Methods: Immunohistochemistry (IHC) was performed using HGS ovarian cancer tumors. Tumor and stromal cell expression of DDR2 was scored. Clinical information was obtained and Kaplan Meier survival curves were generated. DDR2 expression was compared among chemoresistant and chemosensitive populations. Mesothelial cell clearance assays utilizing human omentum-cultured mesothelial cells with and without DDR2 expression were performed with DDR2 expressing tumor cells. Clearance area was calculated and analyzed using student's t test. To determine the effect of metastasis with DDR2 deficient stromal cells, global DDR2 knockout (KO) mice were compared to DDR2 wild-type (WT) mice when a DDR2 expressing murine tumor cell line was injected intraperitoneally. Intraperitoneal spread was quantified using tumor number, size, weight and volume of ascites.
Results: IHC tissue specimens were divided into two groups: survival <3 years and >5 years. Patients living <3 years had higher stromal and tumor DDR2 expression when compared to those living >5 years (mean stromal DDR2 IHC score 82% vs 49%, P<0.0001, mean tumor DDR2 IHC score 82% vs 66%, P<0.0001). Patients with high (>60%) stromal DDR2 staining in both primary and metastatic biopsy sites had worse overall survival and progression free survival compared to patients with low (<60%) stromal DDR2 staining [median OS 171.4 vs 34 months (P<0.0001) and median PFS 54.1 vs 21.5 months (P=0.0001)]. Chemoresistant patients had significantly higher DDR2 in the primary tumor (mean IHC score 78% vs 69%, P=0.04), primary stroma (74% vs 54%, P=0.0004), metastatic tumor (85% vs 68%, P<0.0001), and metastatic stroma (79% vs 65%, P=0.02) than the chemosensitive group. In the mesothelial clearance assay model, human ovarian cancer cells plated above DDR2 deficient mesothelial cells had less tumor cell clearance than cells plated above DDR2 expressing mesothelial cells (P=0.01). For the metastasis mouse model, DDR2 KO mice had less intraperitoneal spread of ovarian cancer cells than DDR2 WT mice by tumor nodules >1mm (P=0.02), volume of ascites (P=0.03), and tumor weight (P=0.02).
Conclusions: Our results indicate that tumor and stromal cell expression of DDR2 promotes ovarian cancer metastasis, chemoresistance, and survival, thus making DDR2 a potential target to guide future therapy.

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Poster #37

Obstetrics and Gynecology resident interest in and perceptions of Gynecologic Oncology

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Objectives: To assess resident interest in the field of Gynecologic Oncology and determine perceptions of Gynecologic Oncology when compared with Obstetrics and Gynecology and related subspecialties.
Methods: A survey was designed using Qualtrics and distributed to Obstetrics and Gynecology residents in the United States. It featured questions regarding demographics and perceptions of Gynecologic Oncology when compared to Obstetrics and Gynecology and other subspecialties. Survey questions were adapted from a paper by Siddigghi et al (2008) studying resident and fellow perceptions of female pelvic medicine and reconstructive surgery. 257 residents received the survey with a 34% response rate after one send-out.
Results: Most participants were female (88.76%), White (64.04%), Christian (53.41%), and married (48.28%). 12.64% were definitely considering a Gynecologic Oncology fellowship. The top three factors that increased interest in the field of Gynecologic Oncology were complex/challenging surgery, comprehensive care, and the ability to perform both surgery and clinical medicine. The top three factors that decreased interest in the field were the work schedule, end of life care, and critical care. When compared with general Obstetrics and Gynecology, the field of Gynecologic Oncology was felt to have much more research potential and impact on personal time; and somewhat more prestige, intellectual challenge, stress, and income potential. When compared to other Obstetrics and Gynecology subspecialties, Gynecologic Oncology was felt to have an increased impact on personal time and stress level. Gynecologic Oncology was felt to be somewhat more competitive to enter. Gynecologic Oncology was thought to be similar when compared to other Obstetrics and Gynecology subspecialties with regard to length of training, research potential, technological developments, and sense of satisfaction.
Conclusions: As the population continues to age, the incidence of cancer will continue to increase. The field of Gynecologic Oncology is in demand and will continue to grow and will need new members in the coming years. Understanding the factors that influence decisions to enter the field is crucial in recruiting strong new members from residency programs.

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Poster #38

Natural anti-carbohydrate human IgM for cancer immuno-therapy

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Objectives: Recently, there is a significant heightened interest in post-translational glycosylation of tumor cell. The cancer glycomics have differentiated them from the normal cells. Hence, tumor surface glycan becomes an attractive target for immunotherapy. Human VH4-34 gene-encoded IgM mAbs, 216 (hybridoma-produced) and 55.5 (recombinant CHO-produced), bind to the straight-chain poly-N-acetyl-lactosamine (SC-PNAL) glyco-epitope. SC-PNAL decorates a small group of proteins that include CD147 and CD98. A recent study demonstrates the presence of SC-PNAL on PD-L1 that are exploited to disinhibit cytotoxic T cells. Besides PD-L1, SC-PNAL is also expressed human B-cells, a subset of T-cells (including T-regs), and macrophages. We have studied the immunoregulatory properties of VH4-34 encoded SC-PNAL (human IgM) targeting mAbs in altering the tumor immune environment towards anti-tumor immunity.
Methods: We used two mouse syngeneic models; a cervical, lung cancer TC-1 model and OVCA HM-1 model. Dual treatment with cisplatin and mAb55.5 was undertaken in a subcutaneous and peritoneal model for TC-1 and HM-1 respectively. The tumor was treated with intra-tumoral or intraperitoneal drug administration. The tumor size, weight, drug toxicity and survival were monitored. Tumor explants and associated lymphoid tissue (draining lymph nodes, spleen), blood were taken at appropriate time. Immune-profiling was done with FACS.
Results: We show significant tumor volume reduction and increased survival in both models. Analysis of tumor infiltrating lymphocytes demonstrates a significant increase in CD8+ T-cells and decrease in T-regs in mice treated with both CDDP and mAb55.5. The immunoregulatory mechanism of targeting a sugar ligand by VH4-34 encoded IgMs is discussed.
Conclusions: 1) Natural occurring mAb has specificity to both liquid and solid tumor and immune cell surface glycan. 2) These mAbs have immunoregulatory properties. 3) Can be a novel treatment of gynecologic cancers.

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