



Research article

A potential role for metastasis-associated in colon cancer 1 (*MACC1*) as a pan-cancer prognostic and immunological biomarker

Ye Hu[†], Meiling Wang[†], Kainan Wang[†], Jiyue Gao, Jiacy Tong, Zuowei Zhao* and Man Li*

Department of Oncology & Department of Breast Surgery, The Second Hospital of Dalian Medical University, Dalian 116023, China

[†] The authors contributed equally to this work.

* **Correspondence:** Email: dmuzhaozuowei@163.com, man_li@dmu.edu.cn; Tel: +86041184671291; Fax: +86041184672130.

Supplementary

1. Supplementary materials and methods

1.1. Gene mapping and protein structure

We obtained the genome location of *MACC1* in UCSC genome browser (<http://genome.ucsc.edu/>) [1]. The module of “HomoloGene” function (<https://www.ncbi.nlm.nih.gov/homologene/>) of NCBI (National Center for Biotechnology Information) was used to analysis the conserved functional domain of *MACC1* across different species. Meanwhile, we use the constraint-based multiple alignment on-line tool of NCBI (<https://www.ncbi.nlm.nih.gov/tools/cobalt/>) to performed the phylogenetic tree of *MACC1*.

1.2. Gene-drug interaction network analysis

The Comparative Toxicogenomics Database (CTD) was constructed for chemotherapeutic drugs that reduce or increase the mRNA or protein expression levels of the certain genes [2]. We searched *MACC1* in CTD database and screened drugs which may interact with *MACC1* expression. And we used the Cytoscape Version 3.5.1 to visualize the gene-drug interaction networks.

1.3. Immune checkpoint-associated genes analysis

The *immunedconv*, an R package integrating six types of algorithms, was used to estimate the relationship of different infiltrating immune cell types and the *MACC1* expression level of each tumor sample by R package. The results are presented as a heat map. $P < 0.05$ is considered statistically significant. The version of R software using in this article is R-4.0.3.

2. Supplementary figure legends

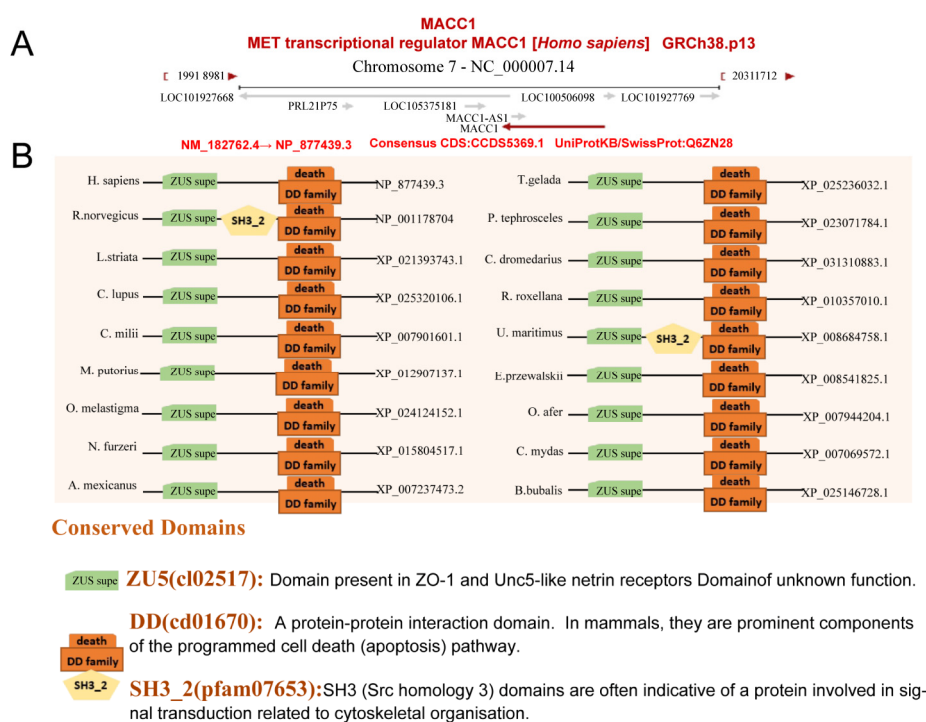


Figure S1. Structural characteristics of *MACC1* in different species. Genomic location of *MACC1*; (B) The conserved domain of *SND1* between different species.

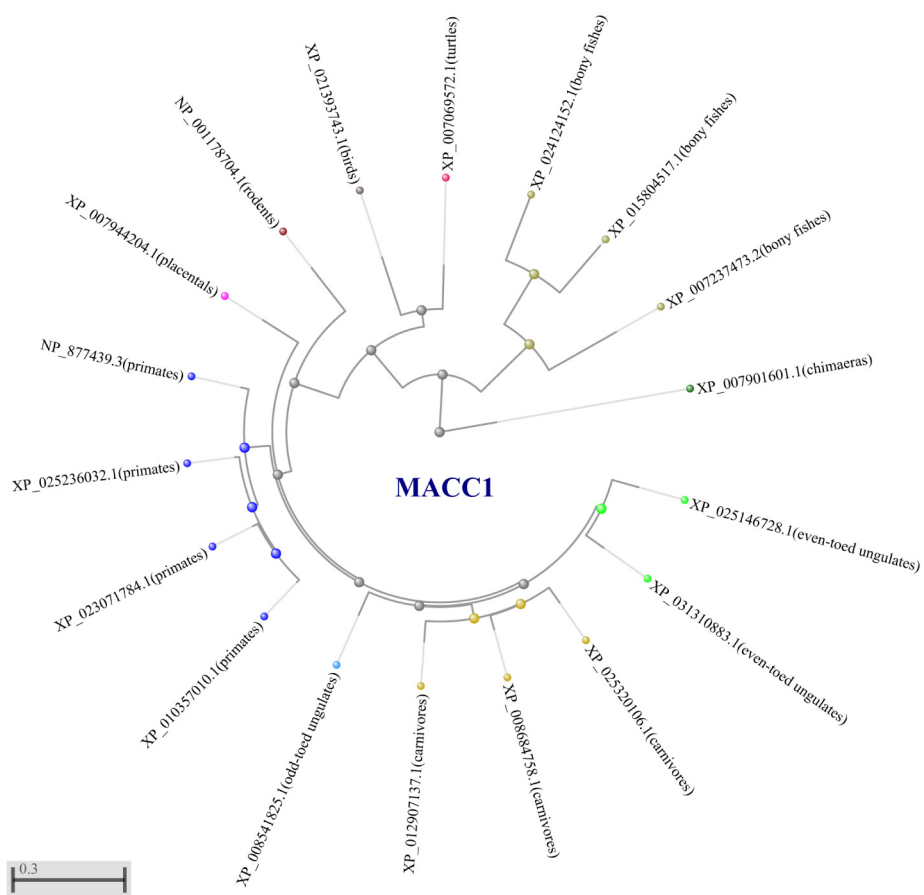


Figure S2. Phylogenetic tree of *MACC1*. The phylogenetic tree of *MACC1* in different species.

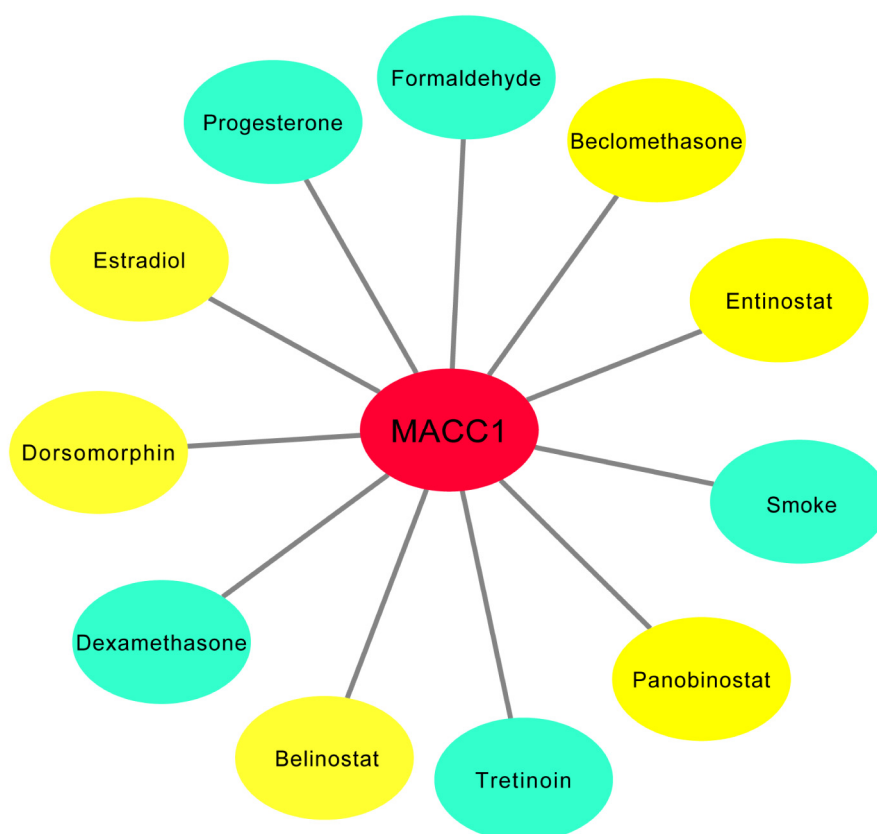


Figure S3. Based on CTD database, *MACC1*-drug interaction analysis was performed. Color yellow, drugs increase the expression of *MACC1*; Color green, drugs decrease the expression of *MACC1*.

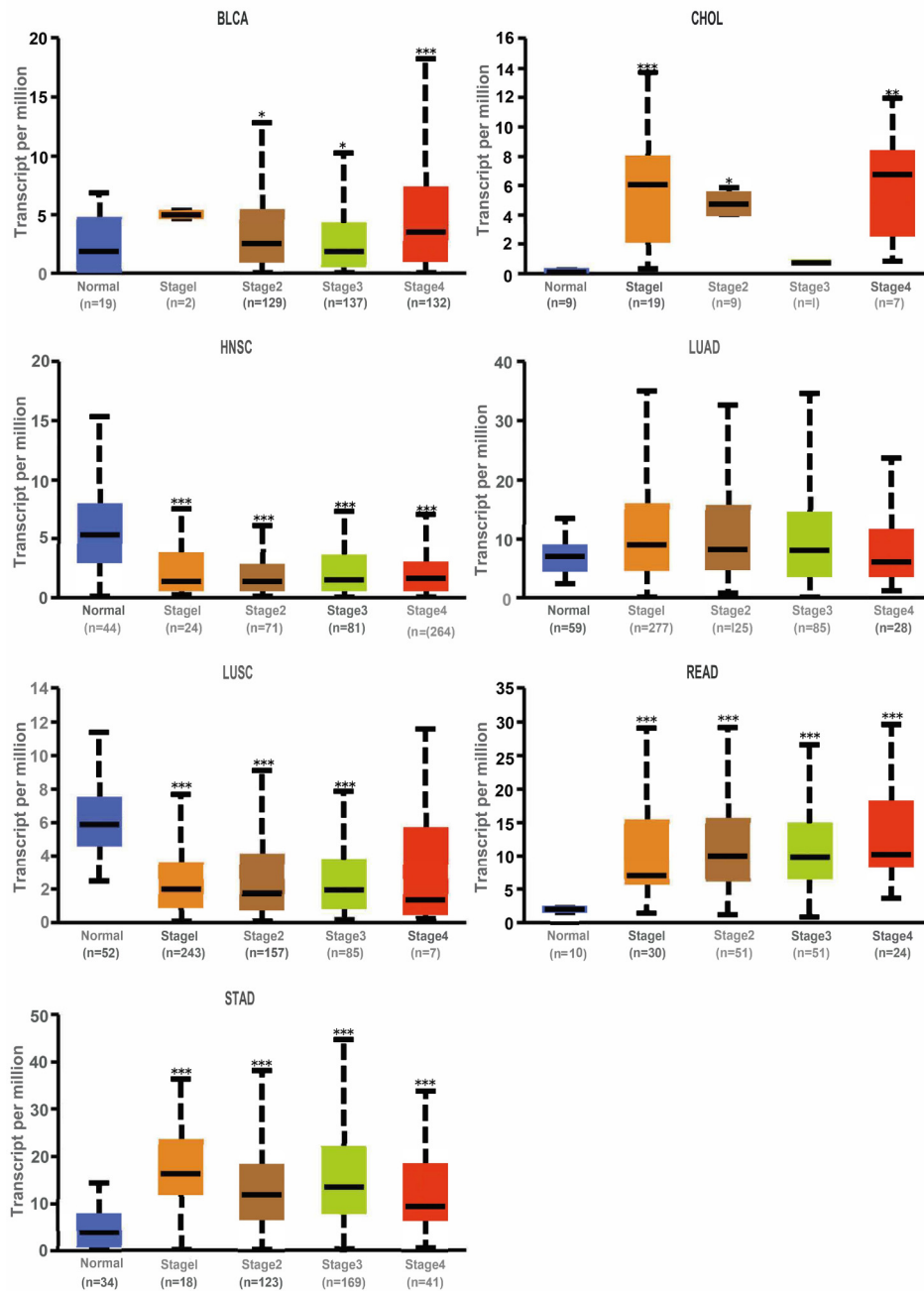
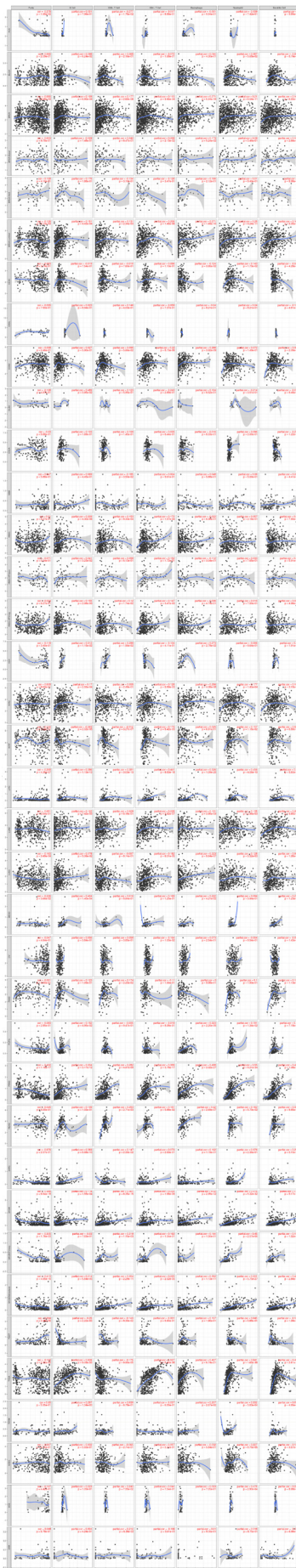


Figure S4. Relationship between expression levels of *MACCI* and different pathological stages of BLCA, CHOL, HNSC, STAD, READ, LUSC, LUAD. The first asterisk above the first error line represents a comparison to normal tissue. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.



Continued on next page

Figure S5. Correlation between *MACC1* and immune infiltration level. The relationship between *MACC1* and six immune cells (B-cells, CD4+ T-cells, CD8+ T-cells, macrophages, neutrophils, and dendritic cells) in 30 types of tumors except LGG and STAD.

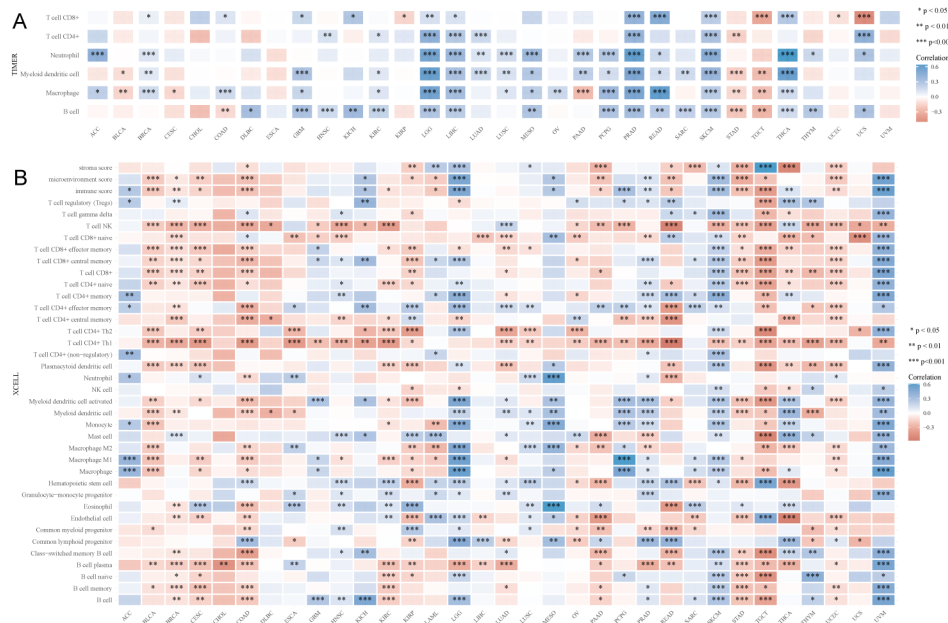


Figure S6. The relationship between *MACC1* and diverse infiltrating lymphocytes across 33 tumors using the TIMER and XCELL algorithms.

Reference

1. W. J. Kent, C. W. Sugnet, T. S. Furey, K. M. Roskin, T. H. Pringle, A. M. Zahler, et al., The human genome browser at UCSC, *Genome Res.*, **12** (2002).
2. A. P. Davis, C. J. Grondin, R. J. Johnson, D. Sciaky, J. Wiegiers, T. C. Wiegiers, et al., Comparative Toxicogenomics Database (CTD): update 2021, *Nucleic Acids Res.*, **49** (2021), D1138–D1143.