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INTRODUCTION

- The colorectal cancer (CRC) is a major worldwide public health problem known by a high incidence rate between both men and women (1). Over the tumor progression neoplastic cells acquire migratory, invasive and metastatic ability. This occurs through the loss of cell-cell adhesion and apical-basal cell polarity with subsequent actin cytoskeleton rearrangement (2).
- Cofilin-1 (Cfl-1) is the major regulatory protein responsible for the turnover of F-actin. Cfl-1 depolymerizes the actin filament and participates of its dendritic nucleation induction and branching, these events are involved at the initiation of the first steps of migratory cycle (2).
- Cfl-1 is necessary to the embryonic development and the impairment in its regulation leads to serious consequences into tissue homeostasis (3,4). Cfl-1 role at the cytoskeleton dynamic needs to be clear, though. Furthermore, it is necessary to elucidate how its expression profile is under different stages of the tumor progression. Thereby, we could propose new therapeutics interventions in the CRC treatment.

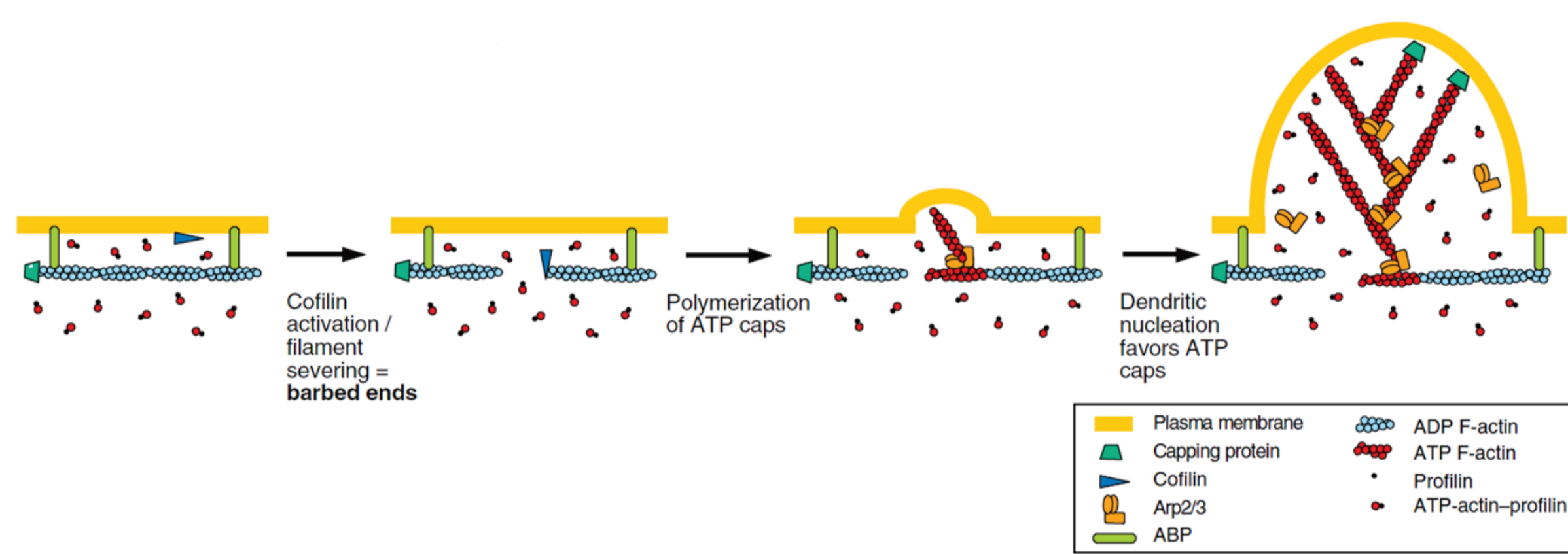


Figure 1- Schematic representation of cofilin-1 activity in a membrane protrusion. (DesMarais et al., 2005)

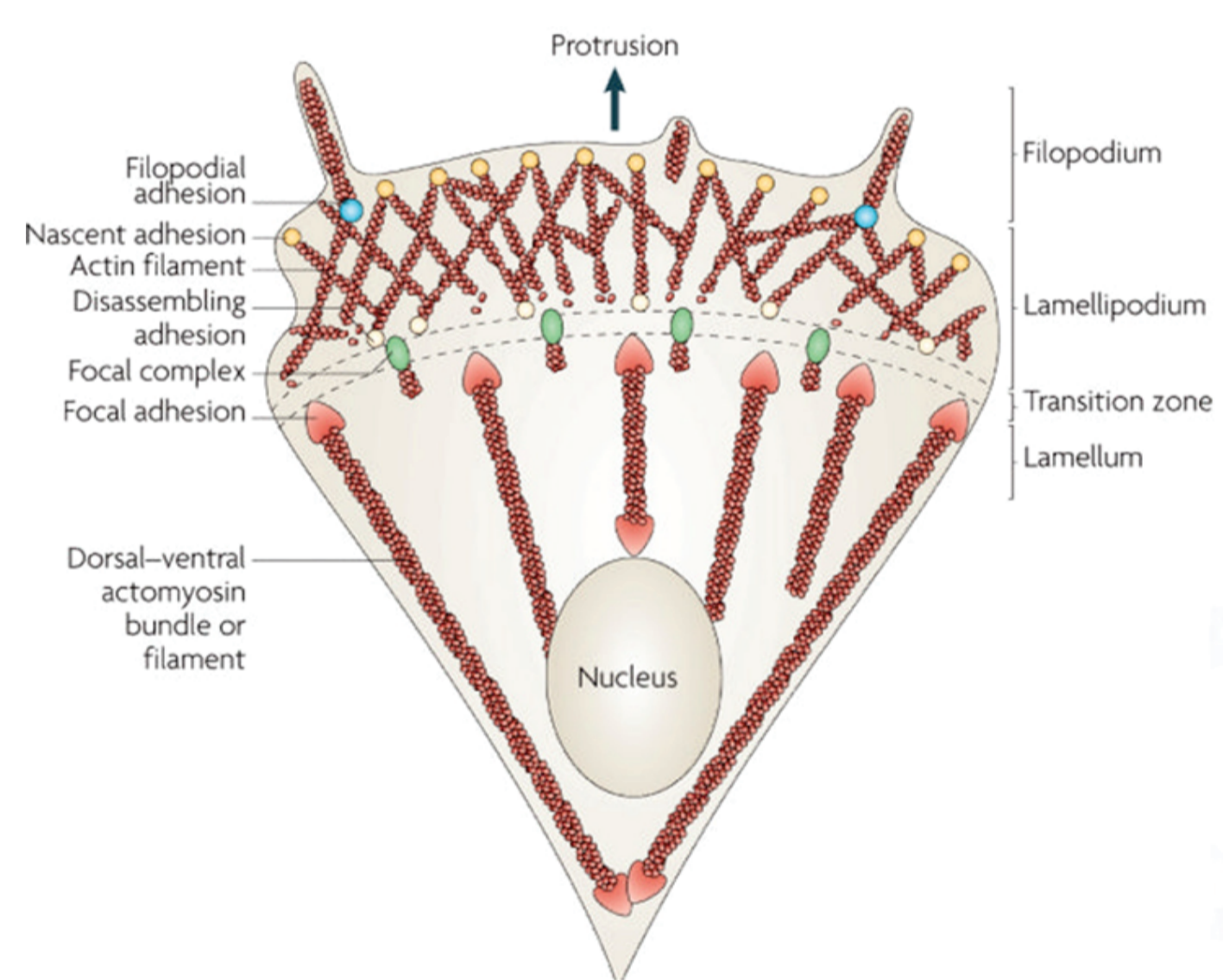
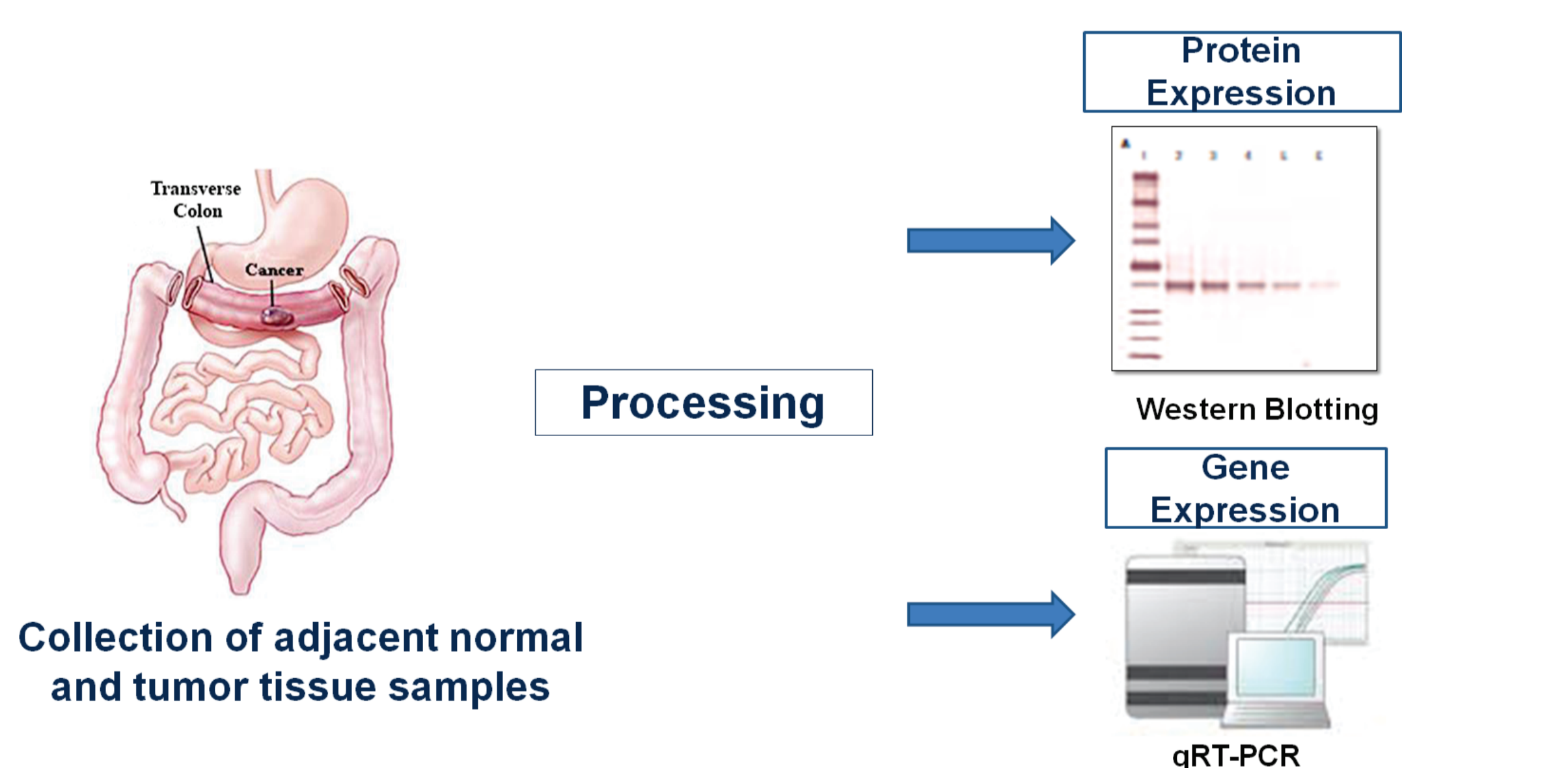


Figure 2- Schematic representation of the main elements of a migratory cell. (Parsons et al., 2010)

OBJECTIVE

Analyze the Cfl-1 expression profile on samples of CRC patients under different stages of the tumor progression.

METHODS



RESULTS

Table 1- Clinical Pathology Data

Age		Tumor Location		Patient's Total	
≤50	4 (9,30%)	Ascending Colon	25 (58,14%)	44	
>50	39 (90,7%)	Transverse Colon	3 (6,98%)		
Gender		Descending Colon	4 (9,30%)		
Female	24 (55,81%)	Sigmoid Colon	7 (16,28%)		
Male	19 (44,19%)	Rectum	4 (9,30%)		
Stage (AJCC* v.7)		Tumor Grade			
0	0 (0%)	Well Differentiated	2 (4,65%)		
I	5 (11,63%)	Moderately Differentiated	30 (69,77%)		
II	14 (32,56%)	Poorly Differentiated	4 (9,30%)		
III	23 (53,49%)	Mucinous Adenocarcinoma	7 (16,28%)		
IV	1 (2,32%)	Patient diagnosed with FAP**			
		Age	44 years old		
		Gender	Female		
		Stage (AJCC v.7)	IIB		
		Surgical Procedure	Total Colectomy with Ileostomy Surgery		

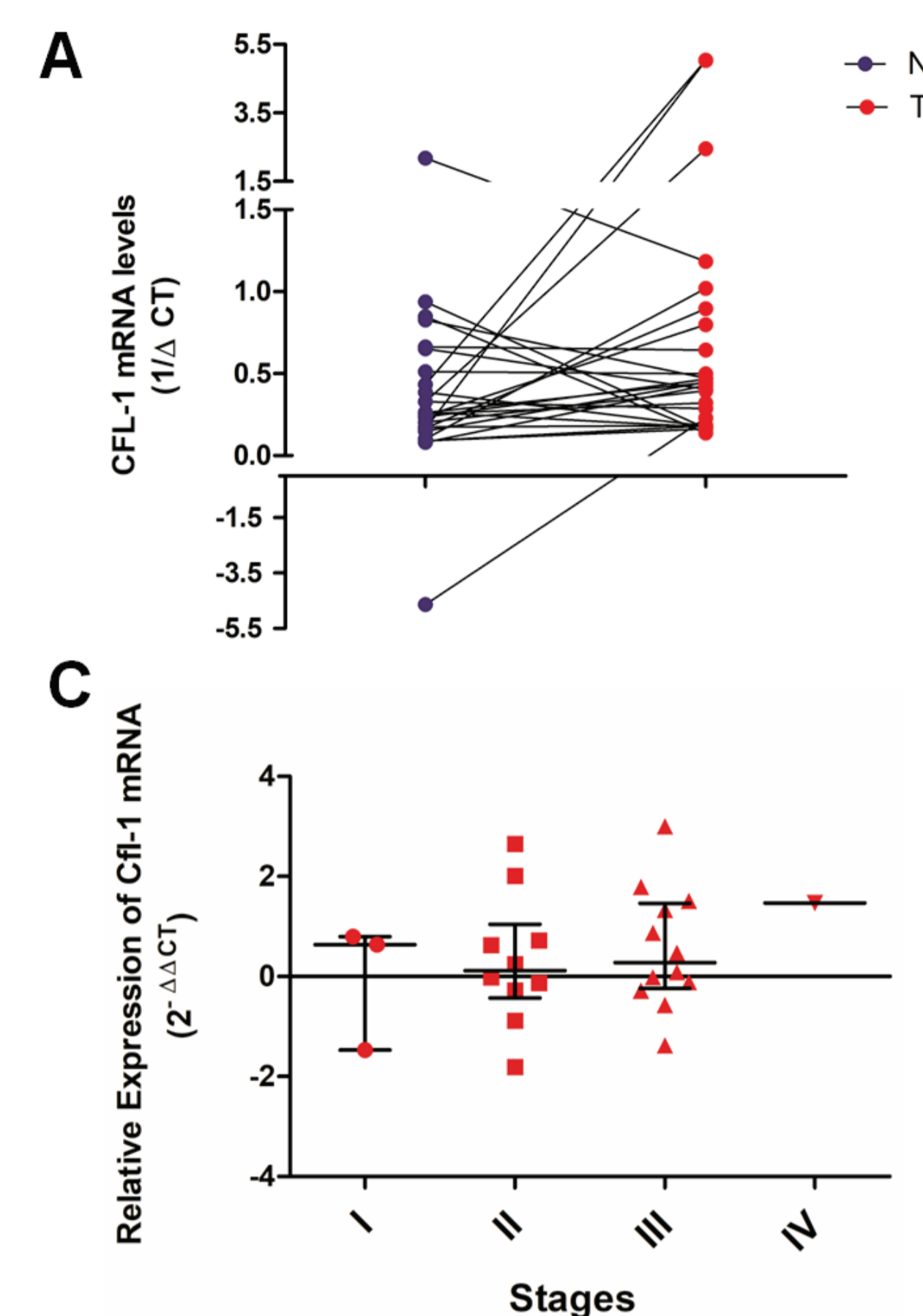


Figure 3- (A) Comparing of Cfl-1 mRNA expression of normal adjacent (NA) tissues and tumor tissues (T) samples from patients diagnosed with CRC. (B) Cfl-1 mRNA expression on tumor tissues and its corresponding normal adjacent tissues, median with interquartile are represented. Both analysis assessed by 1/ΔCT method. (C) Cfl-1 mRNA levels on tumor samples according to the stages of tumor progression, median with interquartile are represented, analysis assessed by 2^{-ΔΔCT} method. Housekeeping: β-actin. N=26.

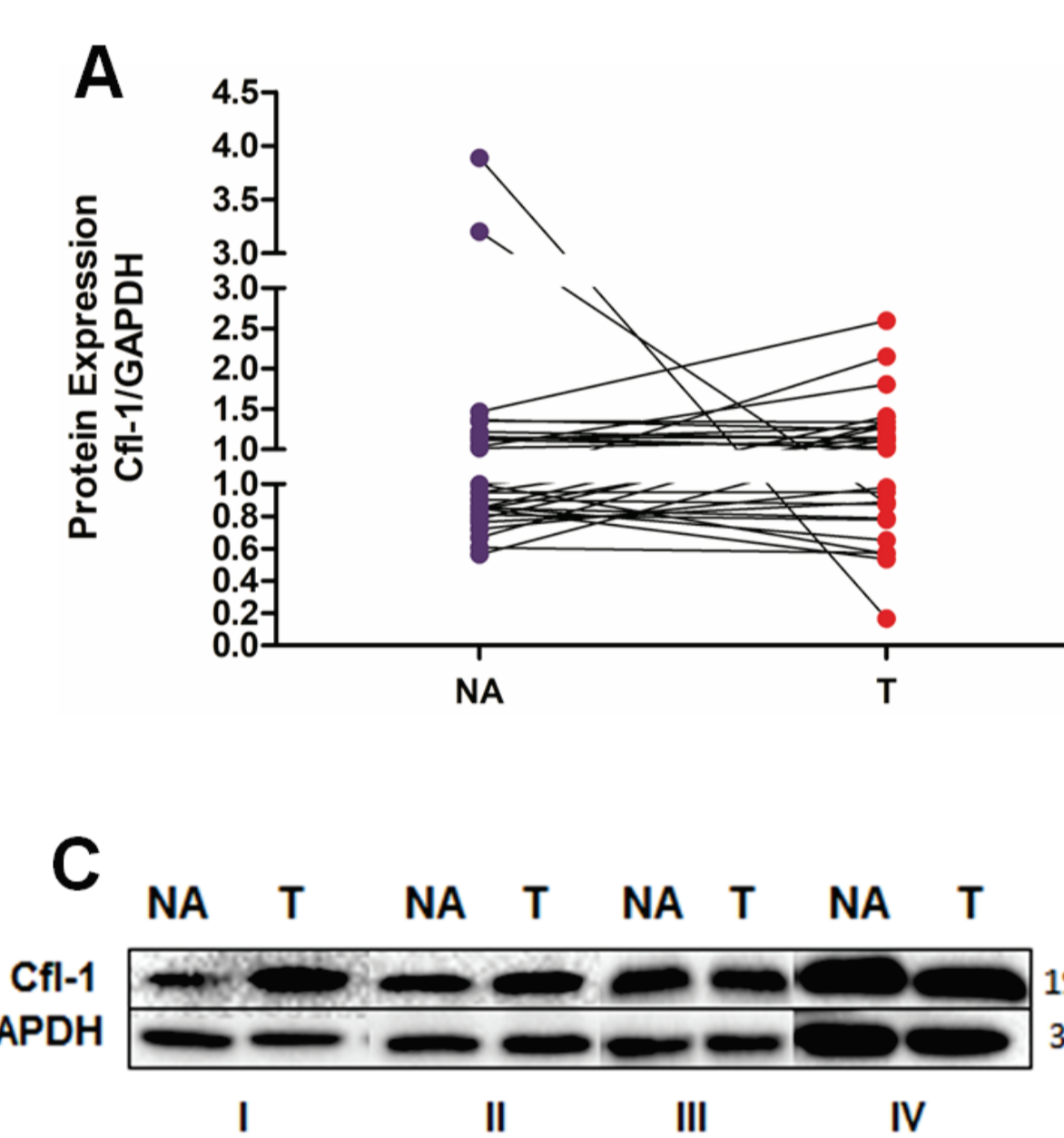


Figure 4- (A) Comparing of Cfl-1 protein expression of normal adjacent (NA) tissues and tumor tissues samples (T) from patients diagnosed with CRC. (B) Cfl-1 protein expression profile according to the stages of the tumor progression, median with interquartile are represented. N=30. (C) Analysis of normal adjacent (NA) and tumor tissue samples (T) under different stages of the tumor progression subjected to Western Blotting assay. Housekeeping: GAPDH.

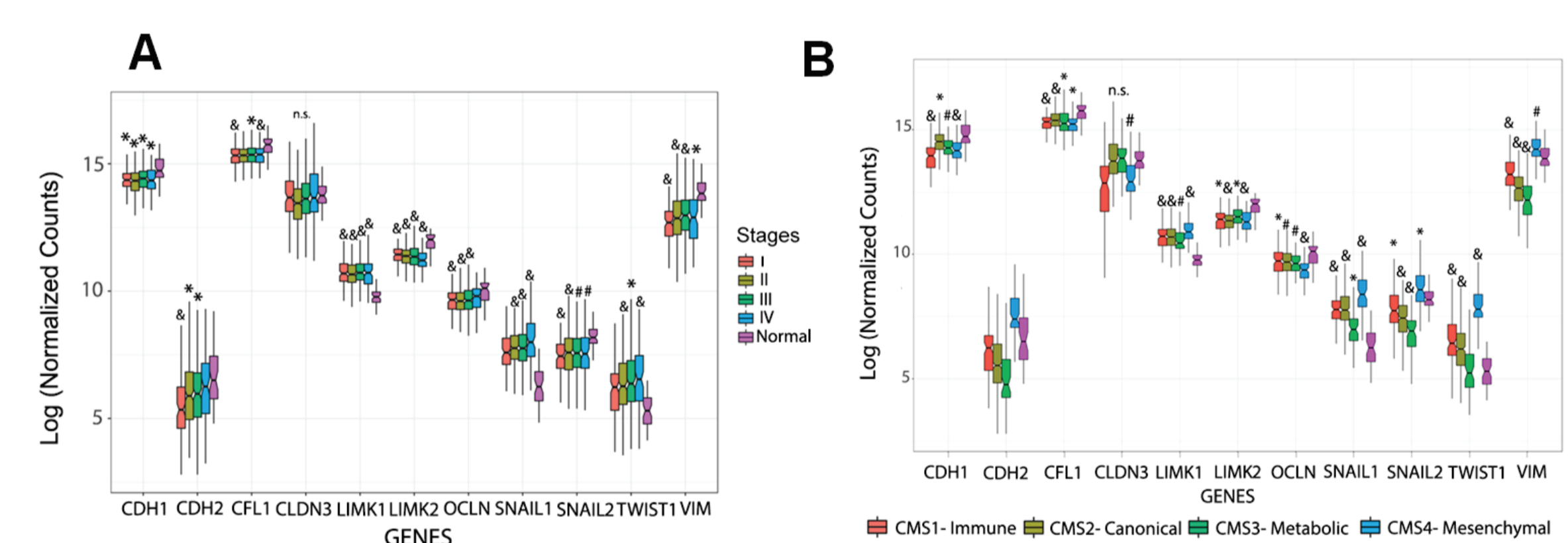


Figure 5- (A) Expression analysis of EMT genes and Cfl-1 signaling pathway regulators according to the CRC stages. (B) Expression analysis of EMT genes and Cfl-1 signaling pathway regulators according to the CRC subtypes. 622 tumor samples and 51 normal adjacent samples assessed. Statistical analysis tests: Wilcoxon rank sum and Bonferroni. * P<0,05; # P<0,001; & P<0,0001.

CONCLUSIONS

These results are not in accordance with previous studies, so we could suggest that on this type of tumor the Cfl-1 regulation might be occurring differently compared to others types of tumor. Datas of these previous studies bring forward indications that the actin cytoskeleton remodeling under Cfl-1 activity is determinant to migration and invasion events of tumor cells. Therefore, further analysis have to be done in order to identify the location and staining pattern of Cfl-1 at the CCR samples in situ and, thereby, to verify if this analysis are useful to identification of patients with a more aggressive tumor profile.

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