

represented on a signal bar display and represented the average cingulate activation during the trial. Unlike many rtfMRI studies, the purpose here was not for participants to interact with the neurofeedback directly. Rather, a feedback summary was shown to participants after each MEMORY and STRATEGY trial as an index of how brain activity changed in response to negative memories/worries and therapeutic strategies. Our goal was not for participants to learn to self-regulate the cingulate cortex, but rather to provide participants with a metacognitive demonstration of strategy efficacy. Participants were given detailed instructions regarding the task design, the role of the cingulate cortex in depression, as well as the hypothesized direction of activation during the MEMORY and STRATEGY phases to help them interpret the neurofeedback. RESULTS/ANTICIPATED RESULTS: Results revealed that “stronger neurofeedback” (defined as the difference between STRATEGY vs. MEMORY trials) correlated with self-reported strategy efficacy ratings immediately following the scan session ( $p < 0.05$ ). More importantly, stronger neurofeedback predicted both self-reported strategy efficacy and frequency of use 1 month following the MRI session ( $p < 0.05$ ). Importantly, this relationship was specific to only those strategies used inside the scanner; and no such relationship was observed at baseline. Neuroimaging results revealed that during the MEMORY phase, activation within inferior frontal gyrus and supramarginal gyrus correlated with baseline BDI score (whole brain, cluster corrected with FSL Flame 1 to  $p < 0.05$ ). During the STRATEGY phase, the periaqueductal gray nucleus, insula, and temporal pole predicted self-reported frequency of strategy use 1 month post-scan session (whole brain, cluster corrected with FSL Flame 1 to  $p < 0.05$ ). DISCUSSION/SIGNIFICANCE OF IMPACT: We believe this study holds promise to provide a powerful demonstration for individuals that strategies used to cope with negative moods can produce significant changes in their brain.

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### Vesicular secretion of suppressor of cytokine signaling 3 by alveolar macrophages is dysregulated in NSCLC patients and its provision inhibits epithelial cell transformation and tumor cell function

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OBJECTIVES/SPECIFIC AIMS: Insufficient endogenous expression of suppressor of cytokine signaling 3 (SOCS3) with subsequent over-activation of its target, the transcription factor STAT3, has been associated with tumorigenesis and cancer development in the lung and other organs. We have observed that a “backup” source of SOCS3 in the lung, namely that secreted in microvesicles (MVs) by alveolar macrophages, is reduced in the bronchoalveolar lavage fluid (BALF) of KRAS mutant mice harboring lung tumors. Here we sought to evaluate levels of SOCS3 in BALF of a cohort of non-small cell lung cancer (NSCLC) patients and to test the effects of vesicular SOCS3 administration on tumor cell transformation and function as potential therapeutic strategy. METHODS/STUDY POPULATION: In total, 22 BALF samples were obtained from healthy volunteers ( $n = 11$ ) as well as patients undergoing diagnostic bronchoscopies for suspected lung cancer ( $n = 11$ ). SOCS3 levels in the BALF were determined by ELISA after brief sonication to disrupt vesicles. In vitro experiments utilized the human adenocarcinoma cell line (A549) or human G12V mutant KRAS-expressing rat lung epithelial cells (RLE-G12V). Proliferation, Fas ligand (FasL)-induced apoptosis, and chemical transformation with *N*-methyl-*N*'-nitro-*N*-nitrosoguanidine (MNNG) or cigarette smoke extract (CSE) were assessed by CyQuant assay, annexin V staining, and soft agar assay, respectively. For SOCS3 rescue, epithelial cells were treated with natural alveolar macrophages-derived MVs (isolated via ultracentrifugation) or synthetic unilamellar liposomes containing human recombinant SOCS3 for at least 1 hour before assay. RESULTS/ANTICIPATED RESULTS: SOCS3 levels were significantly reduced in BALF samples of patients determined to have NSCLC as compared with healthy volunteers ( $186.6 \pm 26.74$  vs.  $395.6 \pm 74.31$  pg/mL,  $p = 0.015$ ,  $n = 11$ ). Addition of exogenous SOCS3-containing liposomes had the capacity to significantly inhibit MNNG and cigarette smoke extract-induced transformation and colony formation in soft agar. Exogenous SOCS3 provided in liposomes or in natural MVs significantly induced apoptosis (both in the presence and absence of FasL) and inhibited basal proliferation of A549 cells. DISCUSSION/SIGNIFICANCE OF IMPACT: These

data identified a novel dysregulation of immune surveillance in the form of decreased SOCS3 secretion in the tumor-bearing lung that may contribute to tumorigenesis via sustained STAT3 activation. Future studies will focus on the mechanism underlying this defect and whether rescuing SOCS3 secretion can inhibit cancer progression in vivo.

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### What genes are involved in the brain food reward circuitry: Findings from a large candidate gene analysis

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OBJECTIVES/SPECIFIC AIMS: The food reward circuitry regulates hedonic eating especially in relation to palatable hypercaloric foods, which can lead to chronic overeating and consequent overweight and obesity. Evidence supports that there is considerable overlap within the brain reward circuitry between palatable hypercaloric food intake and substance addiction. The goal of this study was to identify associations between addiction-related genes and body mass index. We hypothesized that addiction-related genes potentially participate in the food reward circuitry if they are associated with obesity traits. METHODS/STUDY POPULATION: A secondary analysis was conducted with 1093 African American adolescents and young adults from the New Mother's Study. Anthropometric, genetic, demographic and lifestyle measurements were available at the 18-year follow-up assessments. A total of 1350 single nucleotide polymorphisms mapped to 127 addiction-related genes were assessed. A total of 186 ancestry informative markers were used to adjust for population stratification. Generalized estimating equation models were used to identify genetic associations, including additive, dominant, and recessive models, and control for correlations within families. RESULTS/ANTICIPATED RESULTS: The participants ranged from 15 to 23 years of age. Of them, 42.7% were overweight or obese. Significant associations with body mass index were identified for 13 single nucleotide polymorphisms mapped to 11 addiction-related genes, including LEP ( $p = 0.027 - < 0.001$ ). Most of these genes are involved in dopaminergic, opioidergic, serotonergic pathways, and stress. DISCUSSION/SIGNIFICANCE OF IMPACT: Our results support the role of dopaminergic and opioidergic pathways in the food reward circuitry, and suggest a potential involvement of serotonergic pathways and genes related to stress in the food reward circuitry. Further investigation of the identified genes will facilitate delineation and understanding of the brain food reward system and its relationship with obesity.

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### Validation of a novel PD-L1 assay for bladder cancer circulating tumor cells

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OBJECTIVES/SPECIFIC AIMS: Bladder cancer patients being considered for immune checkpoint blockade are often judged on immunohistochemical staining for the checkpoint target protein PD-L1 in the original surgery or biopsy sample. However, sampling error or the clinical evolution of most patients' cancer can render the original PD-L1 assessment no longer accurate. In contrast, circulating tumor cells (CTCs) allow serial noninvasive sampling of the current tumor status throughout a patient's clinical course including those with the highest metastatic potential. We therefore sought to develop a method for quantifying PD-L1 expression in CTCs towards addressing inherent limitations of current UC management. METHODS/STUDY POPULATION: This work utilizes both cancer cell lines as well as patient samples. Positive and negative control cancer cell lines were assessed via “industry standard” antibodies for PD-L1 expression via Western blots and immunofluorescence, and a threshold-based method was developed for reliable quantification. PD-L1 expression was additionally verified via interferon-mediated up-regulation. CTCs isolated from bladder cancer patient samples via a density centrifugation method were then assessed for PD-L1 via the same antibodies. RESULTS/ANTICIPATED RESULTS: We will show preliminary preclinical and clinical data that validates the sensitivity and specificity of our assay. A case study will be presented that illustrate the potential useful of the novel approach we describe and which should be complementary to current clinical practices. In a patient with metastatic bladder cancer, this method effectively detected the PD-L1 expression in CTCs taken at a time coincident to when the patient derived an

excellent response to the PD-L1 checkpoint inhibitor Pembrolizumab. **DISCUSSION/SIGNIFICANCE OF IMPACT:** This work highlights the potential utility of CTCs in the management of bladder cancer. It may be the case that this assay in conjunction with current methods of patient selection for immunotherapy may allow for better response prediction than either method alone.

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### Large patient volume is associated with adverse patient outcomes among those requiring maintenance renal replacement therapy

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**OBJECTIVES/SPECIFIC AIMS:** We set out to describe important associations and outcomes among those requiring maintenance renal replacement therapy with the patient volume per provider. **METHODS/STUDY POPULATION:** Through the combination of several large administrative datasets, including the United States Renal Data System ( $n = 237,485$ ), the American Medical Association Master file ( $n = 62,49$ ), and Medicare data limited to 2012, we compared characteristics of patients, by quintile of patient/provider volume.  $\chi^2$  and logistic regression, adjusted for various patient and provider factors for categorical and continuous variables, was used for baseline comparisons, respectively. Cox regression, adjusted for patient, provider, and socio-economic variables, was used to calculate risks for important clinical outcomes such as kidney transplant listing, transplant receipt, and all-cause mortality. **RESULTS/ANTICIPATED RESULTS:** There is a threshold patient volume at which important clinical outcomes, including kidney transplantation and all-cause mortality, may be influenced. Higher patient volume is associated with adverse patient outcome. Those receiving care from providers with the highest patient volumes are less likely to receive kidney transplantation, live in a more rural area, and be non-White. **DISCUSSION/SIGNIFICANCE OF IMPACT:** There is a need to identify novel and potentially modifiable factors associated with patient outcome among those with end-stage kidney disease on maintenance renal replacement therapy. Provider level variables, such as patient volume, is one such variable. As nephrologists are often tasked with the care of variable numbers of patients on dialysis, a better understanding of this association is an unmet need.

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### A collaborative neurology-emergency medicine rapid outpatient clinic for the management of TIA and minor stroke in the emergency department

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**OBJECTIVES/SPECIFIC AIMS:** Current practice frequently dictates hospitalization for TIA and minor stroke (TIAMS) in order to obtain comprehensive evaluation of stroke risk factors and mechanism. Inpatient hospitalization is often done to expedite workup and to coordinate care although may be associated with nosocomial risks and increased healthcare cost. However, a subset of these patients who do not have debilitating deficits may not require inpatient hospitalization. We conducted a pilot study to assess the feasibility of conducting rapid outpatient stroke evaluations in low risk patients with TIAMS without disabling deficits. **METHODS/STUDY POPULATION:** The rapid access clinic was initiated at a single-site urban tertiary care facility for outpatient evaluation of TIAMS within 24 hours of emergency department (ED) evaluation. Patients were selected using a decision tool identifying presumed low-risk TIAMS seen in the ED. Criteria included medical (e.g., no disabling deficit, no thrombolytic agent given, negative CT for hemorrhagic stroke) as well as social criteria (e.g., patient ability to follow-up as an outpatient). We evaluated rates of noncompliance with post-ED follow-up, need for hospitalization from clinic, and 90 day stroke and health outcome data. **RESULTS/ANTICIPATED RESULTS:** Between December 2016 and December 2017 a total of 93 TIAMS patients seen in the ED were recommended for the rapid access clinic utilizing the decision tool. Of these patients, 94.5% (86) were evaluated within 24 hours of ED discharge. Only 2 patients (2.4%) who received outpatient evaluation required hospitalization;

61 (71.8%) patients had TIAMS on final evaluation in clinic. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Our pilot data suggests that for a subset of patients, rapid outpatient evaluation may be a feasible and safe strategy for TIAMS management. Future work exploring such strategies may help improve TIAMS outcomes and reduce ED crowding and unnecessary hospital admissions.

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### A prospective study of cancer clinical trial availability and enrollment among adolescents/young adults treated at a Children's Hospital or Affiliated Adult Cancer Specialty Hospital

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**OBJECTIVES/SPECIFIC AIMS:** Low cancer clinical trial (CCTs) enrollment may contribute to the poor survival improvement for adolescents and young adults (AYAs, aged 15–39 years) with cancer. Treatment site is thought to exacerbate this problem. This study evaluated whether differences in CCT availability explain lower CCT enrollment depending on treatment site for AYAs. **METHODS/STUDY POPULATION:** This prospective, observational cohort study was conducted at an academic children's hospital and an adult cancer hospital, 2 affiliated sites within a NCI-designated Comprehensive Cancer Center over 13 months. In consecutive AYA patients newly diagnosed with cancer at both site, it was determined whether an appropriate CCT existed nationally, was available locally, and if enrollment occurred. The proportions of AYAs in these categories were compared by site using the  $\chi^2$  test. **RESULTS/ANTICIPATED RESULTS:** Among 152 consecutive AYA patients, 68 and 84 were treated at the children's hospital and adult cancer hospital, respectively. AYAs treated at the children's hospital had similar CCT existence nationally compared with AYAs treated at the adult hospital [36/68 (52.9%) vs. 45/84 (53.6%),  $p = 0.938$ ]. However, a significantly higher percentage of children's hospital treated AYAs than adult hospital treated AYAs had an available CCT [30/68 (44.1%) vs. 14/84 (16.7%),  $p < 0.001$ ]. Enrollment percentages were similarly low in both groups [8/68 (11.8%) vs. 6/84 (7.1%),  $p = 0.327$ ]. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Significantly fewer AYAs treated at the adult hospital had a CCT available, but national existence was similar at both sites. This suggests that institutional barriers to opening CCT have more importance at adult centers.

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### Addressing challenges from missing data in a global quality improvement study

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**OBJECTIVES/SPECIFIC AIMS:** Missing data is a common problem in research studies that may lead to inconclusive or inaccurate results. It may even lead to harm secondary to wrong research conclusions. The purpose of this ancillary study is to measure the differences in missing data following implementation of a variety of mechanisms to improve data quality and documentation in a global quality improvement study. Many of the sites involved in the study were in low-income or middle-income countries with minimal research infrastructure. Missing data is defined as "values that are not available that would be meaningful for analysis if they were observed" (The prevention and treatment of missing data. *New Engl J Med* 367; 14, nejm.org, October 4, 2012). **METHODS/STUDY POPULATION:** All study sites used REDCap software to enter various data points including hospital and ICU admission and discharge dates as well as whether items on a Checklist relevant to processes of care in the ICU were