

ID: 00784

Type: COMUNICACIÓN ORAL

Topic: 6. Liquid Biopsy

The potential use of lavages for endometrial and lung cancer diagnosis

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INTRODUCTION

Tissue biopsies are the most standardized sampling method to diagnose cancer, although it has proved to have limitations and is associated to discomfort and complications for the patients. To overcome these drawbacks, the use of liquid biopsies is currently a rapidly expanding field in translational cancer research. CTCs, circulating-free DNA (cfDNA) and exosomes are likely to contain a wide presentation of molecular data from multiple tumor and metastatic sites, whereas a mutational or pathological analysis of a single biopsy might represent a minor subclone or might even missed the tumor. Among liquid biopsies, proximal body fluids might contain a higher representation of the molecular alterations of the tumor compared to distant body fluids. Peritoneal lavages from endometrial cancer patients and pleural lavages from lung cancer patients are systematically collected during surgery but there is little data available about its potential as liquid biopsy sample.

M&M

For endometrial cancer determination, we analyzed KRAS mutations in paired surgical biopsy, blood and peritoneal lavage supernatants in a cohort of 10 early-stage endometrial carcinoma patients. Additionally, peritoneal lavages of 7 patients with other benign uterine pathology were screened as a control. Circulating-free DNA (cfDNA) of all biopsies was purified using an automatic extractor and mutations determined using a sensitive assay. Surgical biopsies were analyzed using a NGS platform. For lung cancer determination, we isolated exosomes from pleural lavage in a cohort of 5 lung cancer patients and 15 control patients. NanoString technique was used to evaluate 800 miRNAs.

RESULTS

The peritoneal lavages from patients with benign uterine pathologies were negative for KRAS mutations. Regarding the 10 endometrial cancer patients, 6 were stage Ia and 4 Ib. KRAS mutations were found in the hotspots G12X and G13X in the surgical biopsies of 4 patients. Although the standard peritoneal lavages were negative for cancer cells (negative cytologies), KRAS mutations were found in cfDNA isolated from the lavages in 3 patients, two stage Ia and one stage Ib. In contrast, only one patient presented KRAS mutations in blood. In all cases, the KRAS mutations found in cfDNA matched those in paired biopsies. The patient who presented the KRAS mutation in blood and peritoneal lavage progressed and died in less than 6 months. The pleural lavage was useful to isolate exosomes from both tumor and control patients. In all cases, expression of miRNAs was observed.

CONCLUSIONS

We have identified molecular alterations of endometrial and lung cancer in the cfDNA of peritoneal lavages and in the exosomes of pleural lavages, respectively. This finding opens the avenue to the use of proximal bodyfluids for the future implementation of a non-invasive method of diagnosis for endometrial and lung cancer.