P – 315 **ΔNp73 and Δ133p53 in liquid biopsy as early diagnostic markers for colorectal cancer**

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Introduction: Colorectal cancer (CRC) was the most frequent cancer in both men and women in Spain in 2017. Nowadays, 20-30% of patients are diagnosed at an advanced

stage showing a worse prognosis and shorter overall survival. The early diagnosis of the disease would improve the outcome of these patients. Tumor-derived exosomes are emerging as mediators of tumor progression and modulators of metastasis. Hence, the content of these tumor-derived exosomes (mRNA, miRNA and/or proteins) may be used as early diagnostic and prognostic markers. Members of TP53 family translate into different variants with opposite functions. TP73 translates into TAp73 isoforms which show tumor suppressor functions and ΔTAp73 forms that lack the transactivation domain show protumoral activities. TP53 can translate into the variant Δ133p53, which is emerging as a variant with oncogenic functions. Here, we studied ΔNp73, TAp73, and Δ133p53 mRNA levels of serum-isolated exosomes from i) 29 healthy subjects, ii) 51 individuals with premalignant lesions (low and high-grade adenomas) and, iii) 43 CRC patients diagnosed at different stages of the disease. Our main goal was to determine the early diagnostic value of these markers.

Methods: Exosomes were isolated from the serum by subsequent ultracentrifugations and filtration. The quantification of exosomes was performed by a NanoSight NS500 instrument. RNA from exosomes was extracted using SeraMir^{TM} Exosome RNA Amplification kit (System Biosciences). cDNA was synthesized with the Transcriptor First-Strand cDNA Synthesis kit (ROCHE). qPCRs were performed with a LightCycler 2.0 instrument and Fast Start DNA Masterplus SYBR Green I kit (ROCHE). Expression levels were normalized with the exosome concentration. Statistical analysis of the differences in mRNA levels was performed by the Kruskal-Wallis and U-Mann Whitney tests. P-values ≤ 0.05 were considered statistically significant.

Results: ΔNp73 levels were higher in patients with premalignant lesions and CRC, although no significant differences were observed between both groups. Δ133p53 levels were significantly increased in CRC patients but there were no statistically significant differences between the healthy group and the premalignant lesion group. TAp73 mRNA content was negative for all groups.

Conclusion: Our preliminary data showed that ΔNp73 mRNA levels were already overexpressed in serum-isolated exosomes from patients with premalignant lesions and may support its use as an early diagnostic marker in colorectal cancer through liquid biopsy. To our knowledge, this is the first time that Δ133p53 mRNA levels in serum-isolated exosomes were analyzed in cancer, and specifically in CRC. Our preliminary data shows its possible usage as a diagnostic marker. Its is necessary to enlarge our CRC patients series to confirm our data. The identification through a liquid biopsy of early diagnosis markers for CRC may overcome the current handicaps of the fecal occult blood tests.