xenograft, the mice were sacrificed. The cells were counted using fluorescent stereo microscopy (FSM). Percent attachment was calculated based on the number of cells visualized by FSM divided by the number of transfected cells injected. Unpaired student t-test was performed to analyze differences in the percent attachment of the cells. RESULTS/ANTICIPATED RESULTS: The majority of cells were attached to the peritoneum. There was increased attachment of hESCs with OE of CD44v6 compared to control (p=0.03). CD44v6 OE did not change attachment of iEECs. There was no difference in attachment in iEECs or hESCs with OE of CD44s or CD44v3. DISCUSSION/SIGNIFICANCE OF IMPACT: Overexpression of CD44v6 increases attachment of ESCs to PMCs in an in vivo xenograft model. Menstrual endometrial cell type and CD44 variants play a complex role in the development of the early endometriotic lesion.

3468

Predictive biomarkers of platinum-based chemotherapy response in Puerto Rican Hispanics with high-grade serous ovarian cancer.

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OBJECTIVES/SPECIFIC AIMS: High-grade serous ovarian carcinoma (HGSOC) is the most common and malignant histological subtype of epithelial ovarian cancer. While the majority of HGSOC patients initially respond to platinum-based chemotherapy, they often present with recurrent chemoresistant disease, which is extremely fatal. Therefore, there is an urgent need to identify predictive biomarkers of platinum response and to develop rational, targeted therapies to improve the outcome of patients with HGSOC. The objectives of the present study are to profile and assess the clinical significance of MYC network dysregulation in HGSOC. METHODS/STUDY POPULATION: We will conduct a retrospective cohort study of Puerto Rican Hispanics with HGSOC who underwent surgery followed by platinum-based chemotherapy at clinical institutions in Puerto Rico. Medical records, pathology reports, and cancer registries will be reviewed to extract data on clinicopathological features, disease recurrence, and death. For eligible patients, formalin-fixed, paraffin-embedded (FFPE) tissue samples will be processed and analyzed by quantitative Real Time PCR (qRT-PCR) and immunohistochemistry (IHC). RESULTS/ANTICIPATED RESULTS: Expression levels of MYC and MYC-related molecules are expected to correlate with clinicopathological features and prognosis of HGSOC. DISCUSSION/SIGNIFICANCE OF IMPACT: The identification and validation of clinically-relevant alterations in HGSOC, such as dysregulation of the MYC network, will be crucial to guide therapy regimen, maximize clinical benefit, and improve patient outcome.

3506

PRMT5 is a novel therapeutic target to enhance radiation therapy for cancer treatment

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OBJECTIVES/SPECIFIC AIMS: Prostate cancer is the second leading cause of cancer-related death among men in the U.S. and over half of all prostate cancer patients receive radiation therapy (RT). RT induces double-strand breaks (DSBs) in DNA which are lethal to cells if not repaired. While potentially curative, 10% of low-risk patients and 50% of high-risk patients treated with RT still experience tumor recurrence. Thus, identification of novel therapeutic targets to enhance RT will likely reduce prostate cancer mortality. The only clinical approach to enhance RT is androgen deprivation therapy, which targets androgen receptor (AR) signaling; however, its use is limited due to systemic side effects. We recently reported that PRMT5 epigenetically activates AR which led us to investigate if targeting PRMT5 sensitizes prostate cancer to RT. The goal of this project is to determine if PRMT5 is a therapeutic target for prostate cancer radiosensitization and analyze its mechanistic role in response to radiation. METHODS/STUDY POPULATION: To evaluate if targeting PRMT5 may sensitize prostate cancer cells to radiation, we performed a clonogenic assay of irradiated cells. To determine if PRMT5 is required for repair of radiation-induced DSBs, we performed foci analysis via immunocytochemistry. We then used RNA-seq, qPCR, western blot, and ChIP to evaluate a potential epigenetic role of PRMT5 in activating the expression of genes critical to DSB repair. To extend our findings, we analyzed clinical data from around 18,000 of cancer patients encompassing 43 cancer types to assess if PRMT5 expression correlates with the expression of its putative target genes. RESULTS/ANTICIPATED RESULTS: Targeting PRMT5 sensitizes prostate cancer cells to radiation independently of AR status. RNA-seq analysis revealed putative PRMT5 target genes including several involved in DSB repair and G2 arrest. Mechanistically, PRMT5 functions as a master epigenetic activator of DNA damage response (DDR) genes: PRMT5 maintains the basal expression of several DDR genes including BRCA1, BRCA2, and RAD51 and is recruited upon radiation to DDR gene promoters to activate their expression via histone methylation. Targeting PRMT5 decreases expression of these genes at the protein level and hinders repair of radiation-induced DSBs in multiple cancer and non-cancer cell types. Clinically, PRMT5 expression positively correlates with the expression of these DDR genes across all 43 cancer types analyzed. DISCUSSION/SIGNIFICANCE OF IMPACT: PRMT5 acts as a master epigenetic activator of genes involved in DDR and is critical for cells to survive radiation treatment. Importantly, PRMT5 epigenetically activates multiple genes that encode for well-characterized core repair proteins involved in HR (RAD51, RAD51AP1, RAD51D, BRCA1 and BRCA2) and NHEJ (NHEJ1, Ku80, XRCC4, and DNAPKcs), which may explain why PRMT5 is essential to repair IR-induced DSBs in several cell lines. As PRMT5 is overexpressed in many human cancers and its overexpression correlates with poor prognosis, our findings suggest that more efficient DSB repair via PRMT5 overexpression in these cancers may confer survival advantages particularly following DNA damaging treatments. Lastly, because targeting DSB repair is a clinically validated therapeutic approach for cancer treatment, our findings also suggest that PRMT5 targeting may be explored as a monotherapy or in combination therapy with radiation therapy or chemotherapy for cancer treatment.

3204

Renin-Angiotensin System Inhibitors Do Not Improve Survival in Fibrillin-1 Hypomorphic Mice with Established Aortic Aneurysm

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OBJECTIVES/SPECIFIC AIMS: Drugs to attenuate aortic growth are usually not initiated in patients with Marfan syndrome until

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aortic dilation is already present. Therefore, we measured the impact of drugs (the renin-angiotensin system inhibitors losartan and enalapril) on survival and thoracic aortic growth in a mouse model of Marfan syndrome when extensive aortic dilation was already present. METHODS/STUDY POPULATION: Male and female fibrillin-1 hypomorphic (FBN1 mgR/mgR) mice (n=10-12/group) were stratified into treatment groups by aortic diameter at 6 weeks of age to ensure an equivalent average aortic diameter in each group at the start of the study. Osmotic mini pumps filled with PBS (vehicle), enalapril (2 mg/kg/d), or losartan (20 mg/kg/d) were implanted subcutaneously into mice after stratification. Mini pumps infusing drug or vehicle were replaced every 4 weeks for a total duration of 12 weeks. Wild type littermates (n=10) were infused with PBS as a negative control to the Marfan mouse model. Ascending aortic diameters from male and female FBN1 mgR/mgR mice and their wild type littermates were assessed by ultrasound every 4 weeks from 6 to 18 weeks of age. Aortic diameters were measured luminal edge to luminal edge during diastole. RESULTS/ANTICIPATED RESULTS: 6 week old FBN1 mgR/mgR mice exhibited significantly dilated ascending thoracic aortas at study initiation compared to their wild type sex-matched littermates (in males: FBN1 mgR/mgR = 1.87 +/− 0.07mm, wild type = 1.23 +/− 0.07mm; p <0.001) (in females: FBN1 mgR/mgR = 1.56 +/− 0.07mm, wild type = 1.18 +/− 0.07mm; p <0.001). Baseline mortality of FBN1 mgR/mgR mice infused with PBS was 36% in male and 22% in female mice at the time of study termination. Within sex-matched mgR littermates, there was no significant difference in survival between groups treated with PBS, enalapril, or losartan after 12 weeks (p=0.224 for males, p=0.094 in females). In the same groups, no significant difference in maximum ascending aortic diameter was detected after treatment for 12 weeks (in males: PBS=2.69 +/− 0.19 mm, enalapril=2.04 +/− 0.27 mm, losartan=2.42 +/− 0.28 mm; p=0.24) (in females: PBS = 1.92 +/− 0.13, enalapril=1.89 +/− 0.31, losartan=1.98 +/− 0.17; p=0.86). Furthermore, aortic diameters in the FBN1 mgR/mgR mice were found to demonstrate sexual dimorphism. DISCUSSION/SIGNIFICANCE OF IMPACT: This research shows that losartan is not effective when administered after significant thoracic aortic dilation has already occurred in FBN1 mgR/mgR mice. This has important translational implications because losartan is usually not started in patients with Marfan syndrome until significant aortic dilation is already present. Therefore, more research needs to be done to determine the critical time period within which this medicine will be effective if given to patients. In addition, this research demonstrates that male FBN1mgR/mgR mice have a significantly larger aortic diameter than female FBN1mgR/mgR mice. This sexual dimorphism has recently been observed in patients with Marfan syndrome as well. Additional studies for understanding the mechanism underlying this sexual dimorphism have the potential to elucidate new therapeutic approaches for aortic disease.

3503

Restrictive feeding and excessive hunger in young children with obesity: A case series

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OBJECTIVES/SPECIFIC AIMS: The purpose of this case series is to show how helping parents instill a non-restrictive, structure-based (i.e., authoritative) approach to feeding is useful in addressing family food conflicts in a clinical child obesity treatment program. METHODS/STUDY POPULATION: Case reports are presented for 3 young children (two 8-year-old males and one 7-year-old female) with obesity (BMI ≥ 95th percentile for age and sex). Patients underwent family-based treatment at Brenner FIT® (Families In Training), an interdisciplinary tertiary weight management clinic. RESULTS/ANTICIPATED RESULTS: All patients experienced a period of rapid weight gain and/or severe onset obesity. Parents reported a combination of problematic eating behaviors (e.g., sneaking food, frequent complaints of hunger, vomiting from rapid consumption). Families implemented structure-based feeding with a meal-snack schedule and allowed children to eat until they were full from the food provided at meal-snack times. BMI z-score decreased from 2.19 to 2.07 in patient 1 and from 2.43 to 2.09 in patient 2 (follow-up weight was not available for patient 3). DISCUSSION/SIGNIFICANCE OF IMPACT: The improvements observed by our clinical program after families lifted restriction and instituted authoritative feeding is anecdotal evidence for the ecological validity of existing empirical work. Randomized controlled trials are needed to examine causality.

3008

Role of Interferon-gamma in Natural Clearance of Chlamydia trachomatis Infection in Women

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OBJECTIVES/SPECIFIC AIMS: Chlamydia trachomatis (CT) infection can lead to reproductive morbidity in women. Animal models suggest that protection against CT is mediated through the cytokine interferon-gamma (IFN-γ), produced by CD4+ T-cells, which clears CT through intracellular tryptophan depletion. In humans, correlates of protection remain to be elucidated, which hinders chlamydia vaccine development. Natural clearance of CT infection (e.g., clearance before antibiotics) may be an immunological correlate of protection, evidenced by (1) CT clearance without antibiotics; and (2) a 4-fold reduced risk of CT reinfection within 6 months. We have identified women with and without natural clearance of CT infection. By comparing these two groups of women, the role of IFN-γ-mediated natural clearance of CT infection will be investigated. METHODS/STUDY POPULATION: Through collaboration with a cohort study of CT-infected women, we have access to stored specimens from women who naturally cleared CT or had persisting CT infection. Using peripheral blood mononuclear cell (PBMC), we will assess whether natural clearance of CT infection is associated with IFN-γ-producing CD4+ T-cells by stimulating PBMC ex vivo with CT antigens using intracellular cytokine staining. We will also use cervicovaginal lavage (CVL) and untargeted High-Performance Liquid Chromatography-Mass Spectrometry to assess for tryptophan-dependent and -independent metabolic pathways associated with natural clearance of CT infection. RESULTS/ANTICIPATED RESULTS:: To date, IFN-γ has been measured in 10 women who did not clear CT infection, demonstrating that <20% of these women produced significant levels of IFN-γ. Women who naturally cleared CT have yet to be studied. Untargeted HPLC-MS has been performed on 6 women (3 who cleared matched to 3 with persisting CT infection). To date, 11 pathways that are significantly associated with natural clearance have been identified. DISCUSSION/SIGNIFICANCE OF IMPACT: The outcome of natural clearance

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