

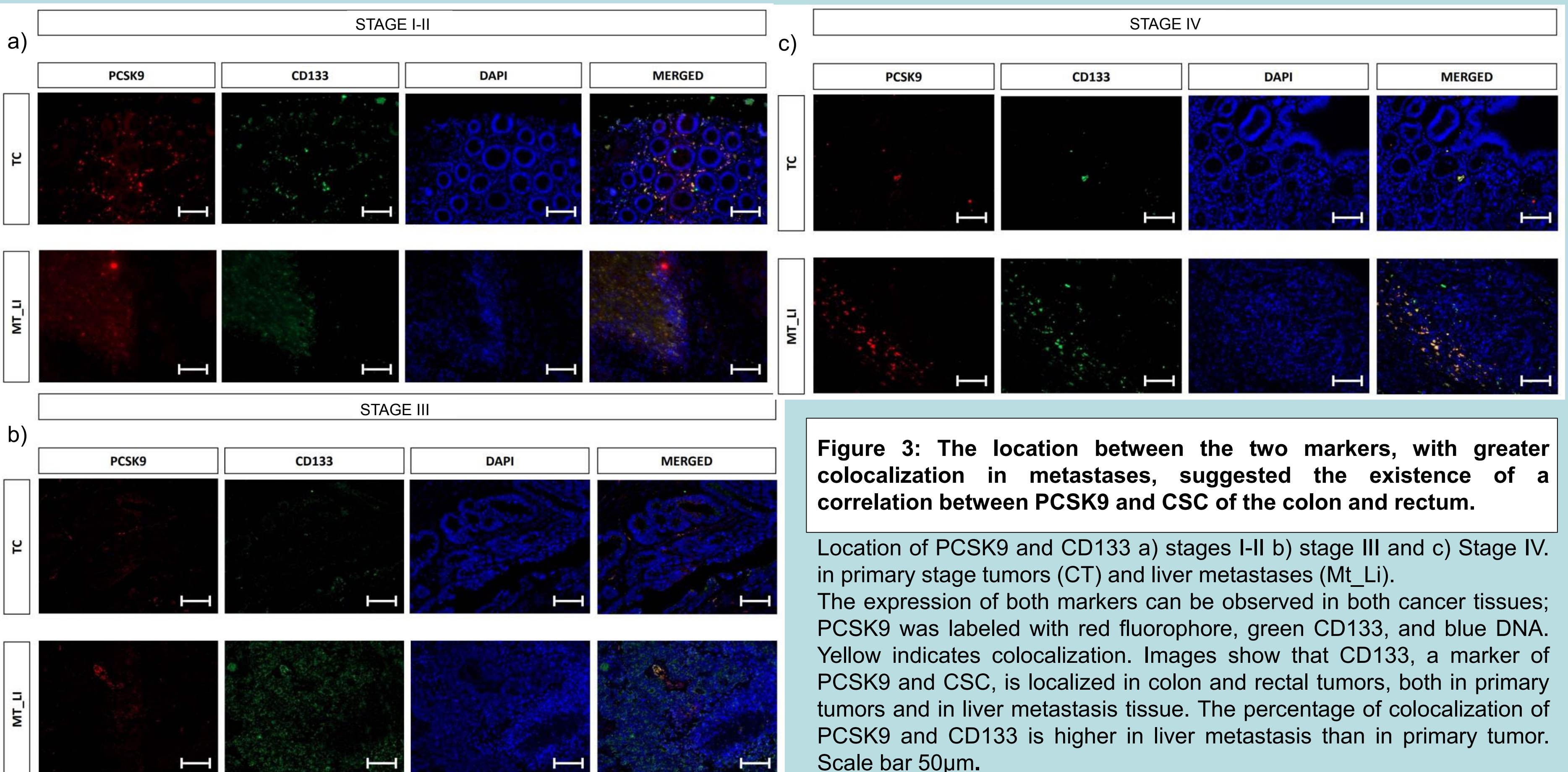
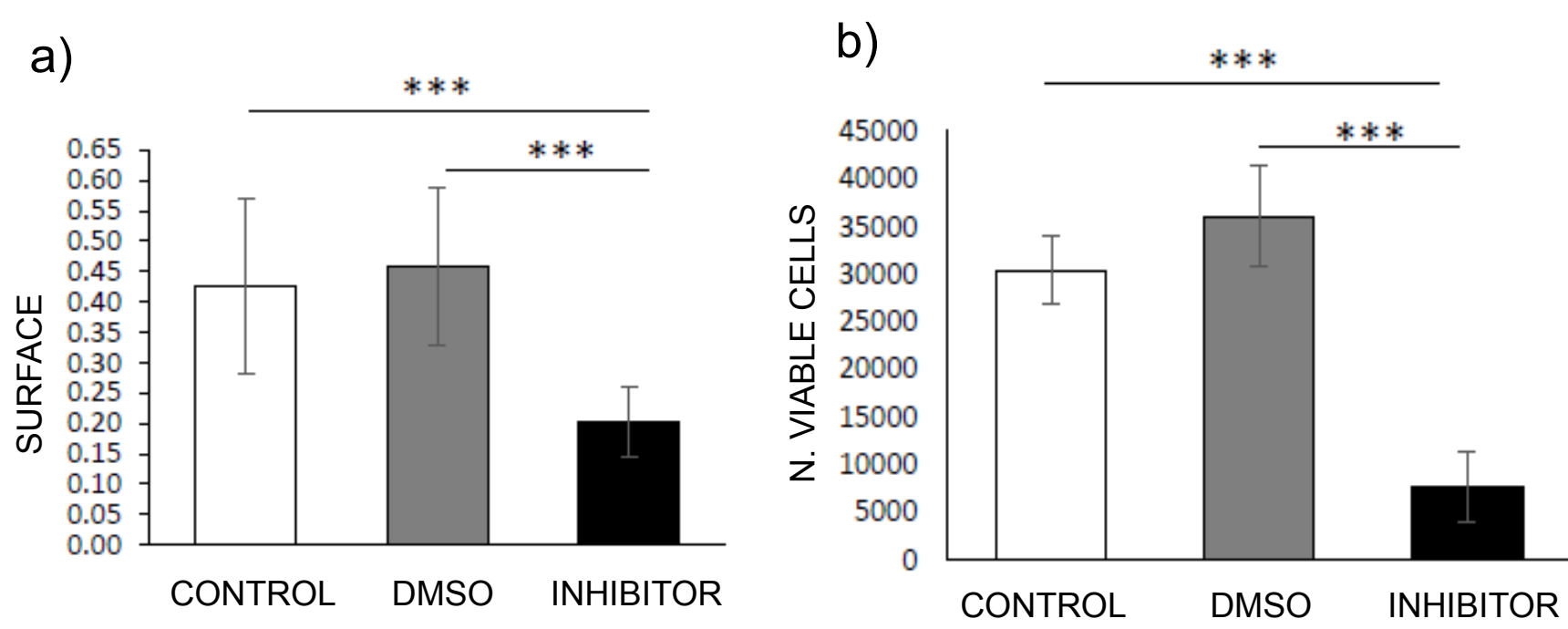
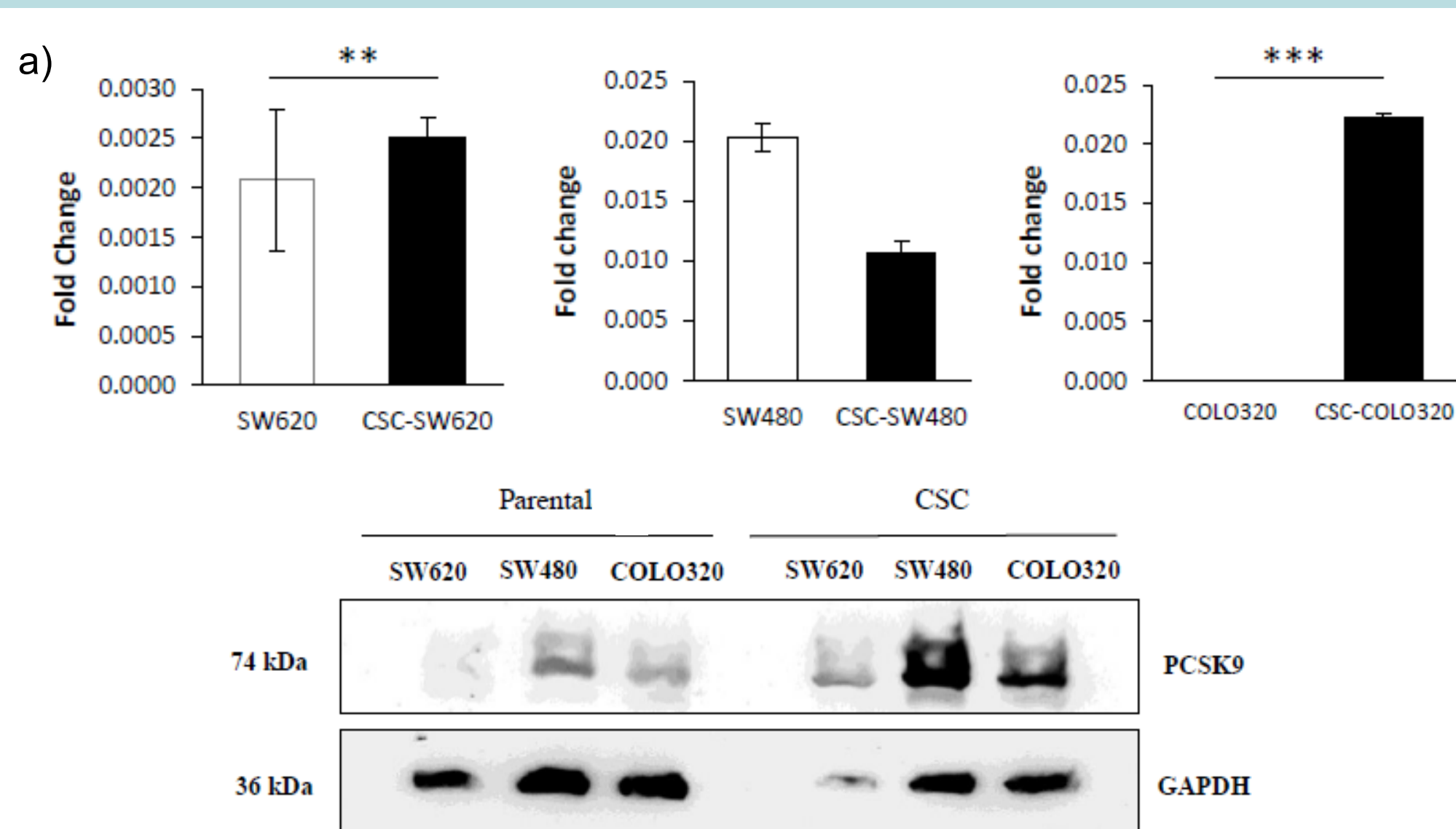
## INTRODUCTION:

Protein Convertases are a family of 9 mammalian serine secreted proteases (PCSK1, PCSK2, FURIN, PCSK4, PCSK5, PCSK6, PCSK7, SKI1, PCSK9) that modulate the biological activity of proteins by removing aminoacide chains. They are involved in the activation of a wide variety of secretory proteins that are essential for the maintenance of homeostasis, such as cytokines, proteases, adhesion molecules and growth factors (GF) and GF receptors, among others. Indeed, it is known that proprotein convertase subtilisin/kexin type 9 (PCSK9) increases circulating levels of low-density lipoprotein (LDL) but emerging investigations revealed also novel functions; including cell apoptosis, inflammatory response, neuronal development and tumor metastasis.

Cancer Stem Cells (CSCs) have been recently pointed out to be responsible for cancer initiation, progression, metastasis, recurrence and drug resistance. This is because any cell of a lineage that is not terminally differentiated, and can still proliferate, can potentially give rise to cancer.

Our study aimed to further elucidate the role of PCSK9 in cancer. Previously, our studies demonstrated a different expression of PCSK9 in CSCs and parental cells from metastatic and non-metastatic human colorectal adenocarcinoma cells lines. After using a PCSK9 inhibitor, PF-06446846, we analyze the expression both at the protein and gene expression levels and we studied the role of PCSK9 on the cellular functions of colon CSC. On the other hand, the co-expression of CD133 (CSC marker) and PCSK9, has been studied by immunofluorescence in biopsies of primary and metastatic tumors.

## RESULTADOS:



## CONCLUSIONS:

- PCSK9 expression was higher in CSCs than in parental cells.
  - Inhibition of PCSK9 significantly decreased CSC viability
  - The location between the PCSK9 and stem cell marker, with greater colocalization in metastases, suggested the existence of a correlation between PCSK9 and CSC of the colon and rectum.
- PCSK9 may play a role in tumor development and metastasis. His inhibition could be potentially use for future cancer therapy.