Identification of novel genes in patient with Barret's Esophagus/Esophageal Adenocarcinoma using bioinformatics

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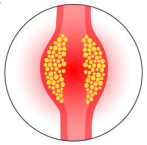
Introduction

- Esophageal cancer is one of the leading causes of death in males in the United States (US).
- Esophageal Adenocarcinoma (EAC) is the most common histological type.
- EAC usually arises from Barrett's esophagus (BE).
- There is a paucity of data on the cellular mechanisms that leads to neoplastic progression in the esophagus.



Aim

To understand the pathophysiology of BE and EAC and identify the genetic changes that drive the neoplastic process.

Methods

- Employed a Search Tag Analyze Resource (STARGEO) platform to conduct two meta-analysis using the National Center for Biotechnology's (NCBI) Gene Expression Omnibus (GEO).
- First analysis compared **175 esophageal biopsies from patients with BE** to **169 healthy esophageal samples** as a control.
- Second analysis **compared 157 esophageal biopsies from patient with EAC** to **127 BE biopsies**.
- Analyzed associated signatures in Ingenuity Pathway Analysis (IPA) to genes that showed:
  1)Statistical significance ($p<0.05$)
  2)An absolute experimental log ratio greater than 0.1 between case and control samples

Results

BE vs Healthy	
Top Up-Regulated Genes	
TSPAN8	1.361
LGALS4	1.248
MUC5AC	1.173
Top Down-Regulated Genes	
SERPINB13	-0.742
SPRR2C	-0.711
CRISP3	-0.723

Table 1: Top genes up-regulated and down-regulated in BE vs Healthy samples

EAC vs BE	
Top Up-Regulated Genes	
SSP1	0.320
INHBA	0.292
MMP1	0.287
Top Down-Regulated Genes	
LIPF	-0.418
GKN1	-0.405
HPGD	-0.399

Table 2: Top genes up-regulated and down-regulated in EAC vs BE samples

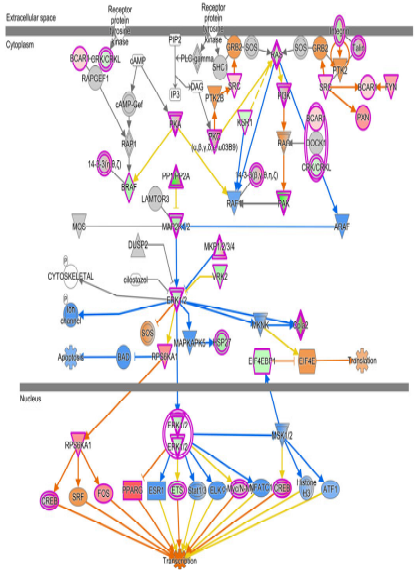


Figure 1: We identified EPK/MAPK signaling pathway as the top canonical pathway. Activation of this pathway an important mediator in metaplasia.

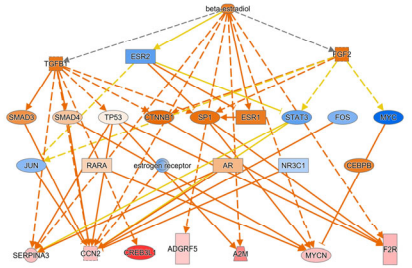


Figure 2: Beta estradiol is associated with the activity of many genes upregulated in BE/EAC.

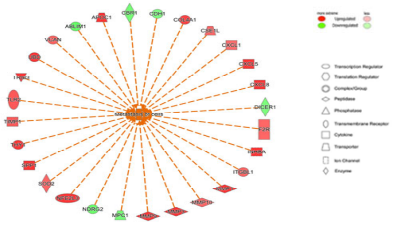


Figure 3: Genes associated with increased risk of metastasis in EAC.

Conclusions

- Our results build off long-described players in BE pathogenesis and provide more support for more recently described genes including:
  1) TSPAN8 2) LGALS5
  3)SERPINB13 4) SPRR2C
- Upregulation of SSP1 is involved in esophageal cancer angiogenesis and inflammation.
- Our analysis illustrates that EPK/MAPK signaling dysregulation is a key component of BE/EAC pathogenesis.
- Dysregulation of beta estradiol function is associated with upregulation of oncogenes leading to tumorigenesis.
- TSPAN8 is an emerging potential therapeutic target in esophageal carcinoma.

Clinical Implication

This study provides more insight to BE/EAC pathogenesis that can suggest possible therapeutic targets or potential markers of disease progression.

References

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