

cfDNA variants profile analysis in a High Grade Serous Ovarian Cancer patient for the search of prognostic biomarkers

Arthur Schenider Oliveira Felipe^{1,2}, Maria Vitória Costa Felipe^{2,3}, Álvaro Percínio Costa^{2,4}, Diogo Gomes da Costa^{1,2}, Thalia Rodrigues de Souza Zózimo², Ramon de Alencar Pereira², Suelen Peixoto Marinho de Deus⁵, Débora Cristina de Freitas Batista^{5,6}, Paulo Guilherme de Oliveira Sallles^{2,5}, Fábio Ribeiro Queiroz², Letícia da Conceição Braga^{1,2}

¹Universidade Federal de Minas Gerais/Instituto de Ciências Biológicas, Belo Horizonte/Minas Gerais, ²Instituto Mário Penna, Núcleo de Ensino, Pesquisa e Inovação, Belo Horizonte/Minas Gerais, ³Faculdade de Minas - FAMINAS, Belo Horizonte/Minas Gerais, ⁴Programa de Pós-graduação de Ciências Aplicadas à Cirurgia e à Oftalmologia, Faculdade de Medicina, Universidade Federal de Minas Gerais, MG, Brazil., ⁵Instituto Mário Penna, Hospital Luxemburgo, Belo Horizonte/Minas Gerais, ⁶Programa de Pós-graduação em Ginecologia, Faculdade Medicina de Botucatu, UNESP, Botucatu/SP.

INTRODUCTION

Ovarian cancer (OC) is the leading cause of death among gynecologic malignancies. This disease is subdivided into different subtypes, of which the High Grade Serous Ovarian Cancer (HGSOC) is the most aggressive (Fig. 1).



Figure 1. Percentage of deaths according to OC subtypes. HGSOC accounts for about 70% of all the death cases of ovarian cancer.

HGSOC is characterized by an elevated mutational burden. Those mutations can affect processes that influence tumor aggressiveness and, consequently, disease prognosis and treatment response (Fig. 2).

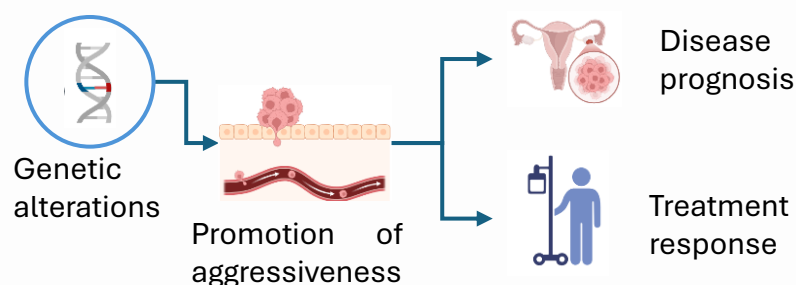
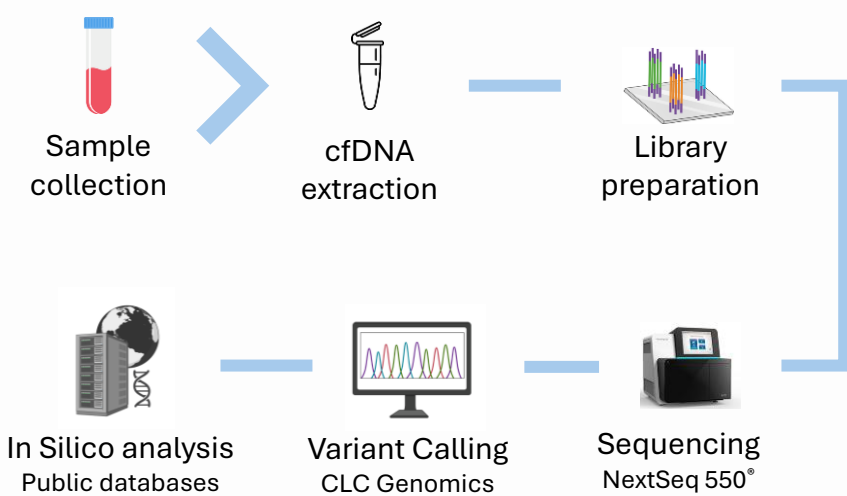


Figure 2. Schematic figure of the effects of mutations in disease progression and treatment.

OBJECTIVE

This study aims to identify genetic alterations that can serve as predictive or prognostic biomarkers for HGSOC.

METHODS



RESULTS AND DISCUSSION

The patient presented advanced HGSOC (IIIC/IVA), G3 histopathological grade, hepatic metastasis, lymphovascular, and capsule invasion. Chemotherapy resulted in a decrease in Ca-125 levels (Fig. 3).

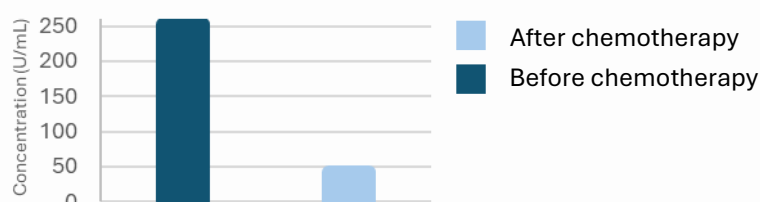


Figure 3. Comparison of Ca-125 levels before and after chemotherapy treatment. Before treatment: 253,70 U/mL, after treatment: 42,40 U/mL

81 unique genes with variants classified at least as possibly damaging by PolyPhen score (≥ 0.5) or with pathogenic/likely pathogenic clinical significance were identified through VEP. Among those 81, we selected 39 genes directly related to the phenotype of ovarian cancer in VarElect (Fig. 4), with the most evident being *WT1* (Fig. 5).

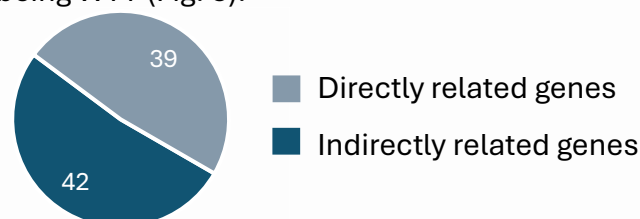


Figure 4. Distribution of the 81 unique genes identified on VEP. 39 genes were directly related to “ovarian cancer” phenotype by VarElect.

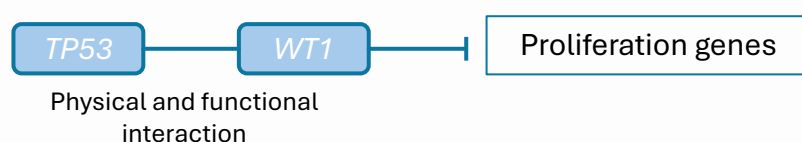


Figure 5. Interaction between *TP53* and *WT1*. The gene most related to ovarian cancer that was found in this patient, according to VarElect.

Furthermore, Analysis in the STRING database for those 39 genes revealed that *WT1*, *PLAU*, *SMARCB1*, *HNF1A*, *LRPPRC*, *ELP1*, *SOX3*, *SP2-AS1*, and *TET2* were mainly related to pathways of transcriptional regulation. While *PLAU*, *COLGALT1*, *LTBP1*, *LOXL1*, *TNXB*, and *ADAM19* were genes related to extracellular matrix (ECM) remodelling (Fig. 6).

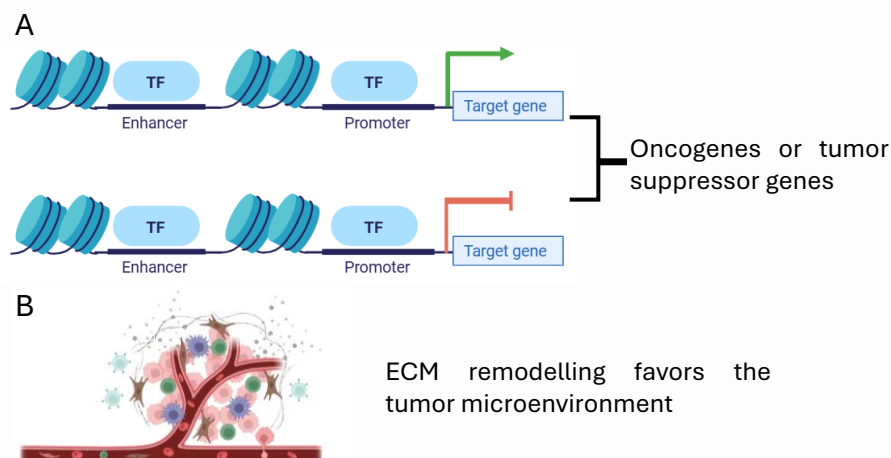


Figure 6. Importance of the main altered pathways observed for tumor development. A) transcriptional regulation. B) EMT remodelling and tumor microenvironment.

CONCLUSION

Studies are in progress to better understand and relate the variant profile of this patient with clinical observations. However, the preliminary results suggest that cfDNA could screen for tumor-related variants effectively.

ACKNOWLEDGEMENTS

We are grateful to all the patients who agreed to participate in this study. We are also grateful to the Brazilian Funding Agencies of the Ministry of Health (PRONON: NUP 25000.020618/2019-35), the Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG; APQ-02564-22), and the Rede Mineira de Pesquisa Translacional em Oncologia (RED 00059-23).

REFERENCES



ACKNOWLEDGMENTS