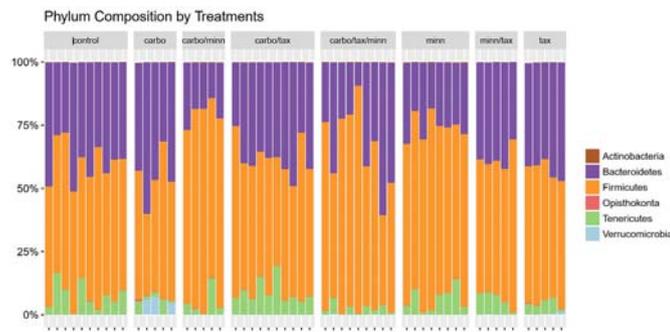


emergence of Verrucomicrobia. Further studies are underway to delineate the role of the microbiome observed.



doi:10.1016/j.ygyno.2019.03.107

Poster #3

Whole genome CRISPR/Cas9 screen identifies established and novel genes required for ovarian cancer dissemination

L.J. Wheeler, Z.L. Watson, T.M. Yamamoto, K.D. Sullivan, B.G. Bitler. *University of Colorado, Denver, Denver, CO, USA*

Objectives: A majority of high-grade serous ovarian cancers (HGSOC) arise from the exfoliation of transformed cells from the fimbriated end of the fallopian tube, indicating that these cells must escape anoikis to disseminate. Our aim was to identify novel genes and pathways critical for HGSOC dissemination.

Methods: We performed a CRISPR/Cas9 whole genome screen of HGSOC cells grown in adherent and suspension settings. 19,050 genes were targeted with at least 6 guide RNAs (gRNA) per gene totaling 123,411 gRNAs. We conducted principal component and differential gRNA expression analyses, as well as Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway and gene ontology (GO) analyses. We completed next generation sequencing of cells grown in adherent and suspension (RNA-seq). Known databases, including Protein Atlas, Oncomine, and The Cancer Genome Atlas, were utilized to refine gene list. We validated a subset of candidate genes, using small hairpin RNA (shRNA) knockdown and cell viability studies. Student t-test was used with threshold of < 0.05 for significance.

Results: CRISPR/Cas9 screen of cells grown in adherent compared to suspension settings identified 15,636 differentially expressed guide RNAs (gRNAs) (adj. $p < 0.05$), mapping to 11,571 genes. 3,395 genes had ≥ 2 targeting gRNAs, suggesting greater significance. RNA-seq analysis of the cells grown in adherent compared to suspension setting identified 804 differentially regulated genes ($p < 0.0001$).

CRISPR/Cas9 and RNA-Seq overlap analysis found 444 genes, representing a 3.2-fold enrichment. Of these genes, 108 had ≥ 2 gRNAs with similar directionality. KEGG pathway analysis of these 108 genes revealed enriched pathways including dorso ventral axis formation (NOTCH signaling), TGFbeta and calcium signaling. GO for biological processes showed enrichment for regulation of cell differentiation and positive regulation of development. In two independent ovarian cancer datasets, Oncomine analysis of the 108 genes revealed a significant enrichment in metastatic associated genes. Utilizing The Protein Atlas, 13 genes predominantly expressed in ovarian cancer were selected for further validation and elucidation of their role in anoikis. All 13 genes were significantly upregulated in suspension cells.

Cross-referencing the 108 genes with TCGA we found the expression of eight genes were significantly correlated with overall survival (Log Rank, $p < 0.05$). Notably, most had not been previously correlated with survival.

Conclusions: CRISPR/Cas9 and RNA-seq uncovered numerous regulators of anoikis escape. Known pathways, including NOTCH and TGFbeta were identified, increasing confidence in our findings. We also found novel regulators of anoikis escape that correlated with overall survival and metastatic disease. This genomic-based endeavor highlights potential new markers and therapeutic targets in HGSOC dissemination.

doi:10.1016/j.ygyno.2019.03.108

Poster #4

Complications and costs of minimally invasive versus open radical hysterectomy for early stage cervical cancer

D. Margul^{a,b}, R. Zandi^b, J. Yang^b, B.L. Seagle^c, A.L. Alexander^c, E.L. Barber^c, M. Kocherginsky^{b,c}, S. Shahabi^c. ^aUniversity of Cincinnati Academic Health Center, Cincinnati, OH, USA, ^bFeinberg School of Medicine of Northwestern University, Chicago, IL, USA, ^cNorthwestern University Feinberg School of Medicine, Chicago, IL, USA

Objectives: Recent results suggest that when compared to open (ORH), a minimally invasive (MIS) approach to radical hysterectomy, results in worse overall survival. Herein, we evaluate the effects of surgical approach on perioperative outcomes including complications and costs. **Methods:** We performed an observational retrospective cohort analysis of 2,830 women cervical cancer recorded in the 2010-2015 Premier database (Premier, Inc.) to evaluate complications and costs. Premier is a comprehensive electronic healthcare database which provides U.S. hospital-based, service-level, all-payer data, in the form of ICD-9 procedure and diagnosis codes and billing data. Premier was used to compare complications, length of stay (LOS), readmission, and costs between surgery types among propensity score matched patients. All p values were 2 sided.

Results: From Premier, 2,830 women had radical hysterectomy: 45.1% ORH and 54.9% MIS. After propensity score matching, 2,433 patients were selected: 51.2% ORH and 48.8% MIS. ORH was associated with longer LOS than RRH or LRH (days, median (IQR): ORH 3 (3-5); MIS 1 (0-2), $P < 0.001$). ORH also had a higher composite complication rate than RRH or LRH (ORH 52.9%; MIS 25.5%, $P < 0.001$), with increased bowel injuries, urinary tract injuries, vascular injuries, respiratory failure, minor infections, electrolyte or fluid disorders, and ileus (all $P < 0.05$) associated with ORH. Thirty-day readmission rates were similar (ORH 2.4%; MIS 1.3%, $P = 0.078$). Total surgical hospitalization costs favored MIS ($P < 0.001$) with median (IQR) values: ORH \$11,545 (8,622-15,461); MIS \$10,636 (8,023-13,640). Additionally, ORH was associated with additional operations during the surgical admission (ORH: 20.9%; MIS 7.8%, $P < 0.001$) with extra bowel and urinary tract surgeries (all $P < 0.001$) associated with ORH.

Conclusions: MIS hysterectomy is associated with decreased morbidity and costs compared to open radical hysterectomy. Though MIS radical hysterectomy is associated with decreased survival, it may still be a reasonable choice for some women who are deemed lower risk. Patients and physicians should consider morbidity when deciding on surgical approach.

doi:10.1016/j.ygyno.2019.03.109

Poster #5

Assessment of the false negative rate of preoperative imaging in cervical cancer patients undergoing primary radical surgery

A. Staley, K. Tucker, P.A. Gehrig, L.H. Clark. *University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*