Proceedings International
Platinum Open Access Journal (ISSN 2668-6384)

Proceedings, Abstract
Volume 4, Issue 1, 2022, 6
https://doi.org/10.33263/Proceedings41.006

Genomic Profile of Pancreatic Ductal Adenocarcinoma Assessed by Deep Next Generation Sequencing of EUS-FNA Genomic DNA and cfDNA Samples †

Razvan Iacob [1,2,3,*], Andrei Sorop [1,2], Bianca Varzaru [2,3], Stefania Bunduc [2,3], Ioana Manea [2,3], Irma Csiki [1,2], Andreea Spiridon [1,2], Diana Constantinescu [1,2], Speranta Iacob [1,2,3], Gabriel Becheanu [1,2,3], Mona Dumbrava [2,3], Adina Croitoru [2,3], Simona Dima [2,3], Irinel Popescu [2,3], Cristian Gheorghe [1,2,3]

[1] Fundeni Clinical Institute, Bucharest, Romania
[2] Center of Excellence in Translational Medicine, Fundeni, Bucharest, Romania
[3] "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
* Correspondence: raziacob@gmail.com;
† Presented at 1st OncoHub Conference – Connecting Scientists for Next Generation Cancer Management (13-15 October 2021, virtual)

Received: 25.10.2021; Accepted: 5.02.2022; Published: 14.02.2022

Abstract: The use of cfDNA for genomic evaluation of PDAC could be of great value in assessing the genetic profile of pancreatic ductal adenocarcinoma in non-resectable cases. The aim of our study was to assess the PDAC genomic profile using targeted deep next-generation sequencing of defined mutation hot-spots in two different DNA templates of PDAC patients - gDNA from EUS-FNA samples and cfDNA, respectively. Genomic profile was assessed in 20 patients by targeted deep next-generation sequencing (NGS) using paired tumor gDNA and plasma cfDNA. Next-generation sequencing was conducted using Illumina NextSeq 500 platform and an AmpliSeq DNA Hotspot Custom Assay, optimized for cfDNA samples, comprising 1284 mutations from 40 genes relevant for PDAC. The mean number of functionally significant variants/sample was 32.2 ± 9.8 for gDNA and 28.6 ± 9.9 for paired cfDNA, respectively. Variant analysis has indicated 27 deleterious germline mutations - 25 missense, one frameshift mutation in PALB2 gene, and one in-frame deletion of CFTR, with excellent concordance between gDNA and cfDNA. The most frequent pathogenic germline variants detected were SYNE1 rs214976 (75%), ERBB2 rs1058808 (85%), and TP53 rs1042522 (90%). Furthermore, 60 pathogenic somatic mutations were detected in our cohort, out of which 26 were not previously described. KRAS (G12R, G12D, or G12V) somatic variants were detected in 75% of cases, with only one pathogenic variant/case. Overall concordance between gDNA and cfDNA NGS sequencing was 92.4% for germline variants and 44% for somatic variants. The genes harboring the highest number of deleterious variants were SYNE1 and TP53.In our study of PDAC patients, EUS-FNA gDNA and cfDNA provided excellent concordance for germline but lower concordance for somatic variants. In our PDAC cases cohort, the NGS panel detected a higher number of deleterious variants in Syne1 and TP53 genes.

Keywords: pancreatic ductal adenocarcinoma; deep next-generation sequencing; liquid biopsy;

Funding

Not applicable.

Acknowledgments

Not applicable.

Conflicts of Interest

The authors declare no conflict of interest.