitivity correlation	Expression data, miRNA-target interaction data	TargetScan, miRTarBase, TCGA	Breast invasive carcinoma
Xu et al., 2015 [4]	Pair-wise correlation	Expression data, miRNA-target interaction data, cancer-associated miRNAs	TCGA, TargetScan, miRanda, PITA, starBase V2.0, MsigDB	Multi-cancer analysis
Zhang et al., 2016 [5]	Establish significance to sensitivity correlation measure [3]	Expression-data, miRNA-target interaction data	TargetScan, miRanda, PITA, RNAhybrid, DIANA-TarBase, mirTarBase, TCGA	Multi-cancer analysis
Cernia, 2017 [7]	Scoring function for ceRNA prediction, SVM for ceRNA classification	Expression-data, miRNA-target interaction data	miRecords, starBase v2.0, miRTarBase, CLASH, TCGA	Multi-cancer analysis
Cancerin, 2018 [8]	LASSO-based method [9], sensitivity correlation	Expression-data, miRNA-target interaction data, Copy number alteration, DNA methylation	starBase v2.0, TargetScan, miRTarBase, InCeDB, DIANA-LncBase v2, TCGA	Multi-cancer analysis
SPONGE, 2019 [10]	multiple miRNA sensitivity correlation	Expression-data, miRNA-target interaction data	TargetScan, miRcode, miRTarBase, DIANA-LncBase v2, TCGA	Multi-cancer analysis

**Supplementary Table 2.** Summary of mathematical modelling methods.

Name, Year	Method	Data type	Database	Case of study
Figliuzzi et al. 2013 [11]	deterministic model	literature model parameters, miRNA-target interaction data	---	Simulated data
Ala et al., 2013 [12]	deterministic model	literature model parameters, miRNA-target interaction data	TargetScan	Simulated data
Chiu et al. 2018 [13].	deterministic model	Expression data, literature model parameters, miRNA-target interaction data	TCGA	Multi-cancer analysis
Miotto et al., 2019 [14]	deterministic model	literature model parameters, miRNA-target interaction data	CLASH interactome	Simulated data
Bosia et al., 2013 [15]	stochastic model	literature model parameters, miRNA-target interaction data	---	Simulated data

**Supplementary Table 3.** Summary of the main databases of ceRNA interactions.

Database	Type	Link	Last Release
ceRDB [16]	Computational prediction	<a href="https://www.oncomir.umn.edu/cefinder/">https://www.oncomir.umn.edu/cefinder/</a>	2011
lnCeDB [17]	Computational prediction/ Experimental validation	<a href="http://gyanxet-beta.com/lncedb/index.php">http://gyanxet-beta.com/lncedb/index.php</a>	2014
spongeScan [18]	Computational prediction	<a href="http://spongescan.rc.ufl.edu">http://spongescan.rc.ufl.edu</a>	2016
miRSponge [19]	Experimental validation	<a href="http://bio-bigdata.hrbmu.edu.cn/miRSponge/">http://bio-bigdata.hrbmu.edu.cn/miRSponge/</a>	2015
lncACTdb 2.0 [20]	Computational prediction/ Experimental validation	<a href="http://www.bio-bigdata.net/LncACTdb/">http://www.bio-bigdata.net/LncACTdb/</a>	2018
ENCORI (previously starBase 2.0 [21])	Computational prediction/ Experimental validation	<a href="http://starbase.sysu.edu.cn/">http://starbase.sysu.edu.cn/</a>	2019

## References

- [1] Sumazin P, Yang X, Chiu H-S, et al. An extensive microRNA-mediated network of RNA-RNA interactions regulates established oncogenic pathways in glioblastoma. *Cell* 2011; 147: 370–381.
- [2] Zhou X, Liu J, Wang W. Construction and investigation of breast-cancer-specific ceRNA network based on the mRNA and miRNA expression data. *IET Syst Biol* 2014; 8: 96–103.
- [3] Paci P, Colombo T, Farina L. Computational analysis identifies a sponge interaction network between long non-coding RNAs and messenger RNAs in human breast cancer. *BMC Syst Biol* 2014; 8: 83.
- [4] Xu J, Li Y, Lu J, et al. The mRNA related ceRNA-ceRNA landscape and significance across 20 major cancer types. *Nucleic Acids Res* 2015; 43: 8169–8182.
- [5] Zhang Y, Xu Y, Feng L, et al. Comprehensive characterization of lncRNA-mRNA related ceRNA network across 12 major cancers. *Oncotarget* 2016; 7: 64148–64167.
- [6] Wang J-B, Liu F-H, Chen J-H, et al. Identifying survival-associated modules from the dysregulated triplet network in glioblastoma multiforme. *J Cancer Res Clin Oncol* 2017; 143: 661–671.
- [7] Sardina DS, Alaimo S, Ferro A, et al. A novel computational method for inferring competing endogenous interactions. *Brief Bioinform* 2017; 18: 1071–1081.
- [8] Do D, Bozdog S. Cancerin: A computational pipeline to infer cancer-associated ceRNA interaction networks. *PLoS Comput Biol* 2018; 14: e1006318.
- [9] Tibshirani: The lasso problem and uniqueness, <https://projecteuclid.org/euclid.ejs/1369148600> (accessed 22 January 2020).
- [10] List M, Dehghani Amirabad A, Kostka D, et al. Large-scale inference of competing endogenous RNA networks with sparse partial correlation. *Bioinforma Oxf Engl* 2019; 35: i596–i604.
- [11] Figliuzzi M, Marinari E, De Martino A. MicroRNAs as a selective channel of communication between competing RNAs: a steady-state theory. *Biophys J* 2013; 104: 1203–1213.
- [12] Ala U, Karreth FA, Bosia C, et al. Integrated transcriptional and competitive endogenous RNA networks are cross-regulated in permissive molecular environments. *Proc Natl Acad Sci* 2013; 110: 7154–7159.
- [13] Chiu H-S, Martínez MR, Komissarova EV, et al. The number of titrated microRNA species dictates ceRNA regulation. *Nucleic Acids Res* 2018; 46: 4354–4369.
- [14] Miotto M, Marinari E, De Martino A. Competing endogenous RNA crosstalk at system level. *PLoS Comput Biol* 2019; 15: e1007474.
- [15] Bosia C, Pagnani A, Zecchina R. Modelling competing endogenous RNA networks. *PLoS One* 2013; 8: e66609.
- [16] Sarver AL, Subramanian S. Competing endogenous RNA database. *Bioinformatics* 2012; 8: 731–733.
- [17] Das S, Ghosal S, Sen R, et al. InCeDB: Database of Human Long Noncoding RNA Acting as Competing Endogenous RNA. *PLoS ONE*; 9. Epub ahead of print 13 June 2014. DOI: 10.1371/journal.pone.0098965.
- [18] Furió-Tarí P, Tarazona S, Gabaldón T, et al. spongeScan: A web for detecting microRNA binding elements in lncRNA sequences. *Nucleic Acids Res* 2016; 44: W176-180.

- [19] Wang P, Zhi H, Zhang Y, et al. MiRSponge: A manually curated database for experimentally supported miRNA sponges and ceRNAs. *Database*; 2015. Epub ahead of print 2015. DOI: 10.1093/database/bav098.
- [20] Wang P, Li X, Gao Y, et al. LncACTdb 2.0: an updated database of experimentally supported ceRNA interactions curated from low- and high-throughput experiments. *Nucleic Acids Res* 2019; 47: D121–D127.
- [21] Li J-H, Liu S, Zhou H, et al. starBase v2. 0: decoding miRNA-ceRNA, miRNA-ncRNA and protein–RNA interaction networks from large-scale CLIP-Seq data. *Nucleic Acids Res* 2013; gkt1248.