# IDENTIFICATION OF MOLECULAR BIOMARKERS IN INTESTINAL AND DIFFUSE GASTRIC ADENOCARCINOMA SUBTYPES

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Introduction
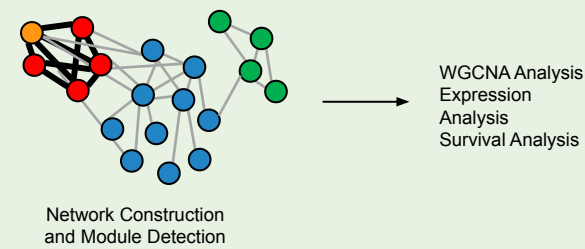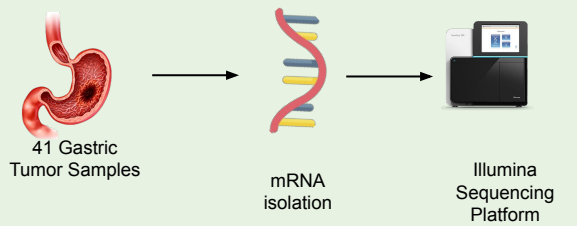

Intestinal   Diffuse
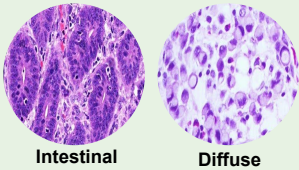
Lauren's histological classification is an important **prognostic factor** in Gastric Cancer (GC) patients undergoing gastrectomy. However, the **molecular characteristics** of the subtypes of this histologic classification **are unclear**.

Thus, there is a search for **new biomarkers** that may be useful in the clinical practice of GC.

Biological networks analysis of **gene expression** patterns might lead to the discovery of putative **"hubs" genes (biomarkers)**, supposed to have important roles in cancer occurrence and consequences.

Material and Methods

41 Gastric Tumor Samples

mRNA isolation

Illumina Sequencing Platform

Network Construction and Module Detection

WGCNA Analysis
Expression Analysis
Survival Analysis

Results

Figure 1. Expression Modules and their top hub genes. The color of the table titles indicate the coexpression groups/modules: Turquoise, Blue and Red modules.

Gene	GS	MM	Score	Gene	GS	MM	Score	Gene	GS	MM	Score
MAD2L1	-0.48	0.92	400	MAP1LC3C	0.42	0.89	393	SHE	0.50	0.63	397
SRP9	-0.38	0.92	398	PARP15	0.47	0.87	392	COL14A1	0.46	0.75	396
TWF1	-0.42	0.92	396	SMARCAL1	0.40	0.90	388	RBMS3	0.44	0.76	395
GLO1	-0.38	0.92	394	ABCC10	0.39	0.92	386	AKT3	0.45	0.74	394
PSMA2	-0.48	0.91	390	C4orf32	0.45	0.87	386	NEGR1	0.49	0.50	392
ERH	-0.43	0.90	390	SHISA9	0.48	0.86	386	WNT2B	0.42	0.60	390
PPIA	-0.42	0.89	388	GRAMD4P3	0.52	0.84	378	ARHGAP28	0.47	0.49	390
SNRPG	-0.44	0.89	386	ZBTB8B	0.36	0.93	373	LIX1L	0.38	0.58	388
USMG5	-0.41	0.89	384	KIR3DX1	0.41	0.86	373	KCNB1	0.38	0.51	386
SF3B6	-0.42	0.88	382	ZNF554	0.37	0.89	372				
RPL39	-0.39	0.88	380	ZNF665	0.43	0.85	372				
C8orf59	-0.42	0.88	378	PCDHA4	0.45	0.85	372				
RPL30	-0.36	0.87	376	ZNF383	0.46	0.84	372				
H2AFZ	-0.41	0.87	374	ANKS3	0.41	0.85	369				
PSMD14	-0.45	0.86	372	TMEM45A	0.51	0.83	369				

*Three **gene coexpression clusters** were identified in the network: **Turquoise, Blue and Red***

Results

Figure 2. Gene Ontology (GO) of the genes present in the coexpression modules related to Lauren's classification. A) GO of Turquoise, B) Blue and C)Red
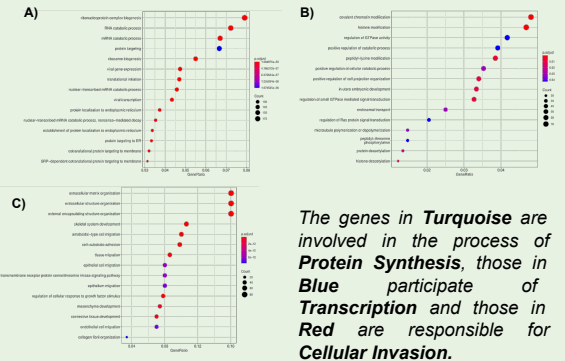
*The genes in **Turquoise** are involved in the process of **Protein Synthesis**, those in **Blue** participate of **Transcription** and those in **Red** are responsible for **Cellular Invasion**.*
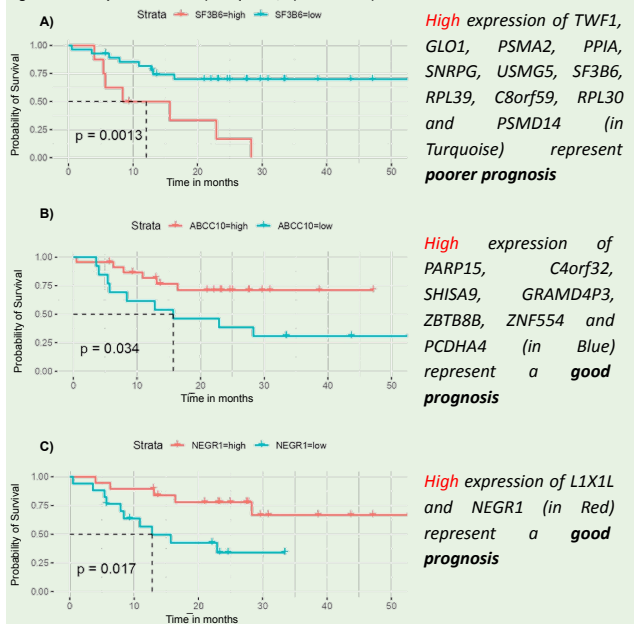
Figure 3. Heatmap of hub gene expression
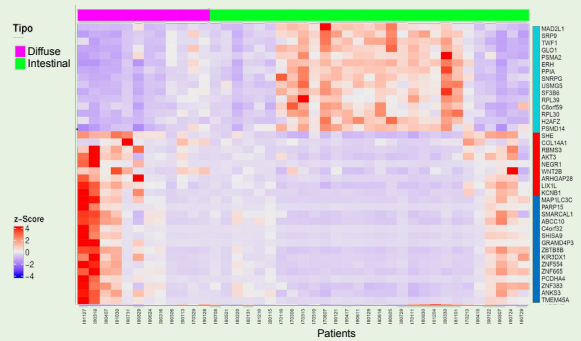
*The expression of genes in the **Turquoise** group discriminate the **Intestinal subtype***

*However, the expression of the hub genes in **Blue and Red** seems to be **similar** in both Lauren's subtypes*

Figure 4. Expression of the hub genes impacts overall survival of GC patients. Example hub genes with impact on OS in A) Turquoise, B) Blue and C) Red.

*High expression of TWF1, GLO1, PSMA2, PPIA, SNRPG, USMG5, SF3B6, RPL39, C8orf59, RPL30 and PSMD14 (in Turquoise) represent **poorer prognosis***

*High expression of PARP15, C4orf32, SHISA9, GRAMD4P3, ZBTB8B, ZNF554 and PCDHA4 (in Blue) represent a **good prognosis***

*High expression of L1X1L and NEGR1 (in Red) represent a **good prognosis***

Conclusions

The hub genes identified in the modules are associated with biological pathways which are important for the histological and functional characteristics of Lauren's subtypes;

Turquoise hub genes are overexpressed in the Intestinal subtype, thus these genes may be related to the development of this subtype;

The hub genes in module Turquoise are related to the prognosis of GC patients;

Although the genes in Blue and Red are not expressed in a single subtype, they have an impact on the overall survival of patients with GC.

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Acknowledgments