FEASIBILITY STUDY COMBINED WITH DIAGNOSTIC TECHNIQUES OF COLORECTAL CANCER SUCH AS ENDOSCOPY, SOLID BIOPSIES AND LIQUID BIOPSIES IN A MURINE MODEL

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INTRODUCTION

The 5-year survival rate for the CRC that is located at the time of diagnosis is 90%, but it can decrease to 68% if it is regionally compromised and to 10% if they are discovered with metastasis. This indicates the need for developing early diagnosis systems. Currently, techniques such as NGS or PCRq serve as support for new research related to the early diagnosis of CRC. The liquid biopsy opens a field of diagnosis and monitoring of the CRC.

OBJECTIVES

To demonstrate the feasibility combining different diagnostic techniques: Liquid biopsy, solid colonic tissue biopsy and endoscopic explorations in a murine CRC model.

MATERIAL AND METHODS

20 animals of type Rattus norvegicus, strain Pirc F344 / NTac-Apcam^{1137} , CRC model developed by RRRC (Rat Resource and Research Center, University of Missouri, Columbia, Missouri), were used in this study: 10 males of 246.6 ± 15.6 grams and 10 females of 162.9 ± 8 grams, all with 2 months of age. The procedure under inhalation anesthesia with Sevoflurane consisted of:

1. Extraction of blood by venipuncture of the lateral coxigeal veins using a 25G needle collected in EDTA tubes for subsequent plasma extraction once centrifuged to 3G for 5 minutes at 4º C.
2. Endoscopic examination using a 2.9 mm optical rigid cystourethroscopy with a total thickness of 5 mm, and a fiberscope of 7.5 Charr.
3. Extraction of the different findings found during the colonoscopy and a biopsy of healthy tissue, using a biopsy forceps through the working channel of the cystourethroscope, fixed in 4% formaldehyde.

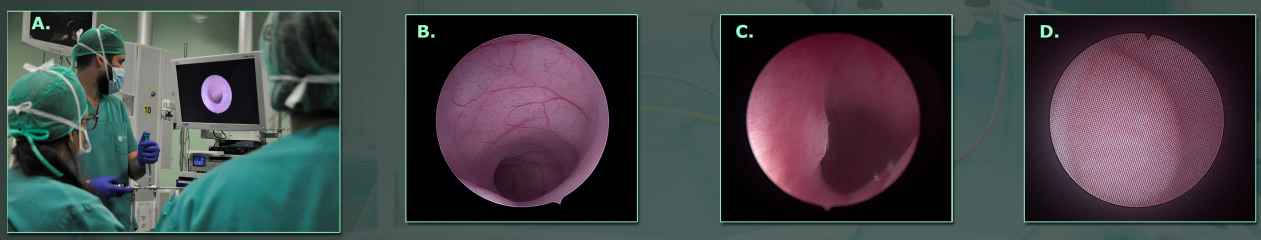

Figure 1. A. Exploration of descending colon by rigid endoscope. B. Healthy tissue in descending colon. C. Polyp in Descending Colon. D. Polyp in Transverse Colon close to splenic flexure, flexible fibroscope image.

RESULTS

30 findings were found along the descending colon and the most distal region of the transverse colon, and 3 polyps in ascending colon. 16 polyp's and 19 healthy's tissues samples were extracted without any perforation or iatrogenic problem. In the blood extractions, plasma volumes of approximately 450-500 microliters of plasma were recollected by extraction, divided into two aliquots, and frozen at -80ºC for subsequent molecular studies.

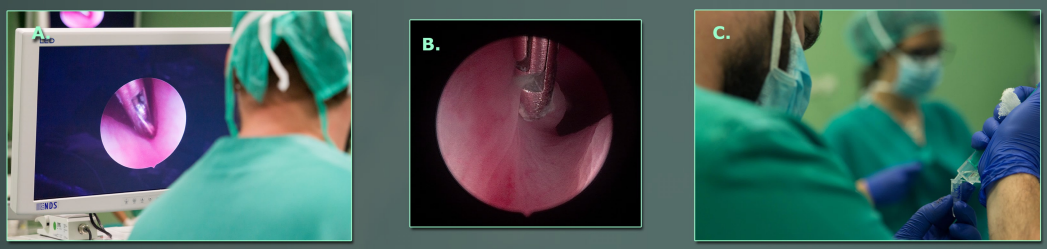

Figura 1. A. Procedure of extraction of biopsies in the colon. B. Biopsy of a polyp in descending colon. C. Collection of tissue samples after biopsy extraction.

CONCLUSIONS

This murine model of CRC allows the realization of studies combining these three techniques for the study of colorectal pathology being possible different molecular studies such NGS or PCRq for the disease's development and appearance. Using the equipment and the refinement techniques allow to develop the procedure in a suitable and safe way.

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REFERENCES

- Benedict M, Neto AG, Zhang X. Interval colorectal carcinoma: An unsolved debate. World J Gastroenterol. 2015;21(45):12735-12741. doi:10.3748/wjg.v21.i45.12735.

- Amos-Landgraf JM, Kwong LN, Kendziorski CM, Reichelderfer M, Torrealba J, Weichert J, Haag JD, Chen K-S, Waller JL, Gould MN, Dove WF. (2007) A target-selected Apc-mutant rat kindred enhances the modeling of familial colon cancer. Proc Natl Acad Sci USA 104(10):4036-4041.

- Irving AA, Yoshimi K, Hart ML, Parker T, Clipson L, Ford MR, Kuramoto T, Dove WF, Amos-Landgraf JM. (2014). The utility of Apc-mutant rats in modeling human colon cancer. Disease Models and Mechanisms, 7(11):1215-1225.

- Bartolí R, Boix J, Odena G. Colonoscopy in rats: An endoscoopic, histological, and tomographic study. World J Gastrointest Endosc. 2013 May 16;5(5):226-30.

- Chen R, Lai LA, Brentnall TA, Pan S. Biomarkers for colitis-associated colorectal cancer. World J Gastroenterol. 2016;22(35):7882-7891. doi:10.3748/wjg.v22.i35.7882.

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