EVALUTION OF INTRATUMOR HETEROGENEITY OF MOLECULAR ALTERATIONS IN ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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INTRODUCTION

- Esophageal cancer is among the ten most incidente and lethal tumors worldwide, ranking as 6th in incidence and 5th in mortality among men.

- Esophageal squamous cell carcinoma (ESCC) corresponds to approximately 90% of esophageal câncer cases in Brazil and the world;

- The high lethality of esophageal cancer is consequence of a late diagnosis, leading to ineffective treatment. By understanding the molecular mechanisms and identifying biomarkers, we can improve diagnosis and prognosis of ESCC pacientes.

- However, its been shown that molecular alterations may occur hetereneously within tumor, what may limit their use as biomarkers in cancer.
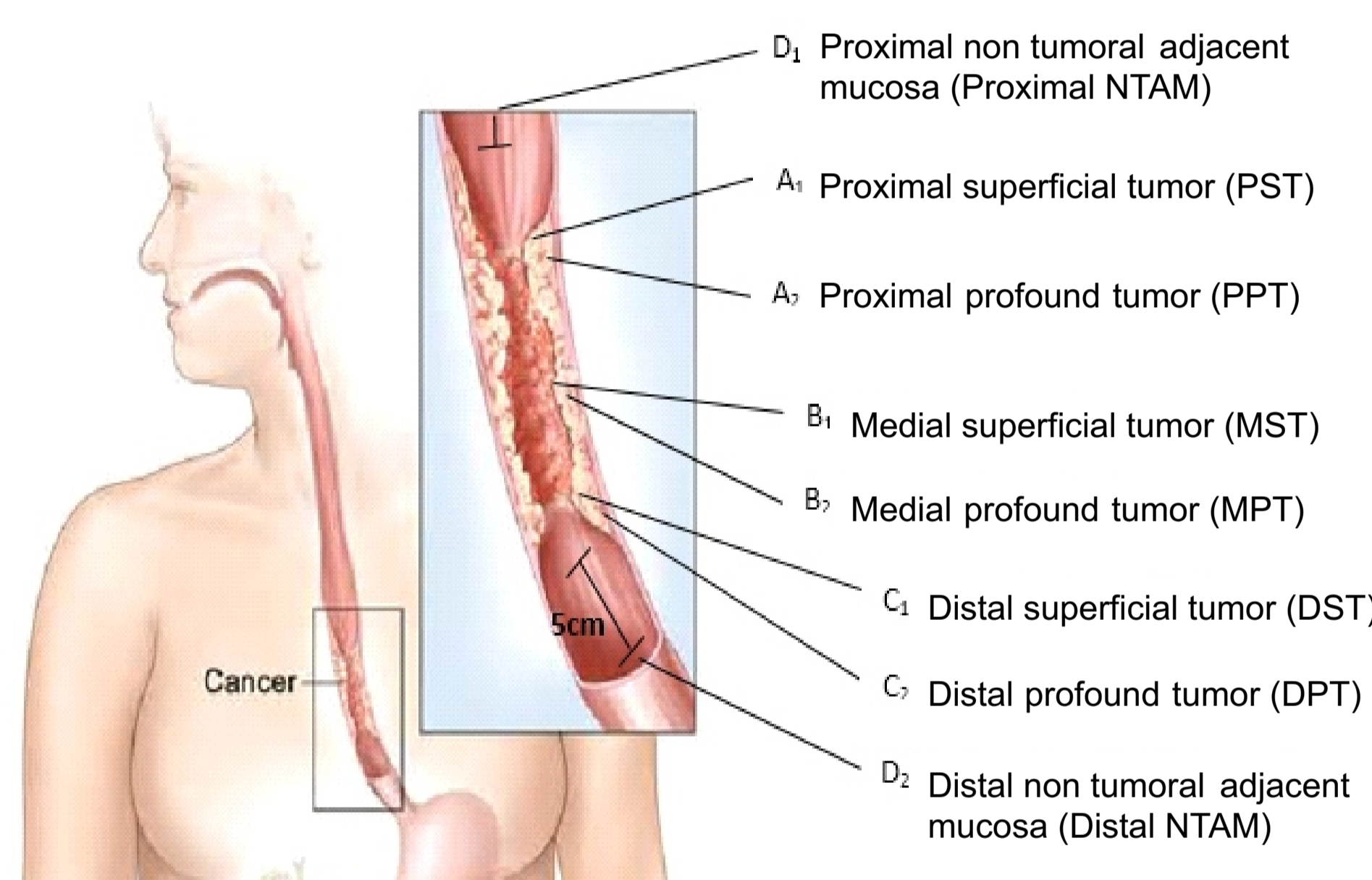

Intertumor Heterogeneity | Intrapaciente Heterogeneity | Intratumor Heterogeneity
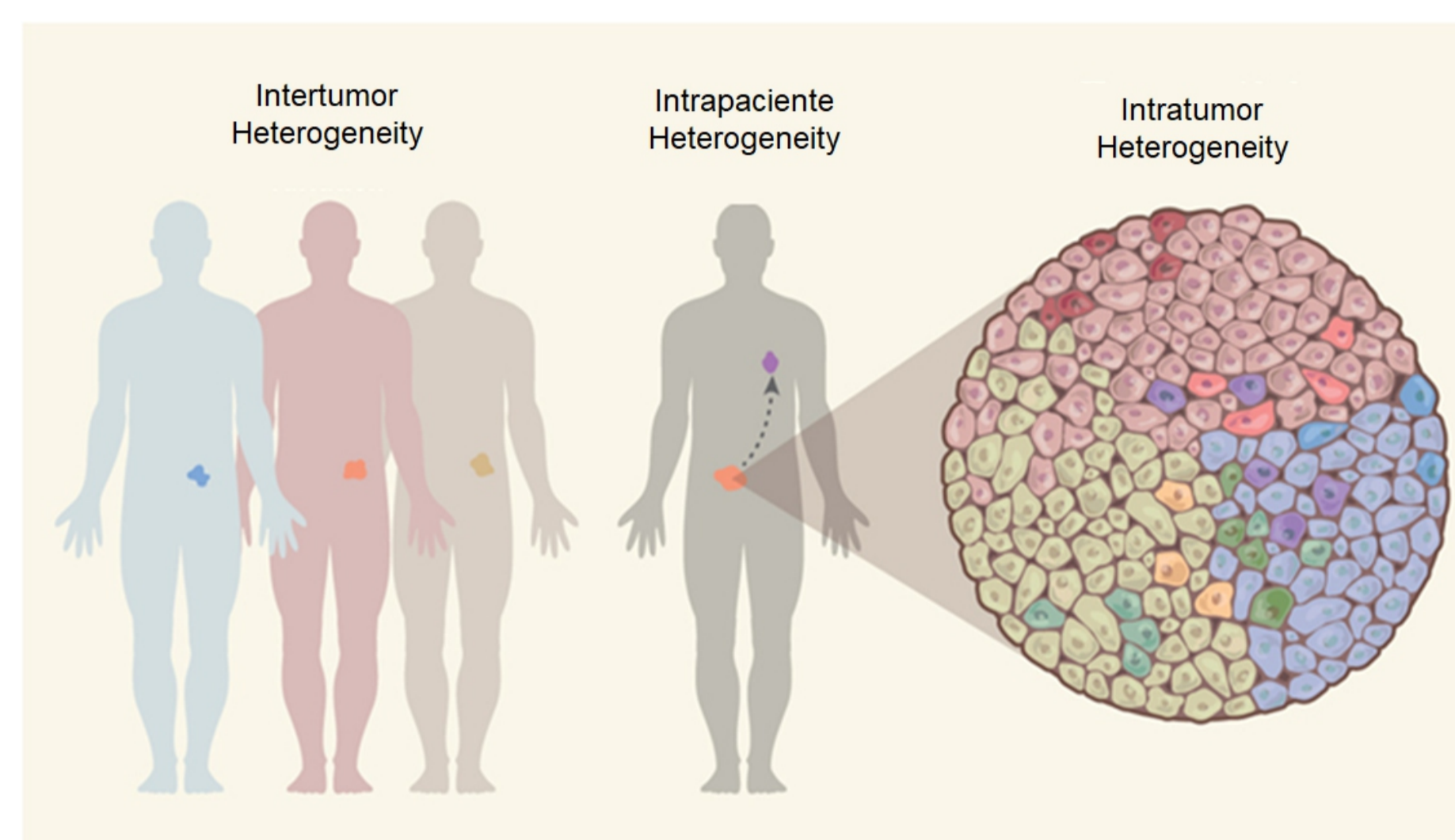
Source: Adapted from Edward J. Fox & Lawrence A. Loeb, 2014.

OBJECTIVE

To evaluate the intratumor heterogeneity of gene expression in esophageal squamous cell carcinoma.

METHODS

Tumor Biopsies

- D₁ Proximal non tumoral adjacent mucosa (Proximal NTAM)
- A₁ Proximal superficial tumor (PST)
- A₂ Proximal profound tumor (PPT)
- B₁ Medial superficial tumor (MST)
- B₂ Medial profound tumor (MPT)
- C₁ Distal superficial tumor (DST)
- C₂ Distal profound tumor (DPT)
- D₂ Distal non tumoral adjacent mucosa (Distal NTAM)

- Biopsies were collected from five patients submitted to endoscopy at the National Cancer Institute (INCA). From the tumor mass of each patient, two fragments (superficial and profound tumor) were collected from three different regions. These regions included a proximal, medial and distal area. When possible, two biopsies from non-tumor adjacente mucosa were also collected from each patient, 5 cm above (proximal) and under the tumor mass (distal);

- Samples were subjected to RNA extraction using Rneasy Mini Kit from Qiagen, then applied to reverse transcription reaction for cDNA synthesis;

- Gene expression was evaluated by quantitative PCR (PCRq).

CONCLUSION

- *BCL3* and *DSG1* demonstrated a homogenous expression decrease in tumors when compared to non-tumor adjacente mucosa.
- *TFF1* and *PI3KR3* presented a heterogenous pattern of expression.
- *IL6*, *FOXM1* and *MET v1* showed homogenous increase of expression in tumors when compared to non-tumor adjacente mucosa.
- The analysis of intratumoral heterogeneity of *MET V2* expression showed great variation between the biopsies of the same patient.
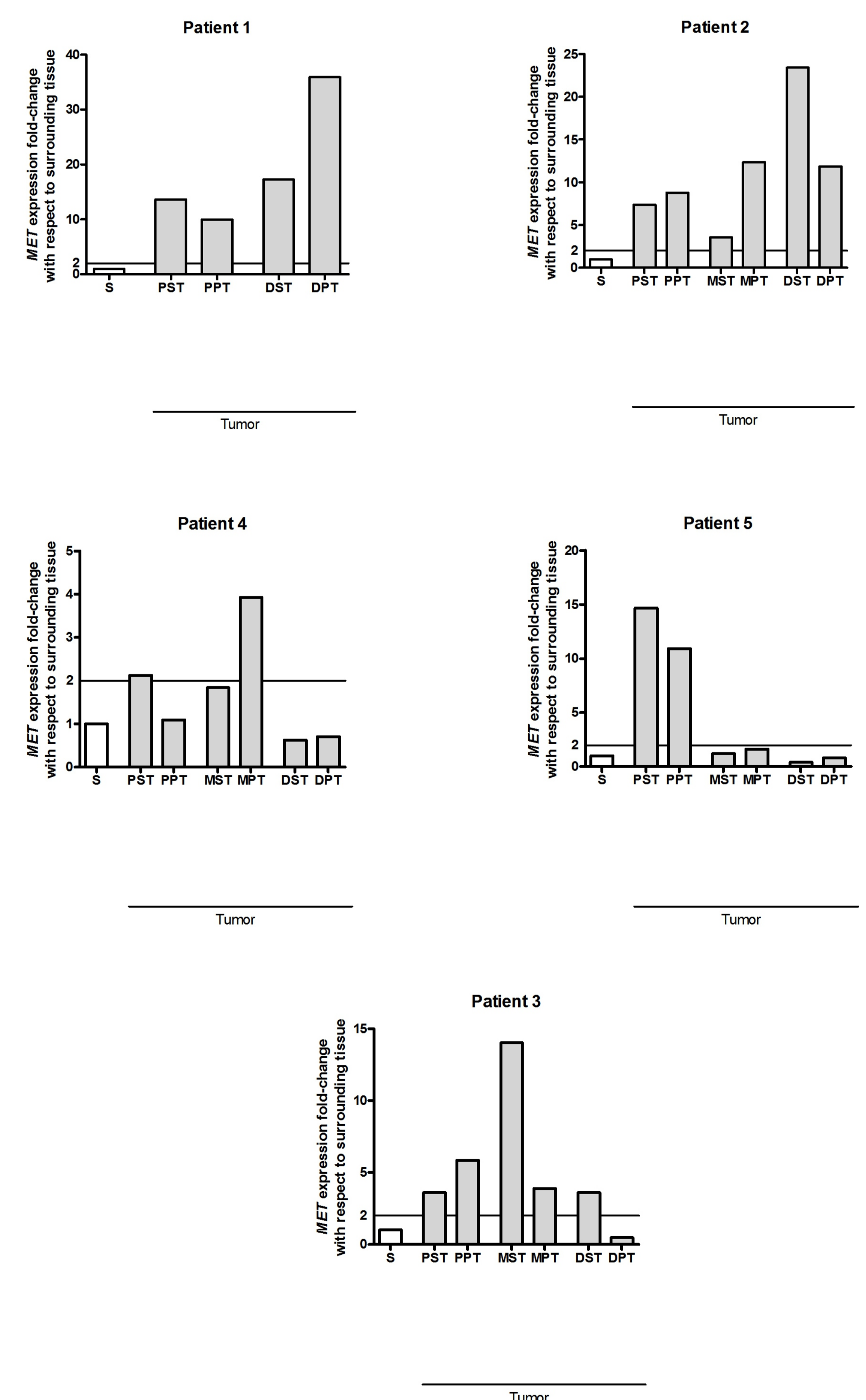
PERSPECTIVES

- To collect samples from additional 5 patients.
- To analyze the gene expression pattern of *BCL3, TFF1, FOXM1, DSG1, IL6, PI3KR3* and *MET-v2* in all cases.

RESULTS

Gene expression analyses in patient 1
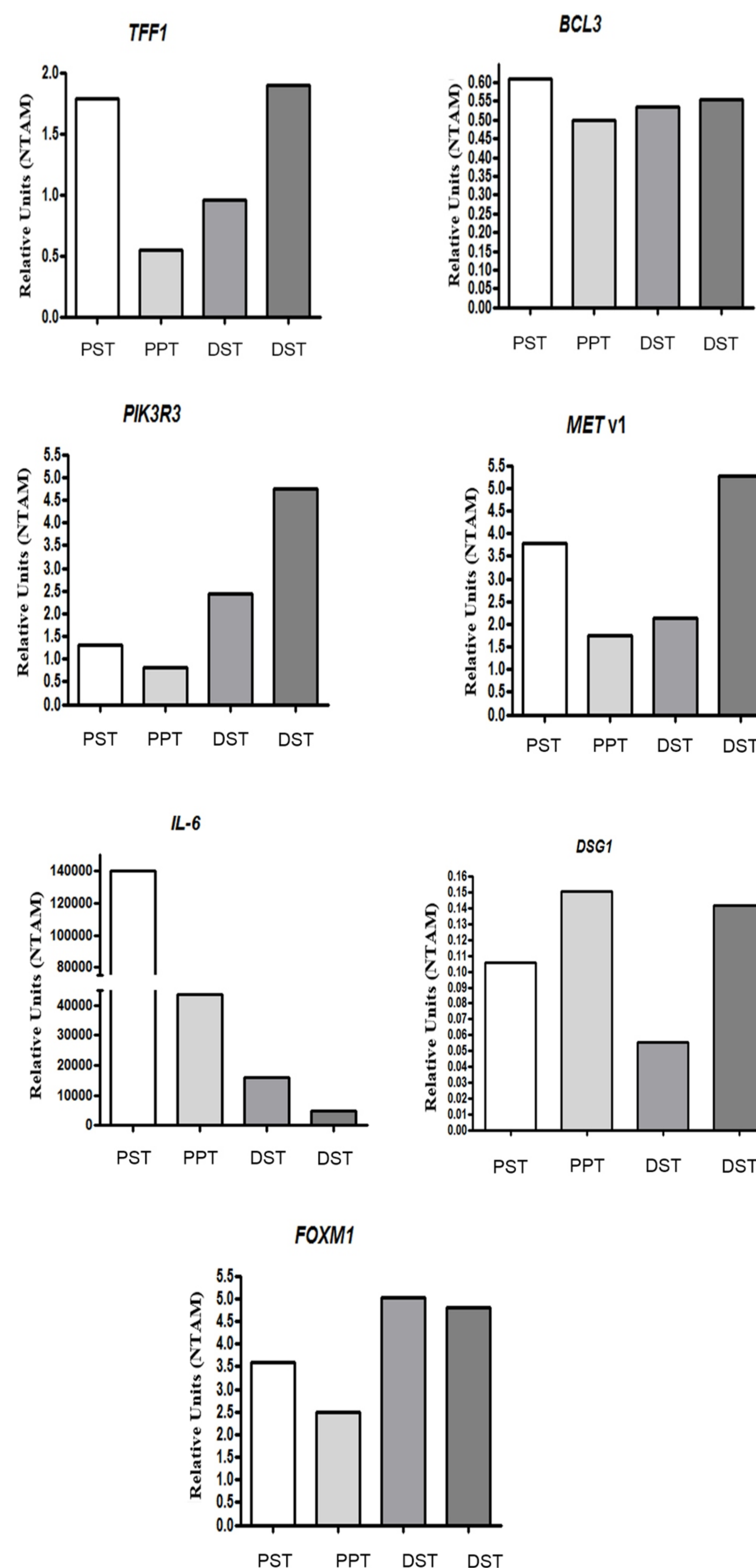
MET v2 Gene expression analisys in samples from 5 patients

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Projeto Gráfico: Área de Edição e Produção de Materiais Técnico-Científicos / INCA

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