SPRY2 AND RESPONSE TO FOLFOX/CAPOX IN METASTATIC *KRAS* MUTATED COLORECTAL CANCER

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Background

• **Chemotherapy** with fluoripyrimidine in combination with either oxaliplatin or irinotecan remains the mainstay of treatment for **metastatic colorectal cancer** (CRC) but their outcomes are mixed, with **no** clear validated **response predictors**.

• It is known that the docking/scaffold protein **SPRY2:**

1. Modulates the EGFR signaling pathway.
2. Regulates cellular apoptosis in response to DNA damage.
3. Is up-regulated in CRC, especially in the *KRAS* mutant status.

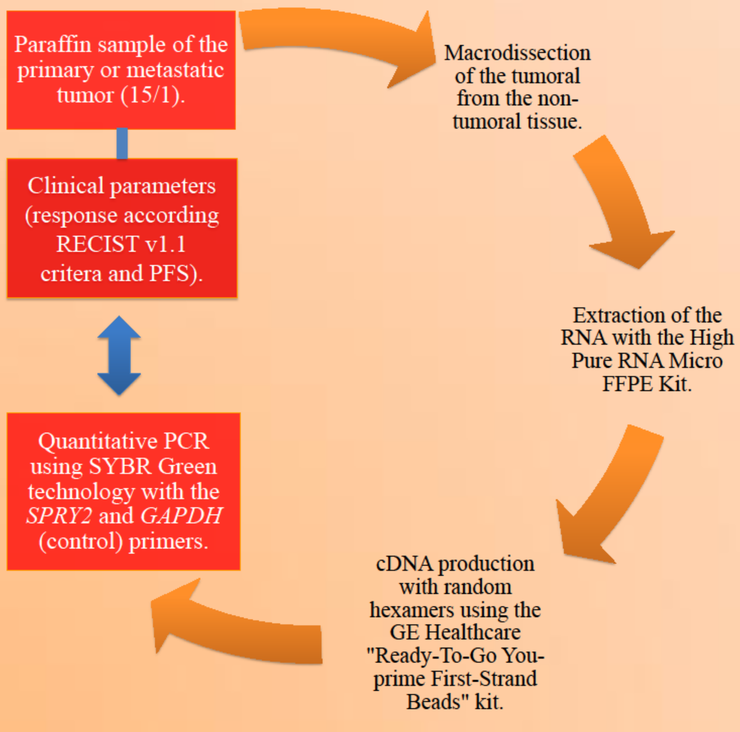
In this study we are going to assess **SPRY2 as a key determinant of response to standard chemotherapy in CRC.**

Methods

Retrospective study of metastatic CRC patients (16) harboring *KRAS* mutation.

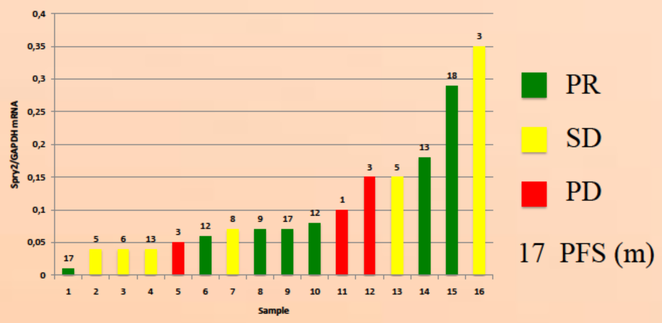
Treated in Institut Català d'Oncologia during the period of 2009-2013.

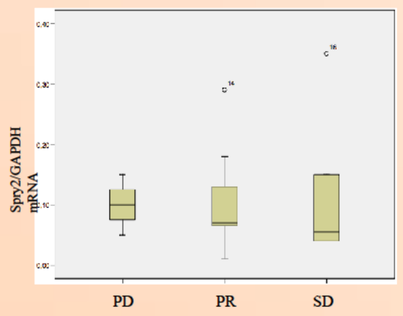
With fluoropyrimidine and oxaliplatin-based chemotherapy (FOLFOX or CAPOX) in the first or second line (10/6).



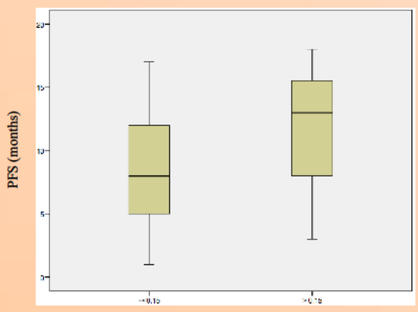
Results

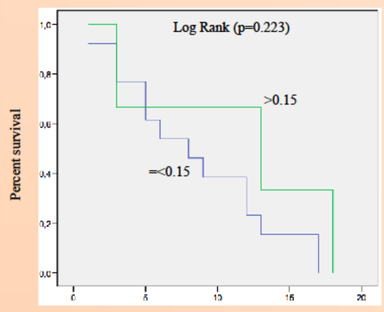
The best radiological response reached was partial response (PR) in 7 patients, stable disease (SD) in 6 patients and progression disease (PD) in 3 patients. The median of progression free survival (mPFS) was 8.5 months (IC95 [2-13]). The median of the expression of *SPRY2* (mRNA SPRY2/mRNA GADPH) was 0.07 with a rank of 0.01-0.35.



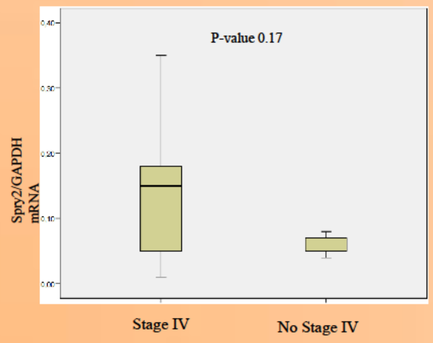


Most of them had levels of expression lower than 0.15 with a mPFS of 8 months but 3 patients had higher levels (2 PR and 1 SD with a mPFS of 13 months). Be mentioned that despite having low values of *SPRY2*, patients could achieve 38% of PR.

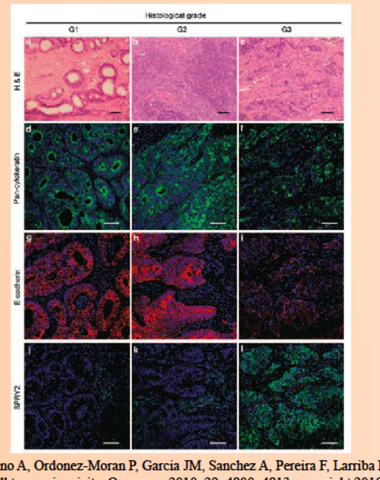




The 9 stage IV patients at diagnosis had a median of the expression of *SPRY2* of 0.15, higher than the 0.07 of the 7 patiens with localized disease at diagnosis.



As described in the study in colon cancer patients of Barbachano et al, SPRY2 is upregulated in undifferentiated high-grade tumors.



Reprinted by permission from Macmillan Publishers Ltd: [ONCOGENE] Barbachano A, Ordonez-Moran P, Garcia JM, Sanchez A, Pereira F, Larriba MJ et al. SPROUTY-2 and E-cadherin regulate reciprocally and dictate colon cancer cell tumourigenicity. Oncogene 2010; 29: 4800–4813, copyright 2010.

Conclusions

• As it has been described before, ***SPRY2* seems to be overexpressed in more aggressive CRC**: in the high-grade undifferentiated tumor in the study of Barbachano et al, and in the stage IV in our study.

• On the other hand, with this preliminar data with few patients, **we can not conclude that the level of expression of *SPRY2* is directly linked to tumor response** to FOLFOX / CAPOX in CRC. The study of more patients is currently on-going.

• The **role of *SPRY2* in cancer is complex**, orchestrating a multilayered regulatory system and mediating a crosstalk among different signaling pathways that remains to be further elucidated.

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