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The Cancer Control Challenge:
Better Understanding It to Better Face It

EXPRESSION OF *MYC/MAX/MAD* AXIS IN GASTRIC ADENOCARCINOMA

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Introduction: The *MYC/MAX/MAD* transcriptional axis is essential for regulating cellular proliferation, differentiation, and apoptosis. Dysregulation of *MYC* is frequently implicated in tumorigenesis, and its overexpression is associated with poor prognosis in several cancers. However, the transcriptional balance between *MYC* and its antagonistic partners, such as *MAX* and members of the MAD family (*MXD1-4, MXI1*), remains poorly understood in gastric adenocarcinoma. **Objectives:** To investigate the expression patterns and diagnostic relevance of *MYC*, *MAX*, and *MXD1-4* in gastric cancer (GC) in comparison to healthy gastric tissue. **Methods:** We analyzed RNA-seq data from 142 gastric tissue samples. Of these, 74 tumor samples were obtained from patients treated at the Hospital Universitário João de Barros Barreto (CAAE 47580121.9.0000.5634), and 68 normal samples were retrieved from the PRJNA1054173 project, available through the NCBI BioProject database (https://www.ncbi.nlm.nih.gov/bioproject/?term=PRJNA1054173). Transcript quantification was conducted using Salmon v1.10.1, and differential expression analysis was performed using DESeq2 v1.40.2 in R v4.3.1. Variance stabilizing transformation (VST) was applied for downstream visualizations, including PCA (ggfortify v0.4.16), boxplots (ggplot2 v3.5.1), and heatmaps (ComplexHeatmap v2.18.0). Diagnostic accuracy was evaluated through ROC curves using the pROC v1.18.5 package. **Results:** A transcriptional imbalance was observed between *MYC* and the *MAX/MAD* repressors in gastric tumor samples. *MYC* was upregulated, while *MAX* and most *MAD* genes were downregulated (log2FoldChange > 1 or < -1; padj < 0.05). ROC analysis revealed that all members of the *MYC/MAX/MAD* family exhibited potential for sample classification, with AUC values exceeding 0.80. These findings were supported by heatmap clustering and PCA, which clearly separated tumor from non-tumor profiles. **Conclusion:** The *MYC/MAX/MAD* axis shows a distinct and disrupted expression profile in gastric adenocarcinoma. These transcription factors demonstrate high diagnostic potential and merit further investigation as biomarkers and therapeutic targets in gastric cancer.

Keywords: Gastric cancer; Differential expression; Cancer transcriptomics; *MYC/MAX/MAD* network