#375 NETOSIS BIOMARKERS LEVELS IN HIGH-GRADE SEROUS OVARIAN CANCER PATIENTS' BIOFLUIDS: POTENTIAL ROLE IN DISEASE DIAGNOSIS AND MANAGEMENT

[1]Sarai Tomás-Pérez*, [2,3]Julia Oto, [1,4]Aitor Cuadros-Lozano, [2]Raquel Herranz, [1,4]Cristina Aghababyan, [1]Eva González-Cantó, [1,2]Bárbara Andrea Mc Cormack, [2]Fernando Cana, [2]María Castaño, [2]Isabel Alemán-Cabrera, [5]Nuria Santonja, [6]Alejandro Herreros-Pomares, [7,8,9]Antoni Llueca, [3]Martin Götte, [1,5]Josep Marí-Alexandre, [2]Pilar Medina, [1,4,10]Juan Gilabert-Estellés. *[1]Research Laboratory in Biomarkers in Reproduction, Obstetrics and Gynecology, Research Foundation of the General University Hospital of Valencia, Valencia, Spain; [2]Hemostasis, Thrombosis, Arteriosclerosis and Vascular Biology Research Group, Medical Research Institute Hospital La Fe, Valencia, Spain; [3]Department of Gynecology and Obstetrics, University of Münster, Münster, Germany; [4]Department of Obstetrics and Gynecology, General University Hospital of Valencia Consortium, Valencia, Spain; [5]Department of Pathology, General University Hospital of Valencia Consortium, Valencia, Spain; [6]Gynaecological Oncology Laboratory, Department of Oncology, KU Leuven, Leuven, Belgium; [7]Department of Obstetrics and Gynecology, General University Hospital of Castellon, Castellón, Spain; [8]Multidisciplinary Unit of Abdominal Pelvic Oncology Surgery (MUAPOS), General University Hospital of Castellon, Castellón, Spain; [9]Department of Medicine, University Jaume I, Castellón, Spain; [10]Department of Pediatrics, Obstetrics and Gynecology, University of Valencia, Valencia, Spain*

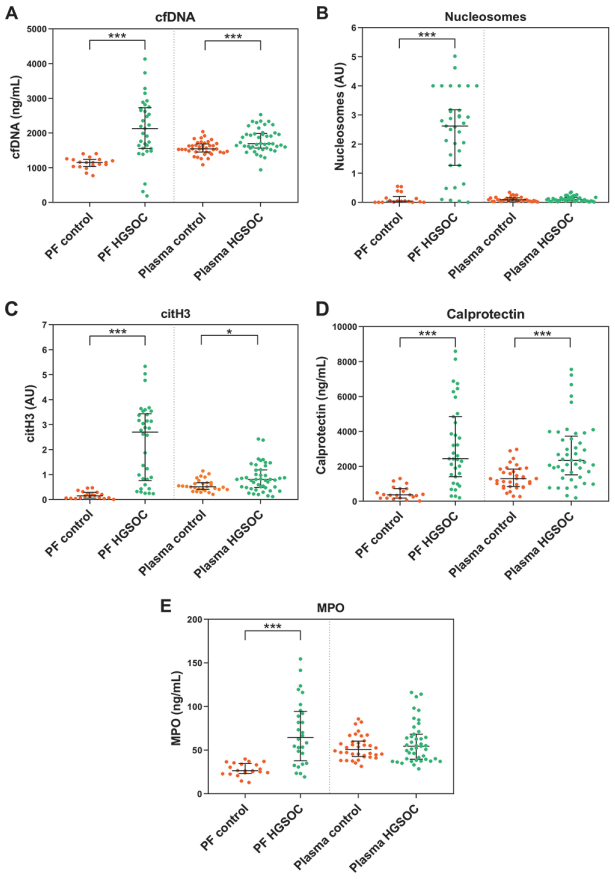
10.1136/ijgc-2023-ESGO.776

Introduction/Background High-grade serous ovarian cancer (HGSOC) is the most lethal gynecological malignancy, partially due to its spread through the peritoneal cavity. Neutrophils are involved in cancer progression by neutrophil extracellular traps formation (NETosis). NETosis has been proposed as a pre-requisite for the establishment of omental metastases in early stages HGSOC. However, its role in advanced stages remains unknown. Therefore, we aimed to characterize a NETosis biomarker profile in biofluids from patients with advanced HGSOC.

Methodology Five biomarkers of NETosis were quantified in plasma and paired peritoneal fluid (PF) samples of 45 patients and 40 control women: cell-free DNA (cfDNA), nucleosomes, citrullinated histone 3 (citH3), calprotectin and myeloperoxidase with specific kits. DNaseI activity was measured with the single radial enzyme-diffusion assay. A NETosis score was created to consider the joint behavior of NETosis biomarkers levels in PF.

Results Compared to control women, HGSOC patients presented a higher concentration of cfDNA, citH3 and calprotectin in plasma, and of all NETosis biomarkers in PF (figure 1). DNaseI was not responsible for the cfDNA increase. These biomarkers showed a strong ability to differentiate both groups, mainly in PF. Interestingly, neoadjuvant treatment (NT) seemed to reduce NETosis biomarkers mainly systemically (plasma) compared to the tumor environment (PF). Our NETosis score allowed to clearly differentiate HGSOC from control women employing a cut-off value of 23% (NETosis score >23 corresponds to HGSOC patients).

Conclusion NETosis biomarkers are present in the tumor environment of advanced HGSOC patients, which might contribute to the progression of HGSOC in advanced stages. Plasma cfDNA and calprotectin could represent low-invasive surrogate biomarkers for HGSOC. NT modifies NETosis biomarkers mainly at the systemic level, but its effect is rather limited in the tumor environment. We have developed a NETosis score that allows the discrimination of HGSOC patients from controls.



Abstract #375 Figure 1 NETosis biomarkers in peritoneal fluid (PF) and plasma samples of patients with high-grade serous ovarian cancer (HGSOC) (n=35 and n=45, respectively) and control women (n=21 and n=40, respectively). (A) cell-free DNA (cfDNA). (B) Nucleosomes. (C) citrullinated histone 3 (citH3). (D) Calprotectin. (E) Myeloperoxidase (MPO). AU, arbitrary units. *** p<0.001; * p<0.05; Mann-Whitney U test.

Disclosures This research was funded by the 'Instituto de Salud Carlos III Fondo Europeo de Desarrollo Regional' (PI20/00075, PI22/01872) and the 'Fundación para la Investigación del Hospital General Universitario de Valencia' (FIHGUV Awards 2021). S. T.-P. is supported by pre-doctoral a grant from the 'Junta Asociada Provincial de Valencia de la Asociación Española Contra el Cáncer (AECC)'; J. O. is supported by post-doctoral a grant from the 'Alexander von Humboldt Foundation'; B. A. M.-C. is supported by a post-doctoral grant from the 'Sociedad Española de Trombosis y Hemostasia (Prime SETH), R. H. is supported by a pre-doctoral grant from the 'Instituto de Salud Carlos III' (FI21/00171); E. G.-C. and I. A.-C. are supported by pre-doctoral grants from the 'Generalitat Valenciana' (ACIF/2020/216 and ACIF/2021/192, respectively). A. H.-P. is supported by a post-doctoral Marie Sklodowska-Curie grant (No. 101064216).