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A.C.Camargo Cancer Center
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Merged microarray meta-dataset displays distinct transcriptional profile for gastric cancer

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Introdução

Gastric cancer (GC) is a highly heterogeneous, a complex disease, and the fifth most common cancer across the world (about one million cases and 784 000 deaths worldwide in 2018). In Brazil, the National Cancer Institute estimated that in 2020 were diagnosed 21.230 new cases of GC (13.360 men and 7.870 women), and approximately 15.000 deaths. The CG is lately diagnosed which guarantee the poor prognosis for GC (the 5-year survival rate is less than 20%, but in early detection can reach 90%). Molecular signature identification is a strong strategy to understand the CG progress.ore, this study aimed to evtranscriptional profile in tumor gastric samples.

Casuística e Métodos

Data collection was performed at Gene Expression Omnibus (GEO) bank to obtain 3 dataset matrices which analyze gastric tumor tissue versus normal gastric tissue, performed microarray using GPL570 platform, and from different sources. Therefore, these three microarray studies were selected to proceed the meta-analyses (GSE66229, GSE54129 and GSE13911). The datasets were merged and a total of 601 samples were classified between gastric and normal tumor tissue models. The merged dataset was applied Combat function for batch correction and then normalized using fRMA functions. The GSEA (Gene set enrichment analysis) platform was used to identify functionally related and enriched genes sets within a list of classifiable genes from cancer samples in comparison to normal samples. Moreover, the survival rates correlated to gene expression in gastric cancer were investigated in GEPIA database (Gene Expression Profiling Interactive Analysis).

Resultados

In total, 3,085 DEGs were matched, including 1,638 up-regulated and 1,447 down-regulated. Among the top-ranked expressed gene with significantly up- or down-regulation, the metadata set showed *AJUBA*, *GPNMB* and *CD80* genes with increased expression in gastric tumor samples compared, while *FBXL13*, *PDILT* and *CCDC69* genes had a decreased expression. In addition, higher expression of *GPNMB*, *ITGB1* and *PTGS2* genes significantly decreased the survival rate in patients with gastric cancer. Furthermore, our metadata, analysed by the hallmark signature on GSEA, showed a enrichment profile for oncogenic hallmarks, such as hallmark_G2M_checkpoint, hallmark_spermatogenesis, hallmark_E2F_targets, hallmark_mitotic_spindle, hallmark_estrogen_response_late, hallmark_epithelial_mesenchymal_transition. These gene sets that were enriched were responsible for several cellular processes important for the gastric cancer cells, which includes cellular proliferation, mitosis, high gene expression modulation, cellular migration and invasion.

Conclusões

The combination of a systematic collection of public microarray data with a comparative meta-profiling approach provided a suitable platform for drawing conclusions. This activation of pathways shows that these genes are important in carcinogenesis and are likely the result of the convergence of several transforming processes in various cellular contexts. Furthermore, the significant overexpression of these genes implies that they might be useful therapeutic targets.

Contato

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Resultados

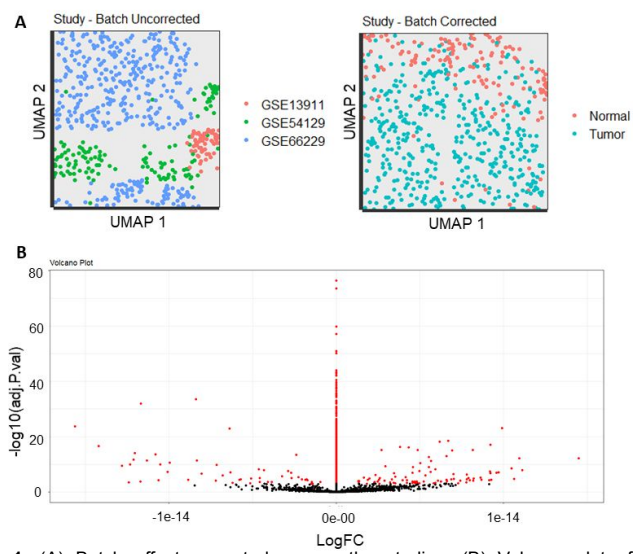

Fig 1. (A) Batch effect corrected among the studies. (B) Volcano plot of differentially Expressed genes (DEGS) in gastric tumor. Red dots represent significant expressed genes.

Table 1. Top 10 up- and down-regulated genes in gastric tumor.

Differentially expressed genes							
Up-regulated				Down-regulated			
Gene Symbol	LogFC	t	Adjusted p-value	Gene Symbol	LogFC	t	Adjusted p-value
AJUBA	1.44E+14	7.80	7.78E-13	**FBXL13**	-1.56E+14	-11.18	2.01E-24
GPNMB	1.11E+14	6.20	1.53E-08	**PDILT**	-1.41E+14	-9.20	2.98E-17
CD80	1.09E+14	7.84	5.74E-13	**CCDC69**	-1.28E+14	-6.83	3.98E-10
ANLN	1.06E+14	4.82	1.61E-05	PDZK1IP1	-1.24E+14	-4.03	4.02E-04
ADGRG7	1.06E+14	4.75	2.22E-05	SCIN	-1.23E+14	-7.05	1.02E-10
BICD1	1.04E+14	6.47	3.44E-09	ITIH5	-1.21E+14	-7.66	1.98E-12
KNL1	9.91E+13	11.01	8.37E-24	NKX2-3	-1.20E+14	-8.46	7.58E-15
ABCD3	9.71E+13	5.89	8.40E-08	ITGB1	-1.17E+14	-4.27	1.59E-04
CENPL	9.57E+13	5.85	1.03E-07	SIGLEC11	-1.16E+14	-13,16	1,33E-32
PTGS2	9.26E+13	4.60	4.17E-05	PTCHD1	-1.13E+14	-7,52	5,07E-12

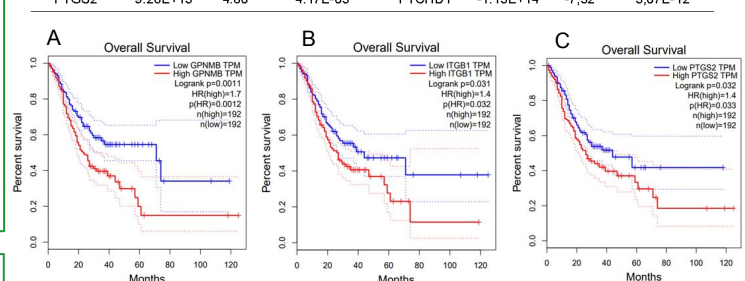

Fig 2. Survival analysis for the genes (A) *GPNMB*, (B) *ITGB1*, and (C) *PTGS2*.

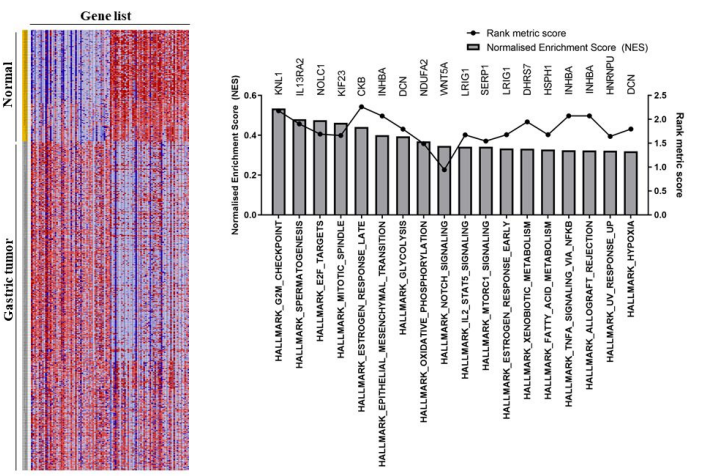

Fig 3. Differentially expressed genes found using Gene Set Enrichment Analysis.