Using Varsome Clinical as a tool for Next Generation Sequencing (NGS) studies of familial pancreatic cancer patients

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Introduction

Familial pancreatic cancer (FPC) is a genetic syndrome that increases the frequency of pancreatic ductal adenocarcinoma (PDAC), with an unknown genetic cause. Some PDAC cases carry inherited germline mutations that enhance their risk of developing pancreatic lesions. Therefore, our objective was to identify potentially pathogenic genetic variants carried by FPC patients that could be associated with the disease.

Material and methods

We selected a cohort of 16 patients, of whom 9 met the criteria of FPC syndrome, 1 had hereditary breast and ovarian cancer syndrome (HBOC) and 6 were classified as sporadic PDAC cases. Panel sequencing was performed using the Sureselect technology (Agilent). The tertiary analysis of data was performed using the Varsome Clinical platform and variants were filtered according to our criteria.

Results

Among the 16 patients, we found interesting variants in 8 of them (50%). 7 FPC cases were negative for the panel, as we did not find variants that met our criteria (43,75%). 88,89% were variants of unknown significance (VUS) and only 11,11% had a likely pathogenic predicted effect. We found that these variants affected genes such as *MLH1*, *MUTYH* or *MSH2* in patients with hereditary syndrome. Sporadic cases harbor variants in other genes such as *TERT*, *CDKN2A*, *ATM* and *POT1*.

Conclusions

Varsome Clinical is an easy-to-use platform for NGS data analysis with multiple possibilities and a powerful source of information about the variants of interest for the researcher.

The genetic basis of FPC can be explained in some cases by previously described genes such as mismatch repair (MMR) genes, but there are many cases that are still undetermined. Thus, further research in larger cohorts of patients is needed to determine the effect of VUS found in this study.

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