Evaluation of intratumoral heterogeneity of molecular alterations in Esophagel squamous cel carcinoma with potential use in the clinic

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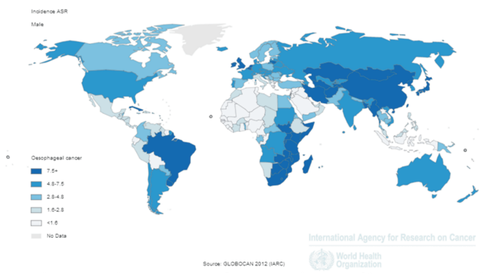
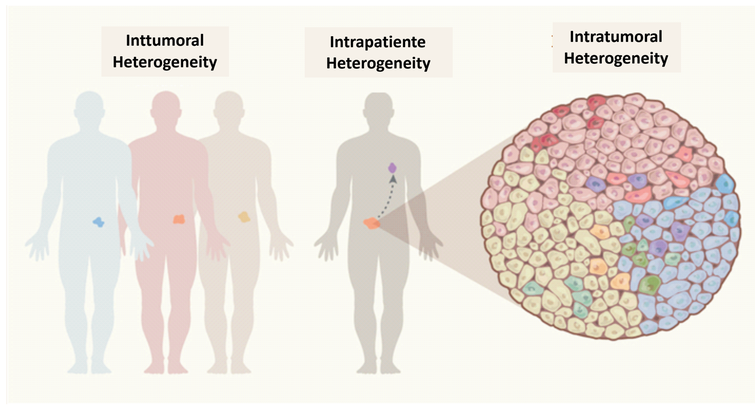
INTRODUCTION

- Esophageal cancer is among the ten types of more incidents and killing tumors in the world, ranking 6th in incidence and 5th place in mortality among men.
- Esophageal squamous cell carcinoma (ESCC) corresponds to approximately 80% of cases of esophageal cancer in Brazil and the world;



- The high lethality of esophageal cancer due to late diagnosis, leading to ineffective treatment. This demonstrates the need for detection of biomarkers and new therapeutic approaches for this disease.
- However, an important barrier to the incorporation of these markers into the clinic is intratumoral heterogeneity.



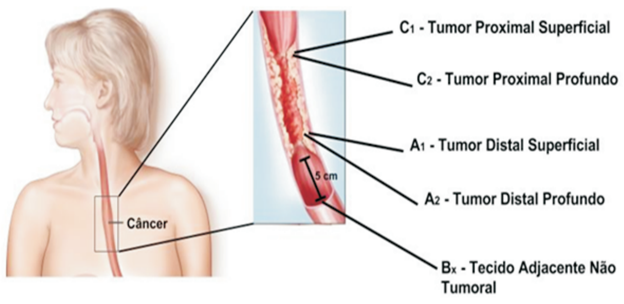
Adapted from Edward J. Fox & Lawrence A. Loeb, 2014.

GOALS

Evaluate the intratumoral heterogeneity of gene expression alterations characteristic of oesophageal squamous cell carcinoma.

RESULTS

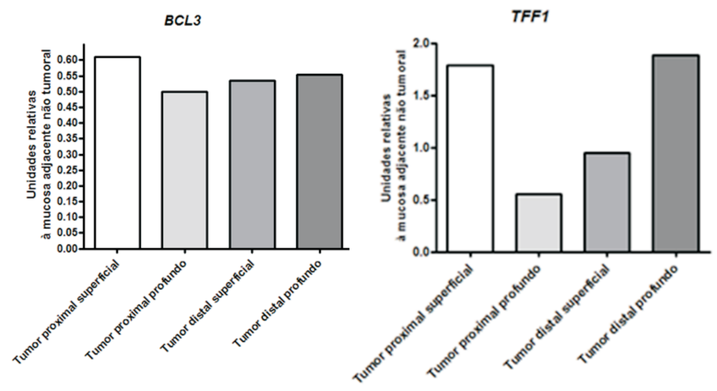
Samples



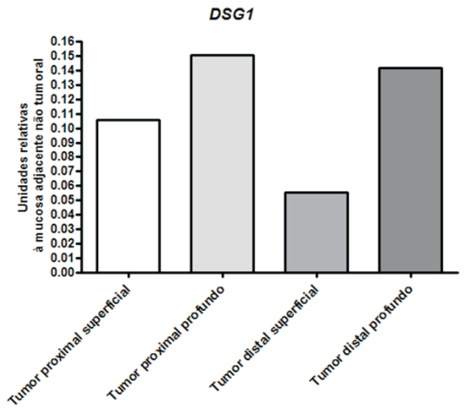
Analysed Genes

Condition	Genes
Early altered during carcinogeneses	*BCL3* *TFF1*
Related to adhesion and differentiation	*DSG1*
Pognostic Biomarkers	*IL6* *FOXM1* *PI3KR3*
Terapeutic Target	*MET*

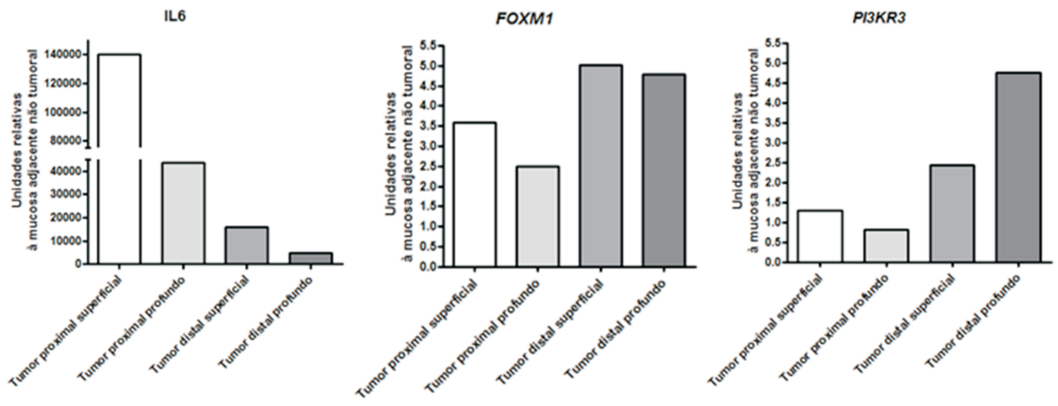
Evaluation of genes early altered during esophagus carcinogenesis



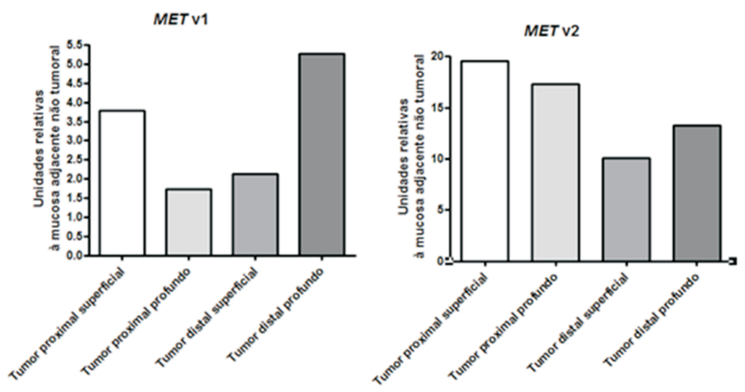
Evaluation of genes related to adhesion and celular differetiation



Evaluation of genes with prognostic biomarker value



Evaluation of genes with potential to target therapy



METHODOLOGY

- The samples were obtained from a 64-year-old male patient, diagnosed with oesophageal squamous cell carcinoma at IIA staging at the time of biopsy.
- From this patient, four biopsies from different regions of the tumor mass were collected and a biopsy of adjacent non-tumor tissue 5 cm from the tumor margin.
- RNA extraction from the CEE biopsies was performed in the BNT-INCA laboratory with the help of the Rneasy Mini Kit (Qiagen), according to the manufacturer's instructions, then applied to reverse transcription reaction for cDNA synthesis.
- The expression of genes were evaluated by quantitative PCR (PCRq) using specifics primers.

PERSPECTIVES

- Increase the number of patients (n) to verify if patterns of heterogeneity are shared among patients.
- Analyze other types of molecular changes, such as methylation profile and mutational profile.
- Evaluate whether patterns of heterogeneity will vary according to different stages.

CONCLUSION

- The expression levels of the BCL3 gene, found altered early during oesophageal carcinogenesis, were homogeneous in the different CEE biopsies evaluated. On the other hand, the expression of TFF1 was variable.
- Expression of DSG1, although heterogeneous among tumor biopsies, was found to be decreased in all CEE regions compared to adjacent non-tumoral mucosa.
- All tumor biopsies evaluated showed increased expression of FOXM1 and IL6, although levels were variable. However, PI3KR3 did not show the same pattern of increase in all tumor regions
- Both MET variants were found to be overexpressed in all tumor biopsies compared to adjacent non-tumoral mucosa. However, the increase of METv2 was more expressive

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