Methods The American Association for Cancer Research’s (AACR) Project Genomics Evidence Neoplasia Information Exchange (GENIE) database version 13.1 was queried via cBioPortal (http://genie.cbioportal.org) for the following gynecologic tumors: epithelial ovarian, sex-cord stromal, germ cell, endometrial, uterine sarcoma, cervical and vulvar/vaginal tumors. PGV frequencies of 27 HRD genes were descriptively reported among these tumors: ATM, ARID1A, ATRX, BRCA1, BRCA2, BARD1, BRIP1, BLM, BAP1, CHEK1, CHEK2, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCL, MRE11, NBN, PALB2, RAD50, RAD51, RAD51B, RAD51C, RAD51D, WRN.

Results A total of 13,312 tumors from 12,804 patients were included for analysis. At least one PGV in an HRD gene was found in 29.6% (3946/13,312) of all samples analyzed, with the highest frequency observed in endometrial tumors (2156/5087, 42.4%), uterine sarcomas (196/704, 27.8%), and epithelial ovarian tumors (1402/6052, 23.2%). There were also substantial rates of HRD PGVs in cervical and vulvar/vaginal tumors, and comparatively lower rates among germ cell and sex cord/stromal tumors (table 1). Across all tumors, HRD genes with the highest frequencies of PGVs were ARID1A (19.6%), BRCA1 (3.9%), BRCA2 (3.7%), and ATM (3.7%).

Conclusion/Implications NGS data demonstrate a substantial rate of somatic PGVs in HRD genes across most types of gynecologic tumors analyzed. These data suggest the need to expand routine functional HRD status assessment beyond epithelial ovarian tumors, and also suggest the need for clinical trials evaluating the efficacy of HRD targeting agents in these cancers.

Abstract PR002/#853 CATECHOLAMINES PROMOTE OVARIAN CANCER PROGRESSION THROUGH SECRETION OF CXC-CHEMOKINES

Introduction Catecholamines such as adrenaline (epinephrine) and noradrenaline (norepinephrine) are hormones that play a critical role in the body’s ‘fight or flight’ response, which is the physiological response to stress. Considerable evidence has accumulated in the last decade to support the notion that chronic stress is closely related to the growth, metastasis, and angiogenesis of ovarian cancer. The purpose of this study was to identify factors that increase the progression of ovarian
cancer and to determine the possibility of inhibiting ovarian cancer progression using novel therapeutics.

Methods In this study, we analyzed the conditioned media in SKOV3 ovarian cancer cell line treated with catecholamine to identify secreted proteins responding to chronic stress.

Results We observed that epinephrine and norepinephrine enhanced the secretion and mRNA expression of CXC-chemokines (CXCL1, 2, 3, and 8). Neutralizing antibody to CXCL8 and CXCL8 receptor (CXCR2) inhibitors significantly reduced catecholamine-mediated invasion of SKOV3 cells. Finally, we found that the concentration of CXCL1 and CXCL8 in the plasma of ovarian cancer patients increased with stage progression.

Conclusion/Implications Therefore, not only can CXCL1 and CXCL8 be used as diagnostic markers for ovarian cancer, but their inhibition also holds promise as a potential therapeutic option for suppressing ovarian cancer progression. Taken together, these findings suggest that stress-related catecholamines may influence ovarian cancer progression through the secretion of CXC-chemokines.