SALL2 expression in colon cancer progression and its association with AXIN2

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INTRODUCTION

SALL2 is a developmental transcription factor involved in the regulation of cell proliferation, migration, and survival. Massive data analyses of cancer versus normal tissues indicate that *SALL2* mRNA is significantly decreased in colorectal cancer **(CRC),** a cancer type characterized by hyperactivation of the Wnt pathway. Interestingly, our unpublished ChIP-seq analyses suggest that SALL2 regulates genes associated with the Wnt pathway, including the negative regulator AXIN2. Currently, there are no studies on the role of SALL2 in CRC.

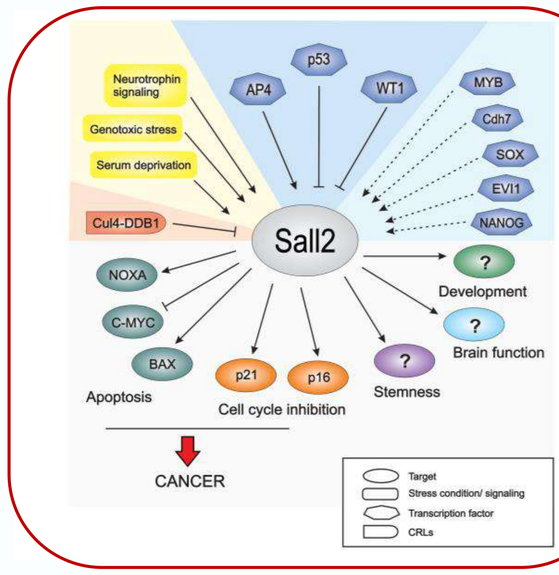


Figure 1- SALL2 regulation and function. Stress conditions activate SALL2. SALL2 regulates cell proliferation and apoptosis by targeting p21, p16, MYC, BAX and NOXA. In addition, SALL2 is involved in development, stemness and brain functions through unidentified targets.

RESULTS

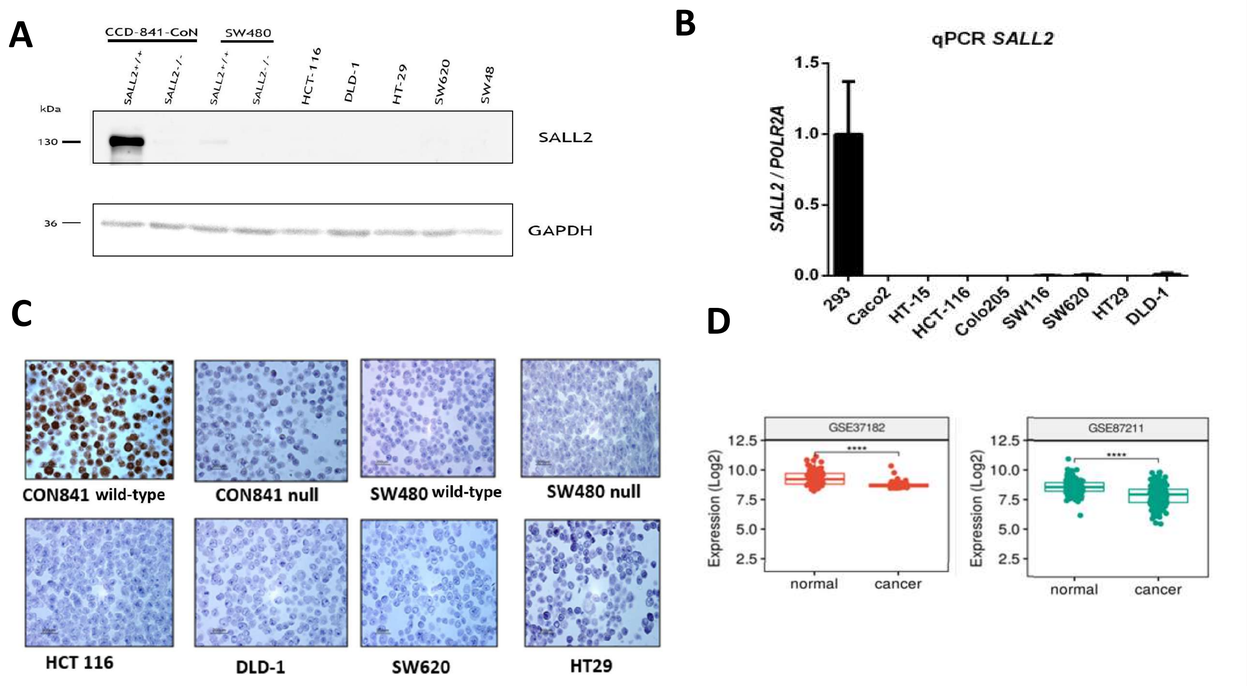
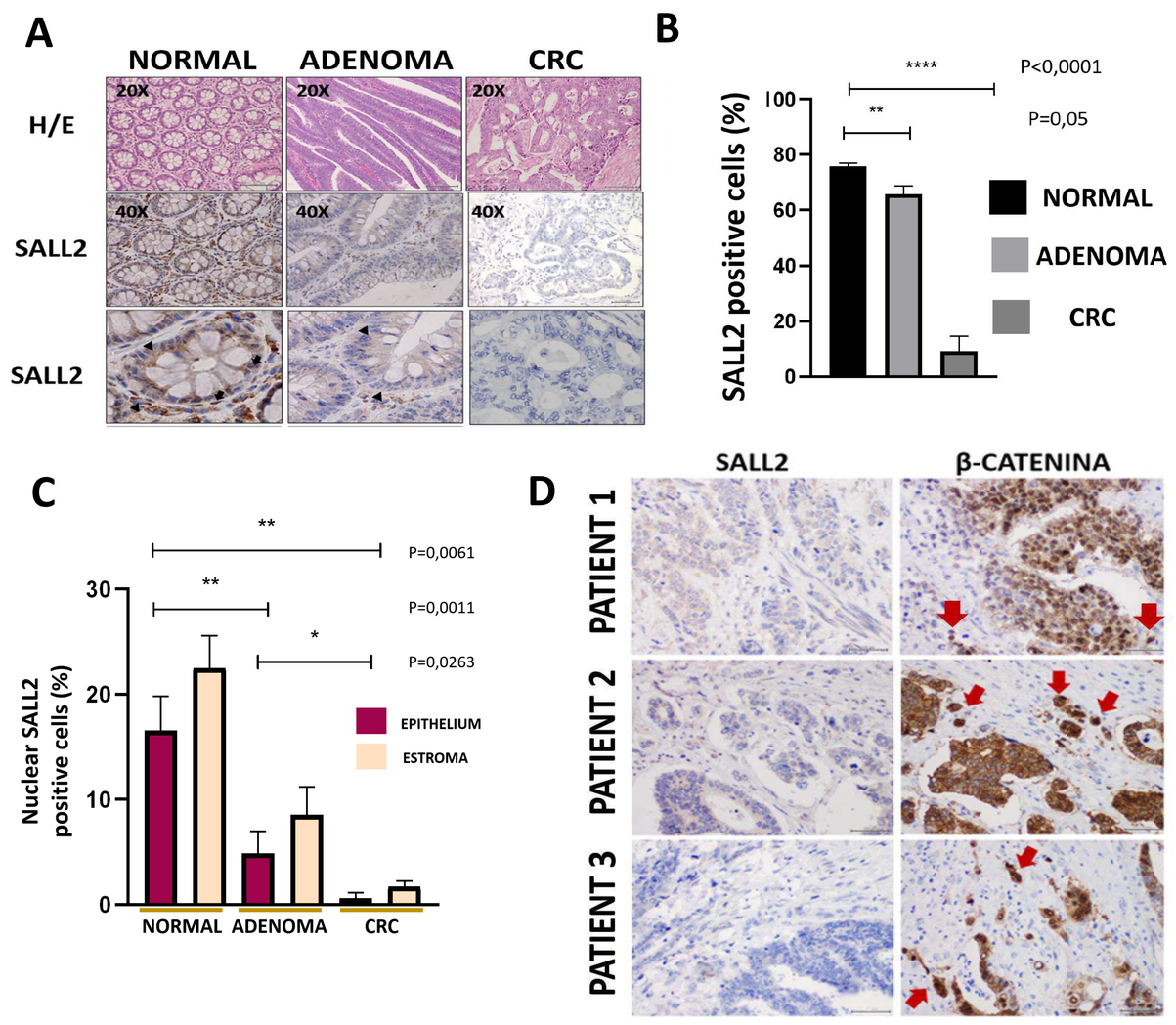


Figure 2- SALL2 expresses in CCD-841-CoN normal colon epithelial cells, but not in CRC cell lines. **(A)** SALL2 immunoblot, **(B)** SALL2 qRT-PCR **(C)** SALL2 Immunohistochemistry **(D)** Massive public data analysis using Limma in R studio with GSE37182 and GSE87211 studies.



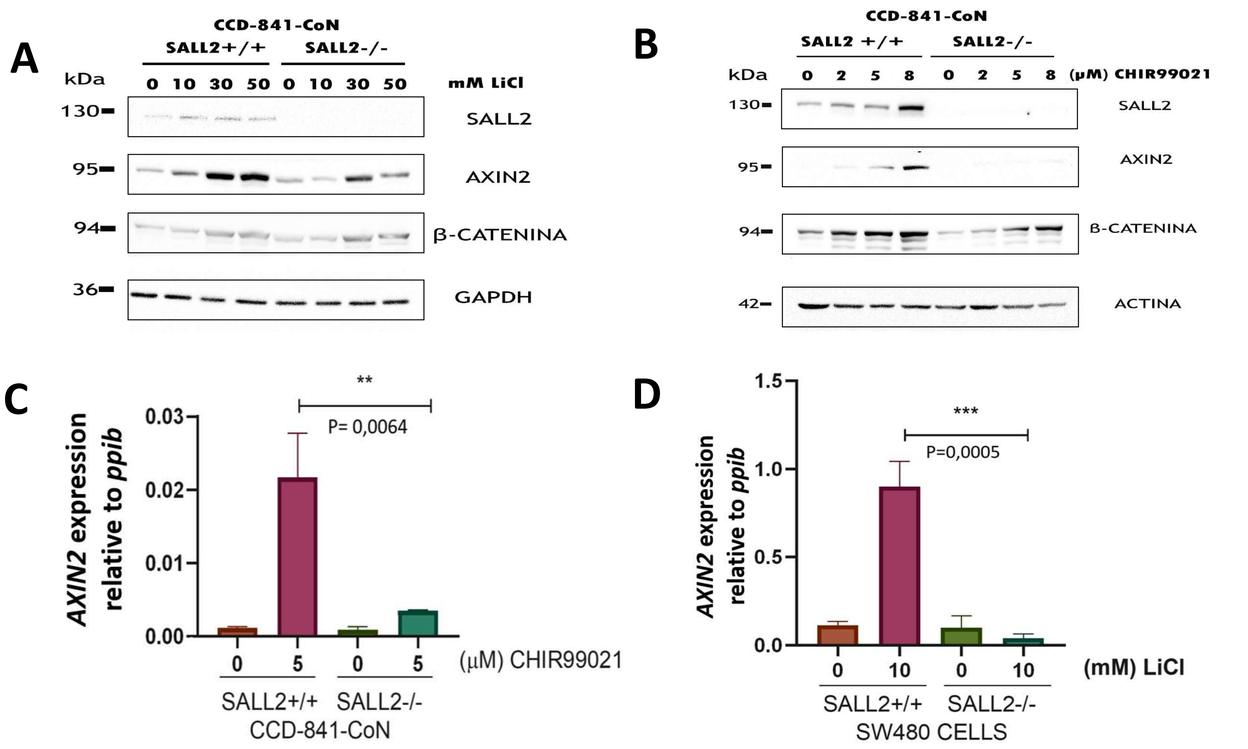


Figure 4. Positive correlation between SALL2 and AXIN2 expression under Wnt pathway activation. SALL2 and AXIN2 immunoblot from CCD-841-CoN cells treated with LiCl **(A)** and CHIR99021 **(B)**. qPCR for *AXIN2* mRNA in CCD-841-CoN treated with CHIR99021 **(C)**, and SW480 cells treated with LiCl **(D)**.

Figure 3. SALL2 expresses in the normal colon but decreases during CRC progression. A-B) *Tissue array* of 130 human samples from Guillermo Grant Bevanete's Hospital shows that SALL2 expresses in normal colon epithelium and stroma, decreases in adenoma, and is absent in CRC. **C)** The nuclear SALL2 expression decreases during progression to CRC. **D)** The absence of SALL2 in CRC correlates with β-catenin in the migratory front (red arrows).

CONCLUSIONS

Our study is the first to evaluate SALL2 protein expression in the colon epithelium and CRC progression. We show that SALL2 expresses in the stroma but decreases in CRC tissues. Besides, AXIN2 expression increases in a SALL2- dependent manner. Since AXIN2 is a negative regulator of the Wnt pathway, loss of *SALL2* could contribute to CRC progression.

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