



# NYC Regional Obesity Forum

NEW YORK CITY  
REGIONAL OBESITY FORUM

## **First Annual Meeting**

Icahn School of Medicine at Mount Sinai  
1468 Madison Ave (btw E 98<sup>th</sup>-101<sup>st</sup>)  
Annenberg Building, Stern Auditorium  
New York, NY 10029

**Monday, September 19<sup>th</sup>, 2016**  
8:30 am – 4:30 pm

**Registration (free) and abstract submission**  
[icahn.mssm.edu/nycrobesityforum](http://icahn.mssm.edu/nycrobesityforum)

 @nycrof2016

# New York City Regional Obesity Forum

Monday, September 19, 2016

Icahn School of Medicine at Mount Sinai - Mount Sinai Hospital

1468 Madison Avenue - Stern Auditorium

8:30-9:00	30min	Arrive, coffee, poster set-up
9:00-9:10	10min	Welcome remarks - Rudy Leibel & Ruth Loos
		<b>Chair:</b> Utpal Pajvani (Columbia University)
9:10-9:30	20min	<b>Short talk 1</b> - Alpana P. Shukla (Weill Cornell) - Food Order has a Significant Impact on Postprandial Glucose and Insulin Excursions
9:30-9:50	20min	Short talk 2 - RT Pickering (Boston Univ) - "Secretory factors produced by cultures of human omental adipose stem cells inhibit adipose differentiation"
<b>9:50-10:40</b>	<b>5 intro+45min</b>	<b>Keynote 1: Barry Levin (Rutgers, New Jersey Medical School) - "Amylin:leptin sensitizer and neurotropic hormone for the treatment of obesity"</b>
10:40-11:10	30min	Coffee/Networking/Poster viewing
		<b>Chair:</b> Gretchen Van Wye (NYC Department of Health)
11:10-11:30	20min	Short talk 3 - Jennifer Woo Baidal (Columbia University) - "Effectiveness of the Massachusetts Childhood Obesity Research Demonstration (MA-CORD) Project: Clinical and WIC Interventions to Improve Body Mass Index among Low-Income Children"
11:30-11:50	20min	Short talk 4 - Henry H. Ruiz (Icahn School of Medicine at Mount Sinai) - "Impaired Autonomic Control of Adipose Tissue Lipolysis is a Major cause of the Chronic Low Grade inflammatory State in Obesity and Diabetes"
11:50-1:30	100min	Lunch/Networking/Poster viewing and presentations (between 12:30 and 1:30)
		<b>Chair:</b> Susan Fried (Icahn School of Medicine at Mount Sinai)
1:30-1:50	20min	Short talk 5 - Harini Sampath (Rutgers University) - Enhanced repair of mitochondrial oxidative DNA damage confers protection against diet-induced obesity and metabolic syndrome
1:50-2:10	20min	Short talk 6 - Reem Z. Sharaiha (New York-Presbyterian Hospital) - Endoscopic sleeve gastroplasty significantly improves body mass index and metabolic complications in obese patients
<b>2:10-3:00</b>	<b>5 intro+45min</b>	<b>Keynote 2: Susan Yanovski (NIH, NIDDK) - "Alcohol Use and Misuse After Bariatric Surgery"</b>
3:00-3:30	30min	Coffee/Networking/Poster viewing
		<b>Chair:</b> Mireille McLean (New York Academy of Science)
3:30-3:50	20min	Short talk 7 - Sarah Stano/Blandine Laferrere (Columbia University) - Effect of meal texture on GLP-1, glucose and hunger after Roux-en-Y gastric bypass surgery
3:50-4:10	20min	Short talk 8 - Gaelle Doucet (Icahn School of Medicine at Mount Sinai) - "Does body mass index impact brain functional organization?"
4:10-4:20	10min	Closing remarks, poster awards

## ORAL PRESENTATIONS

### Short Talk 1

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Food Order has a Significant Impact on Postprandial Glucose and Insulin Excursions
<b>Authors *</b>	Alpana P. Shukla*, Samir H.Touhamy II, Jeselin B. Andono, Anthony J. Casper, Catherine E. Thomas, Rekha B.Kumar, Leon I. Igel, Louis J. Aronne
<b>Institutional Affiliations For Each Author. *</b>	Weill Cornell Medicine, Weill Cornell Medicine & Institute of Human Nutrition, Weill Cornell Medicine & Institute of Human Nutrition, Weill Cornell Medicine, Weill Cornell Medicine, Weill Cornell Medicine, Weill Cornell Medicine, Weill Cornell Medicine
<b>Corresponding Author Email *</b>	aps2004@med.cornell.edu

#### Structured Abstract \*

**Background:**In a previous pilot study using a typical Western meal, we demonstrated that ingestion of protein and vegetables before carbohydrate leads to lower postprandial glucose and insulin excursions upto 120 min compared to eating carbohydrate first in a meal. In this follow up study, we seek to examine the effect of food order on post-prandial plasma glucose and insulin excursions in the setting of three commonly followed meal patterns with extended follow-up to 180 min. The study is ongoing;data for the first 7 subjects are presented below.

**Methods:**7 overweight/obese subjects (BMI 25–40kg/m<sup>2</sup>) with type 2 diabetes(HbA1c  $\leq$  8%) on metformin were studied using a within subject crossover design. After a 12 hour fast, subjects were randomly assigned to consume an isocaloric meal with the same composition on 3 separate days in one of the following food orders: carbohydrate(bread) followed 10 minutes later by protein(chicken) and vegetables, protein and vegetables followed 10 minutes later by carbohydrate or all meal components eaten together as a sandwich. Blood was sampled for measurement of glucose and insulin at baseline and at 30 min intervals upto 180 min after the meal.

**Results:**The incremental areas under the curve for glucose(iAUC 0–180) were similar, though the carbohydrate first pattern demonstrated greater glycemic variability with higher peak at 60 min and lower nadir at 180 min. The average incremental glucose peak following ingestion of protein and vegetables first was 51% and 45% lower compared to eating carbohydrate first or eating all meal components together as a sandwich respectively. The iAUC 0–180 for plasma insulin also was significantly lower when vegetables and protein were consumed first followed by carbohydrate compared to other meal conditions.

**Conclusions:**Food order has a significant impact on post-prandial glucose and insulin excursions and may be an effective strategy to attenuate postprandial glucose spikes and glycemic variability in patients with type 2 diabetes with implications for improving insulin sensitivity.

## ORAL PRESENTATIONS

### Short Talk 2

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Secretory factors produced by cultures of human omental adipose stem cells inhibit adipose differentiation
<b>Authors *</b>	Pickering RT*, Fried SK, Layne M, Jager M, and Lee MJ
<b>Institutional Affiliations For Each Author. *</b>	Dept of Medicine and Graduate Program in Nutrition and Metabolism, Boston Univ. Sch. Medicine.
<b>Corresponding Author Email *</b>	lee.mijeong@gmail.com

#### Structured Abstract \*

**Background:** The size of visceral adipose tissues (VAT) is associated with risk for metabolic disease. As compared to abdominal subcutaneous (Abdsc), VATs have a limited capacity to expand by hyperplasia, leading to adipocyte hypertrophy, inflammation and tissue dysfunction. As expected, omental (Om) adipose stem cells (ASCs) after addition of a potent adipogenic cocktail (Insulin, dexamethasone (Dex), IBMX, rosiglitazone), only 30% of Om ASC differentiate, compared to over 70% in Abdsc.

**Methods:** To test the hypothesis that secretory factors produced by Om ASCs inhibit differentiation, we treated well differentiating Abdsc ASCs with conditioned media (CM) obtained after culture for 24h from paired samples of Om and Abdsc ASCs (n=13) or control media. Differentiation was assessed by triglyceride content and ATGL protein expression.

**Results:** CM from Om ASCs suppressed differentiation more potently than Abdsc CM ( $46 \pm 10$  vs  $21 \pm 5\%$  suppression, n=13,  $p < 0.05$ ). In addition, the magnitude of the inhibitory effect correlated with the capacity of donors cells to differentiate ( $R^2 = 0.4$ ,  $p < 0.01$ , n=17). We previously found that genes in the TGF $\beta$  signaling pathway were enriched and less well downregulated by Dex in Om, so we assessed their levels in the CM. Protein levels of Activin A and TGF $\beta$ , known inhibitors of adipogenesis, were higher in Om ASC CM (Activin A ( $74 \pm 16$  AU in Om vs  $9 \pm 4$  AU, n=14,  $p < 0.05$ ) and TGF $\beta$  ( $30 \pm 4$  vs  $10 \pm 1$  pM, n=14,  $p < 0.05$ ), and basal Smad2 phosphorylation levels were higher in Om than Abdsc ASCs. Blocking TGF $\beta$  signaling using the TGFBR1 antagonist SB431542 or siRNA mediated knockdown of SMAD proteins markedly improved differentiation of Om ASCs. Dex decreased Activin A and TGF $\beta$  secreted into CM in both depots and the ability of Dex to decrease SMAD2 phosphorylation was lower in OM ASCs. Furthermore, Dex increased expression of TGFBR3 which can modulate TGFBR1 activation of SMAD signaling.

**Conclusions:** Taken together these data suggest that the activation of TGF $\beta$  signaling contributes to the poor adipogenic capacity of Om ASCs via autocrine or paracrine mechanisms, and that Om ASCs are less sensitive to the proadipogenic effects of glucocorticoids, possibly restraining healthy expansion of VAT.

## ORAL PRESENTATIONS

### Short Talk 3

<b>Abstract Topic Category *</b>	Population Health and Epidemiology
<b>Abstract Title *</b>	Effectiveness of the Massachusetts Childhood Obesity Research Demonstration (MA-CORD) Project: Clinical and WIC Interventions to Improve Body Mass Index among Low-Income Children
<b>Authors *</b>	Jennifer Woo Baidal, MD, MPH1,2*, Meghan Perkins, MPH2, Shikha Anand, MD, MPH3, Jo-Ann Kwass, MS4, Neil Kamdar, MA2, Rachel Colchamiro, MPH4, Steven L. Gortmaker, PhD5, Kirsten Davison, PhD5, 6, Candace Nelson, ScD4, Thomas Land, PhD4, Elsie M. Taveras, MD, MPH2
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<b>Corresponding Author Email *</b>	jw3286@cumc.columbia.edu

#### Structured Abstract \*

**Background:** Childhood obesity is highly prevalent, disproportionately affects racial/ethnic minority and low-income children, and represents a major threat to public health. The aim of this research is to examine the extent to which the intervention components delivered through primary care and through the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) in two MA communities resulted in reduced age- and sex-specific body mass index (BMI) z-scores among 2–12 year old children vs. children in a comparison community.

**Methods:** In 2011, the Massachusetts Department of Public Health along with academic and community partners launched the MA-CORD study, a multifaceted initiative to prevent childhood obesity among low-income children. In two MA communities, we implemented evidence-informed interventions in the federally qualified community health centers (FQHC), WIC programs, early care and education, schools/after-school programs, and across the community. One MA community, with similar population income distributions, served as the comparison. Using the electronic records of the FQHCs and WIC, we assessed BMI z-scores pre-intervention (prior to January 2013) and at least one post-intervention implementation time point (after June 2013 through August 2015). FQHC sample sizes were 1377 in Intervention site #1, 117 in Intervention site #2, and 2441 in the comparison site. WIC sample sizes were 639 in Intervention site #1, 197 in intervention site #2, and 627 in the comparison site. We used linear mixed models to examine BMI z-score change over a 2-year period in each intervention site vs. the comparison site.

**Results:** Compared to children in the comparison FQHC, children in Intervention site #1 had a significant decline in BMI z-scores following the start of the intervention (–0.06 units/year; 95% CI: –0.09, –0.03;  $p < 0.001$ ). Compared to children in the comparison WIC group, children in Intervention site #1 also had a decline in BMI z-scores (–0.03 units/year; 95% CI: –0.05, 0.00;  $p = 0.05$ ). We found no evidence of an effect in Intervention site #2. While the design was well powered to detect small changes in BMI z-scores, social and economic hardships at Intervention site #2 led to fewer children seeking their primary care and WIC services than originally planned.

**Conclusions:** The clinical and WIC interventions delivered through MA-CORD were associated with significant improvement in BMI z-scores in one of two intervention communities, compared to a control site. A multi-level, multisector approach to obesity prevention and treatment may improve BMI among 2–12 year old children living in low-income communities.

## ORAL PRESENTATIONS

### Short Talk 4

<b>Abstract Topic Category *</b>	Genetics/Epigenetics/Early Determinants of Obesity
<b>Abstract Title *</b>	Impaired Autonomic Control of Adipose Tissue Lipolysis is a Major cause of the Chronic Low Grade inflammatory State in Obesity and Diabetes
<b>Authors *</b>	Henry H. Ruiz*, Eun Ran Kim, Rudolf Zechner, Qingchun Tong, Christoph Buettner
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#### **Structured Abstract \***

A hallmark of obesity and diabetes is chronic low grade inflammation in multiple organs and tissues. While it is clear that metabolic dysregulation and inflammation are inextricably linked, the mechanistic basis for this association is only incompletely understood. Further, what initiates and fuels inflammation in the insulin resistant state still remains unclear. Here we speculated that obesity leads to hypothalamic insulin resistance resulting in unbalanced sympathetic nervous system (SNS) outflow to WAT driving lipolysis and inhibiting DNL, which in turn leads to systemic inflammation. To test if fatty acids derived from WAT lipolysis are peripheral effectors linking the brain via the SNS to the control of innate immunity, we investigated if selective ATGL (adipose triglyceride lipase) deletion in WAT or pharmacological ATGL inhibition prevents obesity induced meta-inflammation. Genetic deletion of ATGL from WAT or pharmacological inhibition of ATGL prevented HFD-induced WAT and liver inflammation. Furthermore, we have generated a novel mouse model of inducible tyrosine hydroxylase (TH) gene deletion that is restricted to the periphery, including sympathetic fibers of the peripheral NS, but spares the brain. TH knock out (KO) mice are unable to synthesize catecholamines in the periphery, while CNS catecholamine synthesis remains intact and hence represents a pharmaco-genetic model of sympathectomy. TH KO mice are cold intolerant consistent with functional sympathectomy, yet exhibit no motor or behavioral deficit. In preliminary studies TH KO mice are protected from high fat feeding induced glucose intolerance and insulin resistance. We are currently using this model to assess the role of the SNS in WAT immunity. Our data provides support for the paradigm that impaired WAT function accounts for the close association between dysmetabolic states and chronic inflammation and identifies new strategies to prevent meta-inflammation.

## ORAL PRESENTATIONS

### Short Talk 5

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Enhanced repair of mitochondrial oxidative DNA damage confers protection against diet-induced obesity and metabolic syndrome
<b>Authors *</b>	R. Stephen Lloyd(a), Vladimir Vartanian(a), Nichole Owens(a), and Harini Sampath(b)
<b>Institutional Affiliations For Each Author. *</b>	a) Department of Molecular and Medical Genetics, Oregon Health & Science University, Portland, OR 97239, b) New Jersey Institute for Food Nutrition and Health and Department of Nutritional Sciences, Rutgers University, New Brunswick, NJ 08901
<b>Corresponding Author Email *</b>	sampath@ifnh.rutger.edu

#### Structured Abstract \*

##### Background

Oxidative damage to genomic and mitochondrial DNA(mtDNA) is mainly repaired via base excision repair, a pathway that is catalyzed by DNA glycosylases such as 8-oxoguanine DNA glycosylase (OGG1). While OGG1 has been implicated in maintaining genomic integrity and preventing tumorigenesis, we recently reported a novel role for OGG1 in altering cellular and whole body energy homeostasis. OGG1-deficient (Ogg1<sup>-/-</sup>) mice have increased adiposity and hepatic steatosis following exposure to a high-fat diet (HFD), compared to wild-type (WT) animals. Ogg1<sup>-/-</sup> animals also have higher plasma insulin levels and impaired glucose tolerance upon HFD feeding, relative to WT counterparts. This propensity to obesity is secondary to an alteration in cellular substrate metabolism favoring carbohydrate utilization over fat oxidation, as evidenced by an increased respiratory quotient, reduced fasting ketones, and co-ordinated changes in fat oxidation and TCA cycle genes in livers of Ogg1<sup>-/-</sup> mice.

##### Methods

To delineate the specific contribution of mtDNA repair to overall energy homeostasis, we utilized mice constitutively overexpressing a mitochondrially targeted human OGG1 protein (Ogg1Tg mice). Food intake, body weight, activity, energy expenditure, and body composition were monitored in WT and Ogg1Tg mice under both chow-fed and HFD-fed conditions. Additionally, hepatic lipid accumulation, inflammatory changes in adipose tissue, changes in mitochondrial abundance, and glucose tolerance were determined in HFD-fed animals.

##### Results

Chow-fed Ogg1Tg mice are significantly leaner than age-matched WT and Ogg1<sup>-/-</sup> counterparts. In addition, Ogg1Tg mice are markedly protected from diet induced obesity and features of the metabolic syndrome, including insulin resistance and hepatic lipid accumulation. Markers of inflammation in adipose tissue are significantly reduced in Ogg1Tg mice. The reduction in body weight in Ogg1Tg mice is accompanied by both a significant reduction in food intake, as well as an increase in overall energy expenditure.

##### Conclusions

These studies indicate a novel and critical role for mitochondrial DNA repair in modulating energy balance by regulating both food intake and energy expenditure.

## ORAL PRESENTATIONS

### Short Talk 6

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Endoscopic sleeve gastroplasty significantly improves body mass index and metabolic complications in obese patients
<b>Authors *</b>	Reem Z. Sharaiha MD MSc1, Alpana Shukla MD2, Nikhil A. Kumta MD MS1, Monica Saumoy MD1, Andrea Benevenuto NP1, Amit Desai, Amy Tyberg MD1, Rekha Kumar MD2, Leon Igel MD2, Elizabeth C. Verna MD MSc 3, Robert Schwartz MD1, , Michel Kahaleh MD1, Louis J. Aronne MD2

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#### **Structured Abstract \***

**Background:** Endoscopic sleeve gastroplasty (ESG) is a novel, incisionless, minimally invasive bariatric treatment, which reduces the length and width of the gastric cavity to facilitate weight loss. The aim of this study was to evaluate the impact of ESG on total body weight loss (TBWL) and obesity-related comorbidities.

**Methods:** Patients who underwent ESG between August 2013 and March 2016 were included in this prospective study. All procedures were performed with a cap-based flexible endoscopic suturing system (OverStitch; Apollo Endosurgery) to facilitate a triangular pattern of sutures to imbricate the greater curvature of the stomach. The primary outcomes were TBWL at 6, 12. Secondary outcomes included the impact of ESG on metabolic comorbidities.

**Results:** Ninety-one patients were enrolled. The mean age was 43.66 (range 19 – 66), 68% were female. The mean pre-procedure BMI was 40.7 ± 7.0 kg/m<sup>2</sup>. 52 patients reached 6-months follow-up, 29 patients reached 12 months. At six months, the mean percent TBWL was 14.4%, and 17.6% at 12 months. For patients before and 12 months after ESG, there was a statistically significant improvement in HemoglobinA1c (p=0.01), systolic blood pressure (p=0.02), waist circumference (p<0.001), ALT (p<0.001), and serum triglycerides (p=0.02). However there was no significant change in LDL (p=0.79) or serum leptin (p=0.48).

**Conclusions:** ESG is a minimally invasive and effective endoscopic weight loss intervention. In addition to sustained total body weight loss after 24 months, ESG is associated with significant improvements in medical comorbidities including hypertension, diabetes and hypertriglyceridemia.

## ORAL PRESENTATIONS

### Short Talk 7

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Effect of meal texture on GLP-1, glucose and hunger after Roux-en-Y gastric bypass surgery.
<b>Authors *</b>	Sarah Stano, Esmeralda Pierrini, Louis Wu, Sin Nee Ng, James McGinty, Blandine Laferrère*
<b>Institutional Affiliations For Each Author. *</b>	Columbia University Obesity Research Center, Mount Sinai St Luke's Hospital Bariatric Division.
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#### Structured Abstract \*

**Background** The incretin GLP-1 is elevated after gastric bypass surgery (RYGB). This results in enhanced insulin secretion, lower blood glucose and, at times, reactive hypoglycemia. The effect of meal texture on the endocrine and metabolic response to nutrient ingestion after RYGB is unknown. Hypotheses: 1) RYGB Effect: one year post-RYGB, a test meal will result in faster gastric emptying (GE), greater GLP-1 and insulin release, and lower post-prandial glucose levels, compared to pre-RYGB. 2) Meal Texture Effect: One year after RYGB, ingestion of a liquid meal (LM) will result in faster GE, greater GLP-1 and insulin release, and lower post-prandial glucose, compared to an isocaloric meal of solid texture (SM).

**Methods:** Obese subjects were studied before and 1 year after RYGB, and randomized to either the SM (n=9) or LM (n=12) group. Fasted subjects consumed 600kcal meal (53%) of CHO at Hour 0. Blood and visual analog scale (VAS) measurements (150 mm) were collected before and for the 6 hours after meal ingestion at regular intervals.

**Results:** After RYGB, regardless of meal texture, GE was 2.4 times faster, GLP-1 and insulin levels increased and post-prandial glucose levels decreased. The number of hypoglycemia episodes increased only after the LM. Meal texture had a significant effect on GLP-1; the peak GLP-1 was 2.3 times higher after the LM compared to the SM ( $106.1 \pm 67.2$  vs  $45.3 \pm 25.2$  pg/ml,  $p < .05$ ), but there was no significant effect on insulin. Although glucose levels were not statistically different between groups, they tended to be lower after the LM, and more subjects experienced hypoglycemia after the LM (n=7; 58%) than after the SM (n=1; 11%). Despite a ~50 kg weight loss, fasted hunger scores were not different compared to pre-RYGB. SM was more efficient at suppressing hunger and better tolerated than the LM.

**Conclusion:** These data suggest that meal texture, but not calories, plays an important role in eliciting GLP-1 release, the occurrence of hypoglycemia, and hunger control in individuals after RYGB.

## ORAL PRESENTATIONS

### Short Talk 8

<b>Abstract Topic Category *</b>	Neurological
<b>Abstract Title *</b>	Does body mass index impact brain functional organization?
<b>Authors *</b>	Gaelle Doucet*, Nadia Micali, Sophia Frangou
<b>Institutional Affiliations For Each Author. *</b>	Icahn School of Medicine at Mount Sinai,Icahn School of Medicine at Mount Sinai,Icahn School of Medicine at Mount Sinai
<b>Corresponding Author Email *</b>	gaelle.doucet@mssm.edu

#### Structured Abstract \*

**Background:** Despite evidence that obesity is associated with brain dysfunction, the relationship between obesity and the functional organization of brain networks has not been fully explored at rest. We tested the hypothesis that brain functional connectivity (FC) would be associated with the degree of obesity amongst healthy subjects, through a process of network alterations.

**Methods:** We included 496 healthy young adult participants ([22–37] years) from the human connectome project (<http://www.humanconnectome.org>). We preprocessed resting-state fMRI data using a standard pipeline using SPM12. The brain was then parcellated into 638 cortical and subcortical regions. For each individual, we identified groups of brain regions that were densely interconnected by strong FC, employing a k-means clustering algorithm. Based on literature, we tested two partition sizes: 4 and 13 networks. For each individual we calculated two global measures: the variance in community size and the index of spatial similarity. We also calculated two local measures: the within-cluster connectivity (a measure of functional cohesion of a network) and the between-cluster connectivity (a measure of functional integration of the networks). Correlations were computed to test the associations between body mass index (BMI) and the functional measures, for each partition size.

**Results:** The BMI range was [16.8–47.8, average of 26.6]. BMI was positively correlated with age ( $r=0.15$ ,  $p=0.04$ ) and negatively with education ( $r=-0.26$ ,  $p=0.0004$ ). At partition size 4, we revealed that a higher BMI was associated with a less normative brain partition ( $r=-0.14$ ,  $p=0.002$ ). In particular, we found that subjects with higher BMI had both a reduced cohesion (lower within-cluster FC,  $r=-0.12$ ,  $p=0.007$ ) and an increased integration (higher between-cluster FC,  $r=0.15$ ,  $p=0.0009$ ) of the default-mode network (DMN). These effects remain present at partition size 13. In detail, higher BMI was associated with a reduction of the functional cohesion of the posterior and anterior parts of the DMN, as well as the salience network and the fronto-parietal central executive network. In contrast, high BMI was associated with high functional integration of the anterior DMN and the central executive network with the rest of the brain. These associations persisted after correcting for age and education.

**Conclusions:** Our results indicate a progressive loss of definition of brain networks with higher BMI. Specifically, the high-level cognitive networks seem to loose both functional cohesion and segregation from the rest of the brain as BMI increases. These findings highlight brain resting-state FC abnormalities that might underpin executive dysfunction in obese individuals.

## POSTER PRESENTATIONS

### Board 1, Poster 1

<b>Abstract Topic Category *</b>	Genetics/Epigenetics/Early Determinants of Obesity
<b>Abstract Title *</b>	Leptin independent regulation of body weight
<b>Authors *</b>	Alicja A. Skowronski, Rudolph L. Leibel, Charles A. LeDuc*
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#### Structured Abstract \*

**Background:** Maintenance of reduced body weight is associated with reduced energy expenditure per unit metabolic mass in mice and humans. Lowered leptin, due to decreased fat mass, provides a primary signal for this response, however, leptin deficient (Lep(ob/ob)) mice (and Zucker rats) also reduce energy expenditure following weight reduction, and necessarily, do so in a non-leptin dependent manner.

**Methods:** We assessed the mechanism for this compensation. Lep(ob/ob) mice were fed ad libitum (AL group; n=21) or restricted to 3 kilocalories of chow per day (WR group, n=21). After losing 20% of initial weight (in approximately 2 weeks), the WR mice were stabilized at 80% of initial body weight for two weeks by titrated refeeding and then released from food restriction to enter the body weight re-gain phase. RNAseq was performed on subcutaneous (SCAT) and perigonadal (PGAT) adipose depots of AL and WR mice when the latter were in the weight reduced state. **Results:** WR mice conserved energy (40% during the day and 65% at night below predicted) and, when released to ad libitum feeding, regained fat and lean mass (to AL levels) within 5 weeks. They did so while their ad libitum caloric intake was equal to that of the AL animals. Prior to release from caloric restriction, the WR mice had a significantly lower respiratory exchange ratio (RER) compared to AL; after release RER was significantly higher than the AL group indicating an anabolic state. RNAseq data showed that 94 genes for the SCAT and 84 genes for the PGAT were both significantly (adjusted P value<0.05) and substantially ( $|\log_2$  fold change|>1.0) different in expression (26 genes are in both groups) between the WR and AL groups. These changes in gene expression will be further investigated to identify a signaling factor(s) that contributes to the energy efficiency in the weight reduced state.

**Conclusions:** Lep(ob/ob) mice, lacking functional leptin, when calorically restricted, reduce their energy expenditure both by lowering their core body temperature and increasing metabolic efficiency; they then recover body weight when released to ad libitum feeding through leptin independent pathways that do not involve hyperphagia. We have identified potential factors responsible for this gain in energy efficiency.

## POSTER PRESENTATIONS

### Board 1, Poster 2

<b>Abstract Topic Category *</b>	Genetics/Epigenetics/Early Determinants of Obesity
<b>Abstract Title *</b>	A Role for Fto in Klf15-regulated adipogenesis
<b>Authors *</b>	Jayne F. Martin Carli*, Charles A. LeDuc, Claudia A. Doege, Yiyang Zhang, Rudolph L. Leibel
<b>Institutional Affiliations For Each Author. *</b>	Columbia University, Columbia University, Columbia University, Columbia University, Columbia University
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#### Structured Abstract \*

##### Background:

SNPs in the first intron of FTO have been implicated in obesity by multiple large scale GWAS. While the causal variant and even the gene or genes in this locus responsible for this association are still unclear, expression of Fto in adipose tissue indicates that it may play a role in adipocyte function and/or development.

##### Methods:

We knocked down Fto in both 3T3-L1 preadipocytes as well as primary human adipose stromal cells (ASCs) prior to differentiation and analyzed their development into adipocytes by Oil Red O staining, gene expression studies and flow cytometric analysis of Nile Red incorporation. We performed RNA sequencing on Fto knockdown preadipocytes to identify early targets of Fto.

##### Results:

Fto knockdown in preadipocytes inhibited differentiation into mature adipocytes, in both human ASCs and murine 3T3-L1s due to decreases in total cell number, as well as in the percentage and lipid filling of mature adipocytes. RNAseq in 3T3-L1 preadipocytes identified a significant increase in an inhibitor of adipogenesis, Klf2, in the Fto knockdown condition. There was no corresponding increase in KLF2 expression in human preadipocytes. However, an expression screen of KLF family members in human ASCs revealed a decrease in KLF15 expression following FTO knockdown which was also observed in 3T3-L1 adipocytes. The decrease in Klf15, a pro-adipogenic transcription factor, is consistent with the observed phenotype of impaired differentiation. Fto is a purported m6A RNA demethylase, which may regulate stability or splicing of its targets. Treatment of mature 3T3-L1 adipocytes with Actinomycin D to inhibit transcription did not reveal impairment in stability of the remaining Klf15 transcript. Additionally, expression analysis of splice variants did not indicate alternative splicing of Klf15. The mechanism(s) by which Fto influences Klf15 expression is under analysis.

##### Conclusions:

The loss of Fto inhibits expression of pro-adipogenic Klf15, thereby limiting adipogenesis in both human and murine cells. Effects on both energy intake and adipocyte development have been implicated in the strong association of non-coding sequence variants in FTO with human adiposity. Mechanistically, these effects appear to be conveyed by regulatory functions of these sequences on vicinal genes such as RPGRIP1L and IRX5. The possible role (if any) of the FTO protein, itself, in these processes remains unclear. Our data do suggest a role for FTO in adipose tissue development and lipogenesis.

## POSTER PRESENTATIONS

### Board 1, Poster 3

<b>Abstract Topic Category *</b>	Genetics/Epigenetics/Early Determinants of Obesity
<b>Abstract Title *</b>	The role of SNORD116 in the neuro-molecular pathogenesis of Prader-Willi syndrome
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<b>Structured Abstract *</b>	
<p><b>Background:</b> Prader-Willi syndrome (PWS) is caused by loss of paternally expressed genes in an imprinted region of chromosome 15q. The protean physiological and behavioral phenotypes of this disorder remain unexplained. Rare microdeletion PWS patients define a 91 kb minimum critical deletion region encompassing only three genes: SNORD109A, IPW, and SNORD116.</p> <p><b>Methods:</b> Induced pluripotent stem cells (iPSC) were generated from skin cells of one micro (118 kb) and three large (5–6 Mb) deletion PWS patients. Pluripotent stem cells were differentiated to neurons using a modified dual smad inhibition protocol. A PWS region MS-MLPA assay was used to measure copy number and DNA methylation content in iPSC and iPSC-derived neurons. Islet cell types were quantified from pancreatic sections of P0.5, P30, and adult wild type and Snord116p-/m+ mice.</p> <p><b>Results:</b> Maternal DNA methylation for genes within the PWS region was sustained following iPSC reprogramming and differentiation to neurons from unaffected control, PWS microdeletion, and PWS large deletion. Genes within the PWS minimum critical deletion region remained silenced in both PWS large and microdeletion iPSCs following reprogramming. PWS is associated with hyperphagia, delayed cognitive development, neuroanatomical and, endocrine abnormalities including diabetes. Mice with a paternal deletion of Snord116 (Snord116p-/m+) display many of the endocrinopathies present in PWS, impaired motor learning, and growth deficiency. We identified neuroanatomical defects in iPSC-derived neurons of individuals with PWS, and mice congenitally deficient for Snord116. iPSC-derived neurons from PWS patients, and neurons from Snord116p-/m+ mice, had smaller soma and decreased numbers of neurites. Reduced neuron cell body size was apparent in utero and persisted until at least 4 weeks of age in Snord116p-/m+ mice. The reduction in neuronal soma size was associated with smaller neuronal nucleoli. There were also developmental defects in the endocrine pancreas of Snord116p-/m+ animals that persisted into adulthood (≥20 weeks). Snord116p-/m+ mice had smaller pancreatic islets; within the islets, the percentage of δ-cells was increased, while the percentage of α-cells was reduced. In Snord116p-/m+ isolated islets, Sst and Hhex were upregulated while Ins1, Ins2, Pdx1, Nkx6-1, and Pax6 were downregulated. There was a 3-fold increase in the percentage of polyhormonal cells in the neonatal islets of Snord116p-/m+ mice, which was due primarily to an increase in cells co-positive for somatostatin. Snord116 may play a role in islet cell lineage specification.</p> <p><b>Conclusions:</b> Overall, this work suggests that hypomorphism for Snord116 may play an important role in the neuro-structural and metabolic phenotypes of PWS.</p>	

## POSTER PRESENTATIONS

### Board 1, Poster 4

<b>Abstract Topic Category *</b>	Genetics/Epigenetics/Early Determinants of Obesity
<b>Abstract Title *</b>	Human adipose transcriptome reveals non-conserved long intergenic noncoding RNAs that modulate adipocyte metabolic function
<b>Authors *</b>	Xuan Zhang*, Chenyi Xue, Jennie J. Lin, Jane F. Ferguson, Sager Gosai, Yumiao Han, Christine Hinkle, Wenjun Li, Benjamin A. Garcia, Brian D. Gregory, Raymond Soccio, John Hogenesch, Patrick Seale, Mingyao Li and Muredach P. Reilly
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<b>Corresponding Author Email *</b>	mpr2144@cumc.columbia.edu
<b>Structured Abstract *</b>	<p><b>Background:</b> Long intergenic noncoding RNAs (lincRNAs) are emerging as important modulators of cellular functions and increasingly implicated in human diseases, yet human adipose lincRNAs remain largely unidentified and unexplored for their roles in adipocyte function and obesity. The vast majority of lincRNAs are not conserved in mammals, raising the important question of whether non-conserved adipose lincRNAs in human are functional.</p> <p><b>Methods and Results:</b> Here we performed deep RNA-seq of subcutaneous adipose from 25 humans and identified 1,868 unique lincRNAs expressed in all subjects. Of these, 142 lincRNAs have adipose-enriched expression, 58 have binding of key adipose transcriptional factors, PPAR<math>\gamma</math> and C/EBP<math>\alpha</math> near their loci. Most human adipose-enriched lincRNAs (~85%) are found not conserved in mice yet, and have similar expression levels and binding by PPAR<math>\gamma</math> and C/EBP<math>\alpha</math> relative to conserved adipose lincRNAs. The non-conserved lincAQPEP is the most abundant adipocyte-specific human adipose lincRNA. It is markedly induced during in vitro human adipocyte differentiation, and its expression is increased in obese humans. In addition, chromatin immunoprecipitation sequencing (ChIPseq) confirm high occupancy of PPAR<math>\gamma</math> around lincAQPEP transcription start site in human adipose tissue and cultured adipocytes, suggesting PPAR<math>\gamma</math> may mediate adipocyte-selective lincAQPEP transcription. lincAQPEP knockdown markedly impairs adipogenic differentiation of human adipose stromal cells (ASC). Interestingly, in differentiated ASC-derived adipocytes, lincAQPEP knockdown resulted ~50% decrease in triglyceride content as well as 40-70% reduction of lipogenic gene expression (e.g. SREBF1, FASN, ELOVL6). These data suggest that lincAQPEP may have dual roles in modulating adipocyte differentiation and lipid metabolism. To investigate the molecular mechanisms of its regulatory functions, we performed RNA pulldown assay followed by mass spectrometry and identified hnRNPU (heterogeneous nuclear ribonucleoprotein U) and IGF2BP2 (Insulin-like growth factor 2 mRNA-binding protein 2) as lincAQPEP-interacting proteins. We further validate that lincAQPEP interacts with hnRNPU and IGF2BP2 at distinct subcellular locations to regulate adipocyte differentiation and metabolism. In summary, our data indicate that lincAQPEP, a non-conserved human lincRNA, plays important modulatory roles in adipocyte biology.</p> <p><b>Conclusion:</b> Our studies demonstrate that non-conserved human lincRNA, exhibiting similar abundance and transcriptional regulation as conserved lincRNAs in adipose, may play specific roles in adipocyte function and obesity. In proof of principle, we provide strong evidence for modulatory roles of non-conserved human lincRNA, lincAQPEP, in adipocyte differentiation and metabolism.</p>

## POSTER PRESENTATIONS

### Board 2, Poster 5

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	The DEXLAR study: Rationale and Methods for a Weight-centric Approach to Management of Type 2 Diabetes
<b>Authors *</b>	Alpana P. Shukla*, Leon I. Igel, Rekha B. Kumar, Wanda Truong, Janet L. Feinstein, Rachel Lustgarten, Anthony Casper, Katherine Saunders, Devika Umashankar, Joy Pape, Jonathan Waitman, Paul Christos, Louis J. Aronne
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#### Structured Abstract \*

**Background and Rationale:** Treatment of hyperglycemia in obese patients with type 2 diabetes is both complex and challenging. The addition of insulin with disease progression is associated with further weight gain and worsening insulin resistance. A "weight-centric" approach rather than a "glucose-centric" approach is a therapeutic strategy that may achieve glycemic control by simultaneously addressing obesity— one of the core issues in the pathophysiology of type 2 diabetes. GLP-1 agonists and SGLT-2 inhibitors have independently been shown to improve glycemic control in insulin treated patients resulting in lowering of insulin dosage and weight loss. Exenatide LAR, a once weekly GLP-1 analog, enhances glucose dependent insulin secretion, suppresses inappropriate glucagon secretion and delays gastric emptying resulting in improved glycemic control and weight loss. Dapagliflozin, an SGLT-2 inhibitor causes glycosuria, modest weight loss and lowers blood glucose independently of insulin. It can however cause a paradoxical increase in glucagon concentration with increased endogenous glucose production which can be mitigated by a GLP-1 analog. There has been no study to date examining the efficacy of adding a SGLT-2 inhibitor to a GLP-1 analog in obese, insulin treated patients with uncontrolled type 2 diabetes. We predict that this combination will have an additive/synergistic effect on glycemic control and weight loss.

**Methods:** This is a prospective, randomized, placebo-controlled 24 week trial. The primary objective of the study is to determine the efficacy of Exenatide-LAR and Exenatide-LAR plus dapagliflozin in lowering HbA1c compared with insulin titration in obese, insulin treated subjects with uncontrolled type 2 diabetes. The secondary objectives are to determine the effects on body weight, waist circumference, fasting glucose (FG), fasting lipids, blood pressure and total dose insulin.

75 Subjects with overweight/obesity (BMI  $\geq 27$  kg/m<sup>2</sup>) and type 2 diabetes on basal insulin  $\geq 20$  units per day plus an oral hypoglycemic agent (metformin and /glitazone and / $\alpha$ -glucosidase inhibitor) will be randomized in a 1:1:1 ratio to one of three treatment regimens:

Group 1: Insulin titration + behavioral therapy

Group 2: Exenatide-LAR 2mg q week x 24 weeks + Dapagliflozin placebo x 24 weeks + titrated basal insulin + behavioral therapy.

Group 3: Exenatide-LAR 2mg q week x 24 weeks + Dapagliflozin 5mg QD x 2 weeks followed by 10mg QD x 22 weeks + titrated basal insulin + behavioral therapy.

The study is actively recruiting participants now.

This research is being conducted with support from Astra Zeneca Pharmaceutical LP.

## POSTER PRESENTATIONS

### Board 2, Poster 6

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Three-month feasibility analysis: Non-randomized pilot testing of a technology-assisted weight management intervention among Veterans within the Veteran Affairs (VA) primary care (PC)
<b>Authors *</b>	Nadera Rahman, BA*, Monika Pietrzak, JD, Clare Viglione, MPH, Hedda Boege, Leigh Loving, BS, Katrina Mateo, MPH, Natalie Ricci, MPH, Natalie Berner, BA, Gail Schechter, RD, Melanie Jay, MD, MS

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#### **Structured Abstract \***

**Background:** We developed a technology-assisted, moderate-intensity weight management intervention called Goals for Eating and Moving (GEM) to deliver 5As (Assess, Advise, Agree, Assist, Arrange) weight management counseling within the VA's patient-centered medical home (called Patient Aligned Care Teams (PACT)). Veterans use an online goal-setting tool that generates tailored materials and facilitates in-person and telephone counseling with health coaches who support PACT counseling and referral to VA weight management services. At one-year, we expect that 27% of patients will have clinically significant ( $\geq 5\%$ ) weight loss. We report 3 month outcomes of a non-randomized feasibility study.

**Methods:** Veterans with overweight/obesity and upcoming PC visits were recruited through mailings and phone calls. At baseline, Veterans completed surveys, created lifestyle goals, and had anthropometric measurements. A non-clinical research assistant trained as a health coach using motivational interviewing and following health coach protocols, then provided counseling. The Veterans then received up to 6 telephone coaching sessions with the same health coach until returning for a 3-month in-person study visit.

**Results:** We recruited 11 Veterans to participate in our study (91% male, 46% Black, 27% White, 27% Hispanic, mean age = 55.36 years (SD=15.10), mean BMI=30.1 kg/m<sup>2</sup> (SD=4.47)). Immediately after the baseline health coaching session, 11/11 participants had set lifestyle goals, 8/11 increased or maintained motivation to lose weight, and 11/11 increased or maintained confidence in ability to lose weight. Two participants dropped out of the study and 1 was lost to follow up. At 3 months, a per-protocol analysis found that 8/8 participants engaged in phone coaching (range 2-6 calls, mean of 4 calls). Furthermore, 7/8 participants expressed interest in involvement in intensive weight loss programs at the VA and of those, 1 participant enrolled in and showed continued involvement. Four (50%) participants lost more than 1 kg, 3 of whom (37.5%) had  $\geq 5\%$  weight loss. Two (25%) stayed within 1 kg of their original weight, and 2 (25%) gained more than 1 kg. The mean weight change was -1.33 kg (SD 5.5).

**Conclusion:** This early analysis demonstrates the feasibility and acceptability of this intervention among Veterans, as demonstrated by their engagement in the GEM intervention, increased motivation and confidence, and weight loss. We anticipate that the 6- and 12-month data will show further weight loss. This study has led to process improvements to increase patient retention and engagement. We have begun recruitment for a pilot RCT of the intervention and have applied for future funding.

## POSTER PRESENTATIONS

### Board 2, Poster 7

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Applied systems thinking to build collaborative capacity for wellness programming in urban high schools
<b>Authors *</b>	David W. Lounsbury*, Lynn Fredericks, Camille Gonzalez, Jean Lim, Sara Helper, Sarah Martin, Michelle Brouchard, Judith Wylie-Rosett
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#### Structured Abstract \*

**Background.** Obesity has quadrupled in US adolescents in the past 30 years. To help address this public health problem, we conducted a school-based intervention to promote wellness programming in N=8 New York City high schools. Although high schools are ideal settings for engaging adolescents, they are diverse, complex systems and therefore present many potential opportunities for, and challenges to, health promotion. We hypothesized that each school's potential to foster healthier choices among the student body could be better understood and managed where systems thinking were utilized by members of local school wellness councils (SWCs). Systems thinking is used to represent interdependencies among parts or elements of a system that may facilitate or inhibit achievement of desired outcomes and goals. Qualitative causal loop diagrams (CLDs) are used to graphically notate the hypothesized dynamics, or causal structure, of a dynamic problem of interest in terms of feedback loops.

**Methods.** Working in partnership with HealthCorps – an in-school program that places full-time trained coordinators in classrooms to mentor and teach high school students – the research team supported facilitation of SWCs in planning, implementing and evaluating wellness activities intended to engage students in skill-building wellness activities. CLDs depicting strategies to build school-level capacity and student-level behavioral change were introduced to SWCs. Over the course of a single academic year, we observed how SWC members applied these tools to choose wellness priorities and subsequently design and execute 'action plans' to mount local initiatives.

**Results.** Two CLDs were disseminated by eight designated SWC coordinators, who filed monthly qualitative progress reports that we used to document SWC processes and outcomes associated with applied systems thinking. The Student CLD represented processes that explained how students' gradual participation in wellness activities at school can help them learn new health-related skills, which comes through trying things out on their own terms (experimentation), building confidence that they can do it (self-efficacy), which in turn can give them the confidence they need to keep doing the health-related skill(s) as well as to share and motivate other students (peers) to start participating in wellness activities, too. The School CLD represented processes that explained how the school as a whole can collaborate to develop and support wellness activities for students, underscoring interdependencies among four elements of collaborative capacity, namely: (1) organizational, (2) relational, (3) member, and (4) programmatic.

**Conclusions.** Results demonstrated utility of integrating a systems thinking approach in school-based wellness programming.

## POSTER PRESENTATIONS

### Board 2, Poster 8

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Obesity Is Linked To Better Survival With Major Infectious Diseases: Concordance Of Results In The Clinic And The Laboratory.
<b>Authors *</b>	Syed F. Mehdi, Navneet Sahota, Amrat Kumar, Farah AlSaati, Vaibhav Patel, Faiza S. Malik, Jesse Roth.
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#### Structured Abstract \*

Obesity promotes inflammation accompanied by the metabolic syndrome, which is typically associated with increases in cardiovascular disorders, diabetes, cancer, and Alzheimer disease, as well as shortened lifespan. In this study, we show that obesity, while having very serious long term deficits, may have short term benefits. We present over 20 epidemiologic studies of six infectious diseases including tuberculosis, pneumonia, American trypanosomiasis, and sepsis that relate increased adiposity with significantly diminished mortality. This benefit was reproduced in mice in preliminary experiments by us and by others. Specifically, adiposity, generated by weeks on a high fat diet, markedly reduced death of mice from (a) trypanosomiasis, a major endemic protozoan disease of Latin America, and (b) sepsis, a major cause of death in the USA. Obesity's well-earned negative reputation growing out of studies of the metabolic syndrome long term in older patients (and the multi-fold expansion of the population over 65), has led the biomedical community to approach very cautiously any suggested benefits of obesity. Based on our collection of epidemiologic studies and of pilot studies in the laboratory, we suggest that adiposity benefits individuals in their struggles with infections throughout most of their lives, an "immuno-metabolic shield" that is especially important in early and middle life. We posit that this protective role is evolutionarily very ancient and continues to the present but has been diminished in relative importance by (i) the containment of infections over the last century; (ii) the multi-fold increase in the proportion of elderly patients in the population; and (iii) the spectacular rise in the prevalence and severity of obesity and the metabolic syndrome.

## POSTER PRESENTATIONS

## Board 3, Poster 9

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Somali, Latino & Hmong "Radio Stories" about Children's Healthy Eating and Exercise: A Pilot Study
<b>Authors *</b>	Chrisa Arcan, Kathleen Culhane-Pera, Shannon Pergament, Khalid Adam, Xai Gao Sheng Chang, Naima Dhore, Hodan Dualeh, Mikow Hang, Nira Ly, Marty Navarrete, Lucky Omaar, Luis E. Ortega, Maira Rosas-Lee, Mai See Thao, Charles Vang, Maria Beatriz Torres
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<b>Corresponding Author Email *</b>	Chrisa Arcan

### Structured Abstract \*

**Purpose:** Following a Community-Based Participatory Research approach, three "Radio Stories," an entertainment health education tool, were developed to inspire Somali, Latino, and Hmong families to make healthy lifestyle changes to prevent type 2 diabetes.

**Methods:** Three dramatic linguistically and culturally-appropriate “radio stories” were developed by interviewing families who had successfully managed their diabetes through lifestyle changes. To test the effectiveness and acceptability of “radio stories,” 123 participants (43 Hmong, 40 Latino, 40 Somali) were randomized to intervention (listened to “radio stories”) and control (listened to audio-taped brochures of relevant health information). Intentions to engage in healthy lifestyle behaviors (16 items) were measured pre and post. Mixed-model analysis of variance was used to examine the intervention effect (net difference) for each survey item.

**Results/Findings:** At baseline, more than 60% of participants reported strong intentions to engage in healthful dietary and physical activity behaviors. Somali and Latino participants were more likely to improve intentions after listening to "radio stories", whereas Hmong participants were more likely to improve intentions after listening to the brochure. After listening to the radio story, Somalis improved their intention to reduce family intake of sugary drinks ( $p=0.003$ ) and fast-food ( $p=0.0008$ ), and eat smaller portions ( $p=0.035$ ), while Latinos improved their intention to reduce family intake of sugary drinks ( $p=0.036$ ) and to manage their stress ( $p=0.006$ ). No statistical significance was found on survey items for Hmong participants.

**Conclusions:** "Radio stories" can be an effective health education method especially among Somalis and Latinos. It could potentially be used for other health conditions and in various health settings.

## POSTER PRESENTATIONS

### Board 3, Poster 10

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Model of energy balance predicts body weight and food intake in obesity/diabetes clinical trials
<b>Authors *</b>	Jangir Selimkhanov*, W. Clayton Thompson, Cynthia J. Musante
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#### Structured Abstract \*

##### Background

One of the major difficulties in anti-obesity drug development is prediction of long-term body weight (BW) loss and the underlying changes in food intake (FI) due to drug treatment. Here, we develop a mathematical model of FI that, along with an energy balance model, can be used to predict long-term BW changes in response to various clinical pharmacotherapies. In addition, we evaluate whether the model can predict the effect of combination therapies with existing approved agents.

##### Methods

A semi-mechanistic model of energy balance and body composition, which relates change in BW to the change in FI, was adapted from Chow and Hall (2008). Expanding on work in Gobel et al. (2015), we incorporated a FI model, which describes initial reduction in food intake due to drug treatment followed by compensation and associated weight-regain, into the energy balance model. We embed the combined FI/BW model in a two-level mixed effects statistical framework and fit it to BW data from published anti-obesity and diabetes clinical trials.

##### Results

The model captured the dose-dependent effects of individual drugs and their combinations on FI and resulting BW changes. Identified model parameters describing FI reduction and BW regain allow for prediction of the magnitude of initial BW loss as well as its long-term durability.

##### Conclusions

The method presented here provides an attractive approach to identifying a set of existing therapies that have the greatest potential for combination and to estimating their BW and FI effect sizes in the future. Additionally, the mechanistic model of FI and BW allows for prediction of long-term BW and FI dynamics based on the observed/predicted initial BW loss.

## POSTER PRESENTATIONS

### Board 3, Poster 11

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Psychological Predictors of Weight Loss and Habit Formation in an Outpatient Weight Loss Program
<b>Authors *</b>	Sabrina M. Jiang*, Betty Kovacs, Rich Weil
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#### Structured Abstract \*

##### Background

Finding successful psychological predictors of weight loss can be challenging. The Three-Factor Eating Questionnaire (TFEQ) and the Overeating Habit Questionnaire (OHQ) are validated surveys used frequently in the obesity field. We were interested to know in this pilot study if these questionnaires, administered to obese adult men and women over the course of a 52-week, hospital-based, outpatient weight loss program, predicted weight loss.

##### Method

We administered the TFEQ (subscales: cognitive restraint, uncontrolled eating, and emotional eating) and the OHQ to two groups of grade 2 and 3 obese adults at the Mount Sinai St Luke's Hospital outpatient weight loss program (Group 1: m = 4, f = 11, avg age = 44.2, avg BMI = 42.9; Group 2: m = 2, f = 11, avg age = 43.9, avg BMI = 40.3). The TFEQ was administered prior to starting the program at baseline (BL) and at week 12 because weight loss in our program at week 12 is a significant predictor of weight loss at week 52. The OHQ was administered at BL and week 52.

##### Results

Group 1 had significant changes in TFEQ subscale scores from week 1-12 (cognitive restraint = +31.3%, p = 0.0016, uncontrolled eating = -14.8%, p = 0.018, emotional eating = -20.8%, p = 0.039). None of the subscale scores at BL correlated with initial weight or BMI, or percent weight change at week 12. However, cognitive restraint score change correlated negatively with percent weight change at week 12 ( $R^2 = 0.31$ , p = 0.03).

Group 2 had significant changes in overeating habit score from week 1-52 (score change = -38.6%, p = 0.028). A negative score is desirable; a lower score means a lower overeating habit. OHQ score at BL had no correlation with initial weight, BMI, nor percent weight change at week 52, but score change from week 1-52 correlated positively with percent weight change at week 52 ( $R^2 = 0.3712$ , p = 0.061).

In group 1, significant changes in OHQ scores occurred from week 1 to week 12 (score change = -18.4%, p = 0.028), but these changes were not correlated with percent weight change at week 52 ( $R^2 = 0.0834$ ).

##### Conclusions

The TFEQ predicted percent weight change earlier in a weight loss program than the OHQ. Because 3-month weight change predicts 52-week weight change, we recommend targeting habit formation earlier in a weight loss program to improve weight loss.

## POSTER PRESENTATIONS

### Board 3, Poster 12

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Coadministration of Canagliflozin (CANA) and Phentermine (PHEN) for Weight Management in Overweight and Obese Adults
<b>Authors *</b>	Priscilla Hollander, <sup>1</sup> Harold E. Bays, <sup>2</sup> Julio Rosenstock, <sup>3</sup> Mary Ellen Frustaci, <sup>4</sup> Albert Fung, <sup>4</sup> Frank Vercruysse, <sup>5</sup> Ngozi Erundu <sup>4</sup> Keith J. Miller presenting as an encore*
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<b>Structured Abstract *</b>	<p>CANA is an SGLT2 inhibitor approved for type 2 diabetes mellitus (T2DM) treatment that increases urinary glucose excretion and provides a calorie deficit, leading to weight loss that has plateaued over 26 weeks in T2DM studies. As CANA may cause increased calorie intake, adding PHEN, an appetite suppressant, may facilitate further weight loss. This 4-arm, 26-week, Phase 2 study evaluated the efficacy/safety of CANA 300 mg + PHEN 15 mg (CANA/PHEN), CANA 300 mg, PHEN 15 mg, and placebo (PBO) in 334 adults without T2DM who had BMI 30 to &lt;50 kg/m<sup>2</sup> or, if with hypertension and/or dyslipidemia, BMI 27 to &lt;50 kg/m<sup>2</sup> (mean weight, 102.9 kg; BMI, 37.3 kg/m<sup>2</sup>). At Week 26, weight loss was statistically superior with CANA/PHEN vs PBO (P &lt;0.001; Figure). CANA/PHEN, PHEN 15 mg, CANA 300 mg, and PBO produced weight changes of -7.5%, -4.1%, -1.9%, and -0.6%. Significantly more patients achieved ≥5% weight loss with CANA/PHEN vs PBO (66.7% vs 17.5%; P &lt;0.001). CANA/PHEN also resulted in a significant PBO-subtracted reduction in systolic BP (-4.2 mmHg; P = 0.015). CANA/PHEN was generally well tolerated, with no new or unexpected safety signals. CANA/PHEN, PHEN 15 mg, CANA 300 mg, and PBO were associated with changes in heart rate of +3.5, +4.1, +0.7, and -0.7 bpm. In conclusion, CANA/PHEN provided significantly greater weight loss vs PBO in overweight/obese adults, suggesting its potential use in chronic weight management.</p>

## POSTER PRESENTATIONS

### Board 4, Poster 13

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Characterizing Eating Behavior of Long-Term Weight Reduced Individuals
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#### Structured Abstract \*

Successful and sustained weight loss is a critical intervention to reduce the morbidity and mortality associated with obesity. While many individuals successfully lose weight, only a very small number are able to maintain it. It has been suggested that the salient behavioral features of Long-term Weight Reduced individuals (LOWER) include persistent intake of a diet low in calories and fat and restricted in diet variety. The purpose of this pilot study is to examine the eating behavior of individuals who have lost a significant amount of weight (i.e., 30 pounds or more) and maintained this weight loss for a significant period of time (i.e., 12 months or longer). To date, nine LOWER individuals and three BMI-matched, non-dieting healthy controls (HC) have participated in an ad libitum laboratory lunch meal. Preliminary results revealed that, on average, LOWER participants consumed an average of  $645 \pm 296$  kcals compared to  $828 \pm 480$  kcals in controls, ( $F(1,10) = 0.64$ ,  $p = .442$ , partial  $\eta^2 = .060$ ), with 25.2% ( $\pm 13.7$ ) of calories from fat compared to 44.0% ( $\pm 6.9$ ) in HCs, ( $F(1,10) = 4.98$ ,  $p = .050$ , partial  $\eta^2 = .332$ ). Mean dietary energy density (kcal/gram) of food consumed by LOWER participants was 0.63 compared to 0.99 in HCs, ( $F(1,10) = 4.68$ ,  $p = .056$ , partial  $\eta^2 = .319$ ). Of the 21 food items presented, LOWER participants consumed a mean of 6 different foods compared to 7 in HCs, ( $F(1,10) = 0.30$ ,  $p = .595$ , partial  $\eta^2 = .029$ ). Initial results suggest that LOWER participants tended to ingest fewer calories, consumed significantly fewer calories from fat and a lower energy density meal than HCs. These data may provide useful insight regarding successful strategies to maintain significant weight loss. Recruitment is ongoing and additional data will be presented.

## POSTER PRESENTATIONS

### Board 4, Poster 14

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Piriform cortex response to milkshake is negatively associated with saturated fat intake
<b>Authors *</b>	Mary V. Burke*, Annika J. Tanke, Dana M. Small
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#### Structured Abstract \*

Food intake is regulated by homeostatic mechanisms as well as hedonic and sensory signals, including olfaction. Amassing evidence links excess consumption of palatable foods high in saturated fat and refined carbohydrates to perturbations in metabolic and hedonic systems involved in the control of feeding. Moreover, high-fat diet was recently shown to produce olfactory sensory neuron loss and alter olfactory- and reward-driven behaviors in rodents (Thiebaud et al., 2014). However, the impact of such diets on chemosensory system function in humans remains a matter for debate. As part of a clinical weight loss trial, we assessed the relationship between perceptual and hedonic ratings for food stimuli, neural response to receipt of a sweet and fatty liquid, and dietary intake of saturated fat and free sugar in overweight and obese participants (11M, 29F; BMI=33.6 kg/m<sup>2</sup>; age=31.1). At baseline, participants tasted a series of flavored puddings and jellos which varied in either fat or sucrose content (puddings: 0%, 3.1%, 6.9%, and 15.6% w/v fat; jellos: 0M, 0.1M, 0.56M, and 1.0M sucrose). Liking and wanting as well as perceived intensity, sweetness, saltiness, fattiness, creaminess, and oiliness were rated using Labeled Magnitude and Visual Analog Scales. In a separate session, we used functional MRI to measure BOLD response to oral receipt of milkshake (MS) vs. a tasteless, odorless solution (TS). Dietary data were collected using a validated semi-quantitative food frequency questionnaire. Preliminary analyses revealed a positive correlation between saturated fat intake and wanting ratings for puddings but not jellos. Greater fat intake was also associated with decreased BOLD response to MS vs. TS in the piriform cortex. This effect was not dependent on age, sex, or BMI, but was abolished when rated wanting for puddings was included as a covariate in the design. Consistent with previous work in animals, these preliminary findings suggest a link between dietary fat intake, chemosensory processing, and food reward.

## POSTER PRESENTATIONS

### Board 4, Poster 15

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Preliminary Studies of Simulated Eating Responses to Dieting Failure and Success Scenarios in a Pre-Bariatric Surgery Population
<b>Authors *</b>	M. Herzog <sup>1</sup> , J.D. Hamm <sup>1</sup> , D. Igudesman <sup>1</sup> , S. Tamura <sup>1</sup> , P. Colon <sup>1,2</sup> , A. Shechter <sup>1</sup> , J. Albu <sup>2</sup> , B. Laferrère <sup>1</sup> , D. Bowman <sup>1</sup> , J.M. Brunstrom <sup>3</sup> , J. McGinty <sup>2</sup> , X. Pi-Sunyer <sup>1</sup> & H. Kissileff <sup>1</sup>
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#### Structured Abstract \*

Personality traits and dimensions (e.g. restraint and disinhibition) of eating affect responses to dieting setbacks and successes, which could impact long-term weight loss. In particular, high emotional reactivity and poor affect regulation can contribute to relapse in response to dieting failure or success. To assess the possibility that proxy measures and eating scenarios could predict potential responses to dieting success and failure we used a portion-selection paradigm as a measure of food intake. It was expected that in response to a hypothetical weight loss failure scenario, as emotionally related disturbance increased, simulated portion size selection of energy-dense foods would increase, and that as eating restraint increased, portion size selection of energy-dense foods would decrease.

Six female and two male obese bariatric surgery candidates ( $\bar{x}$  age = 35  $\pm$  6.90 years, BMI = 44.89  $\pm$  3.58 kg/m<sup>2</sup>) completed a battery of standardized questionnaires to assess emotional functioning and dimensions of eating behavior. Participants were presented with images of six high and six low energy-dense foods on a computer screen and asked to create the portion of each food that they would eat in response to scenarios of weight loss failure and success. Selected portion sizes were regressed from mean-centered questionnaire scores. Given the limited statistical power for a sample size of n=8, a relaxed significance level of alpha=0.1 for Pearson product-moment coefficients was used.

In response to the failure scenario, emotion-dysregulation scores were positively correlated with simulated portion sizes of high energy-dense pizza ( $r=.62$ ,  $p=.1$ ) and potato chips ( $r=.70$ ,  $p=.05$ ), and negatively correlated with low energy-dense grapes ( $r=-.65$ ,  $p=.08$ ). Restraint scores were negatively correlated with portions of pizza ( $r=-.80$ ,  $p=.02$ ), French fries ( $r=-.63$ ,  $p=.09$ ), olives ( $r=-.79$ ,  $p=.02$ ), and potato chips ( $r=-.79$ ,  $p=.02$ ), and disinhibition scores were positively correlated with portion sizes of grapes ( $r=.63$ ,  $p=.09$ ). In response to the success scenario, concern with shape was negatively correlated with portions of apples ( $r=-.65$ ,  $p=.08$ ), turkey ( $r=-.63$ ,  $p=.09$ ) and edamame ( $r=-.72$ ,  $p=.04$ ), and restraint with grapes ( $r=-.66$ ,  $p=.08$ ) and apples ( $r=-.64$ ,  $p=.09$ ). Trait anxiety, emotional eating, and impulsivity did not significantly relate to portion selection in either condition.

These preliminary data suggest that dimensions of eating and emotional reactivity are associated with sizes of selected portions, and these relationships accord with the original predictions. If these responses to the weight gain and loss scenarios in relation to emotional reactivity persist after surgery, they are likely to be predictors of long-term difficulties in maintaining reduced weight.

## POSTER PRESENTATIONS

### Board 4, Poster 16

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Obesity intensifies hepatotoxicity by asparaginase in mice deleted for GCN2 but not ATF4
<b>Authors *</b>	Inna A. Nikonorova (1), Emily T. Mirek (1), Michael P. Goudie (1), Yongping Wang (1), Joseph L. Dixon (1,2), Tracy G. Anthony (1,2)
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#### Structured Abstract \*

Liver dysfunction is a serious adverse effect of asparaginase treatment in patients with acute lymphoblastic leukemia (ALL) that reduces overall survival. Asparaginase depletes circulating asparagine causing rapid tumor regression and induces amino acid stress response mechanisms in normal cells allowing them to adapt. Dysfunction in the amino acid deficiency pathway launched by GCN2 kinase (aka eIF2AK4) results in inability of the liver to adapt to asparaginase and leads to hepatotoxicity. GCN2 kinase is activated by uncharged tRNA molecules that are thought to accumulate in the cells during amino acid starvation. Upon activation, GCN2 phosphorylates eukaryotic initiation factor 2 (eIF2) and inhibits overall protein synthesis. At the same time phosphorylation of eIF2 promotes selective translation of activating transcription factor 4 (ATF4) which reconfigures the cellular transcriptome to alleviate the amino acid stress. A recent clinical report identified obesity as one of the predicting factor for severe hepatotoxicity by asparaginase. Molecular mechanisms of this clinical observation remain to be determined. The focus of our study was to examine the role of the GCN2 pathway on the background of obesity in the development of hepatotoxicity by asparaginase. We induced obesity in wild type, *Gcn2*<sup>-/-</sup> and liver specific-*Atf4*<sup>-/-</sup> (*AlbCre Atf4f/f*) mice and treated them with Elspar L-asparaginase at 0 or 3 IU per gram body weight for 8 days. Biochemical analysis of the liver tissues showed that asparaginase treatment of obese mice resulted in hepatic steatosis and development of advanced endoplasmic reticulum stress, that intensified significantly in *Gcn2*<sup>-/-</sup> but not *AlbCre Atf4f/f* mice. We also found that the mTORC1 activity is inhibited in the livers of asparaginase-treated wild type and *AlbCre Atf4f/f* mice, whereas in *Gcn2*<sup>-/-</sup> livers we observed strong activation of mTORC1 pathway suggesting that GCN2 signals to mTORC1. Overall our study provides important molecular insights into the mechanism of acute liver damage by asparaginase and identifies a novel role for GCN2 in coordinating mTORC1 signal transduction.

## POSTER PRESENTATIONS

### Board 5, Poster 17

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	The effects of a high fructose diet on the gut microbiome, intestinal permeability and inflammatory markers: A controlled clinical intervention study
<b>Authors *</b>	Ryan W. Walker*, Inga Peter, Jeremiah Faith, Jose Clemente, Jeanine Albu, Ruth J. Loos
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#### Structured Abstract \*

**Background:** Americans commonly consume excess amounts of dietary fructose. Added fructose has been shown to have an adverse impact on metabolic health, including increased insulin resistance and type 2 diabetes (T2D) risk. However, the mechanisms that link dietary fructose and metabolic health are poorly understood. Malabsorption of fructose in the small intestine is common in the population, allowing dietary fructose to reach the colon where it may alter the structure of the gut microbiome, increase intestinal permeability and trigger inflammatory responses impacting T2D risk. Using a controlled dietary intervention, this proposal aims to elucidate whether commonly consumed levels of dietary fructose influence metabolic outcomes through altering the gut microbiome.

**Methods:** Twenty healthy, normal weight men and women will be randomized to individualized isocaloric, weight-maintaining diets in a crossover design. Participants will consume a 14-day added fructose diet (25% total daily calories) or an energetically equivalent 14-day added glucose diet after which they cross over to the alternative treatment group. At baseline, within and between treatments we will assess 1) bacterial 16S rRNA sequencing from stool, 2) intestinal permeability, 3) anthropometrics and 4) markers of T2D risk: glucose and insulin, inflammatory cytokines, endotoxemia and liver fat. Germ-free mice will undergo a similar added sugar dietary intervention to study the effects of high fructose on physiology in the absence of gut bacteria. Additionally, uncultured microbiome samples from human participants in the intervention will be transplanted into germ free mice to study the impact of human donor microbiome on mouse physiology in the absence of a dietary intervention.

**Results (expected):** We aim to determine the effects of excess fructose consumption on intestinal permeability, markers of inflammation and the gut microbiome in humans. We expect that the high fructose diet will increase intestinal permeability and plasma markers of inflammation. Abundance, diversity and overall taxonomic profile of the gut microbiome will be altered by the high fructose diet and species that favor fructose as a substrate will proliferate. These effects will be independent of weight gain.

**Conclusions:** Alterations of the gut microbiome by excess dietary fructose may help explain why high fructose consumption is linked to obesity and diabetes. This controlled human clinical study will potentially establish a cause-effect relationship between dietary fructose-induced changes in the gut microbiome, gut health and factors known to increase risk for T2D. Findings could be rapidly translated directly to specific recommendations for prevention and treatment of obesity and T2D.

## POSTER PRESENTATIONS

### Board 5, Poster 18

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	fMRI Visual and Auditory Processing after RYGB and Sleeve Gastrectomy
<b>Authors *</b>	Shaunte Baboumian, 2Spiro Pantazatos, 3Joy Hirsch, 1James McGinty, and 1,4Allan Geliebter
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#### Structured Abstract \*

**Background:** Of the current treatments for obesity, surgery produces the greatest short and long term weight loss. With the marked increase in the number of bariatric surgeries performed, greater understanding of the mechanisms of action is essential. Beyond restrictive and malabsorptive mechanisms, significant neuroendocrine changes occur. We previously reported neural activation changes 1 month post-surgery.

**Methods:** We compared blood oxygen level dependent (BOLD) signals before and 3 months after sleeve gastrectomy and Roux-en-Y bypass surgery in response to both visual and auditory high versus low energy food cues. We also added a very low calorie control group.

**Results:** Postsurgical reductions in fMRI activity were found in key areas of the reward pathway, along with postprandial increases in the satiety hormone GLP-1.

**Conclusion:** Elucidating postsurgical brain activation changes and in relation to satiety hormone GLP-1 could provide a basis for new surgical and pharmacological interventions to produce and maintain long term weight loss.

## POSTER PRESENTATIONS

### Board 5, Poster 19

<b>Abstract Topic Category *</b>	Interventions and Clinical
<b>Abstract Title *</b>	Effects of Simple Distraction Tasks on Food Cravings in Men and Women with Grade 2 and 3 Obesity
<b>Authors *</b>	Richard Weil*, Simon Klebanov, Betty Kovacs, Andrew McClelland
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#### Structured Abstract \*

##### Background

Food cravings play an important role in binge eating and obesity. Cognitive distraction tasks performed in the laboratory such as computer card sorting and Corsi blocks can successfully reduce cravings but are impractical for use in public. It is suggested that future studies identify distraction tasks that can be used in naturalistic settings without the use of computer technology. Furthermore, many studies have clarified that food cravings are associated with visual imagery, but few studies have compared the effects of distraction tasks that incorporate tactile sensation plus vision, and tactile sensation without vision, on changes in food craving intensity and image vividness of food, and especially not in individuals with class 2 and 3 obesity.

##### Method

We tested the effect of four tasks (finger tapping the forehead, finger tapping the ear, toe tapping the floor while seated at a table, and staring at a blank white wall for control) on investigator-induced food cravings and image vividness of 55 obese subjects' four favorite foods ( $m=10$ ,  $f=45$ ; avg BMI = 43.7). For baseline values, subjects' cravings were induced by a script read to them by the investigator and then subjects immediately rated the food craving intensity and image vividness on a 100mm visual analog scale (VAS). Then, for each task (each randomly assigned to one of the foods), subjects performed four 30-sec trials while thinking about the food, followed immediately by rating the craving intensity and image vividness of the food. We used a within subject 4x4 factorial design (4 trials, 1-4, for each condition: control, forehead, ear, and toe tapping). Single factor repeated measures ANOVA was performed for cravings and images to test for changes between baseline and all four trials.

##### Results

Craving intensity and image vividness of the subjects' favorite foods decreased across all four trials and for all four tasks. Mean decrease in VAS craving intensity was -14.0, -14.8, -17.0, and -28.5 for ear, toe, wall, and forehead, respectively. Mean decrease in VAS image vividness was -24.2, -29.7, -32.1, and -39.7 for wall, ear, toe, and forehead, respectively. Repeated measures ANOVA showed that changes in all trials were significant.

##### Conclusions

Four simple 30-sec distraction tasks, two of which can be performed discretely in public (wall and toe), significantly reduced the intensity of food cravings and image vividness of the food in grade 2 and 3 obese men and women. The greatest reductions were observed with forehead tapping.

## POSTER PRESENTATIONS

### Board 5, Poster 20

<b>Abstract Topic Category *</b>	Population Health and Epidemiology
<b>Abstract Title *</b>	Lack of Correlations between BMI, Waist Circumference, and Biomarkers of the Metabolic Syndrome in Men and Women with Grade 2 and Grade 3 Obesity
<b>Authors *</b>	Richard Weil, Simon Klebanov, Xavier Pi-Sunyer, Betty Kovacs
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#### Structured Abstract \*

##### Background

It is widely acknowledged that there is a positive correlation between BMI and biomarkers of the metabolic syndrome. However, large data sets such as NHANES are sometimes reported using BMI's from 20 to an abrupt cut point of 35. That is, the positive association is presented graphically with the biomarker of interest on the Y axis and BMI on the X axis, with no values greater than 35 on the X axis. This presentation leads to the assumption that the curve, frequently presented as J-shaped, would continue to rise as BMI rises beyond 35. In some cases, such as the NIH Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults, BMI cut points as low as 30 are used to present health risks associated with increasing BMI. In other cases, such as in Zhu et al (Am J Clin Nutr 2002;76:743-9), the odds ratios for the presence of obesity-associated risk factors associated with rises in BMI were estimates derived from logistic regression models using NHANES data for white men and women aged 20-90 years, with the reference point set at BMI of 23.7 and 21.8 for men and women, respectively. The results showed an exponentially upsloping line from a BMI of 16 to a cut point of 42. We suggest that these presentations are misleading; that is, there is not always a positive correlation between obesity, determined by BMI, and biomarkers of the metabolic syndrome.

##### Methods

This was a retrospective, cross-sectional chart review of 168 male and female adult patients with an average BMI of 44.0 enrolled in the Mount Sinai St. Luke's Weight Loss Program. Using BMI from 35 to 69.9 as a continuous variable, linear regression correlations were performed for the associations between BMI and LDL, HDL, triglycerides, resting blood pressure, fasting glucose, and total cholesterol. Patients taking medications to control blood glucose, blood pressure, and lipids were excluded from the analyses.

##### Results

We did not find any clinically significant correlations between BMI and metabolic syndrome biomarkers in men and women with BMIs from 35 to 72. Although some statistically significant correlations were found (small effect size), clinically significant correlations were not for BMI versus HDL, LDL, triglycerides, fasting blood glucose or resting blood pressure, and total cholesterol.

##### Conclusions

Biomarkers of the metabolic syndrome and BMI are not always positively associated in men and women with grade 2 and 3 obesity.

## POSTER PRESENTATIONS

### Board 6, Poster 21

<b>Abstract Topic Category *</b>	Population Health and Epidemiology
<b>Abstract Title *</b>	Obesity phenotypes and type 2 diabetes and cardiovascular disease in the UK Biobank
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#### Structured Abstract \*

**Aim:** We aimed to examine association between one or more obesity phenotypes and presence of type 2 diabetes (DM) and cardiovascular disease (CVD) in the UK Biobank, a large population-based study of half million participants in the UK.

**Methods:** We categorized the population into fifteen exclusive groups, based on the combinations of lean/normal/obese phenotypes determined using three anthropometric measures – body-mass index (BMI; <25 kg/m<sup>2</sup>, 25 to <30 kg/m<sup>2</sup> and ≥30 kg/m<sup>2</sup>; \*23 kg/m<sup>2</sup> for South Asians) and sex-, ancestry-specific tertiles of waist-hip ratio (WHR) and body-fat percentage (BF%), e.g. a group of participants would have lean phenotype by all three measures, another group with lean phenotype by BMI but normal/obese by WHR and BF%, and so on. DM and CVD were self-reported and confirmed with the use of medications (DM) and the presence of hospital ICD-10 codes (CVD). Analysis was performed among Europeans (n=472,837), Afro-Caribbeans (n= 8,039) and S Asians (n= 8,067). **Results:** The prevalence of DM and CVD increased with the number of obese phenotypes i.e. from 0.6% and 4.6% among leanest group to 11.7% and 14.6% among the obese by all three measures, respectively. The distribution of the obesity phenotype varied significantly between ancestries, with S Asians less likely than others (8.8% vs 11.2% for Afro-Caribbeans and 16.6% for Europeans) to be lean on all three measures. Significant ancestry-level differences exist in the prevalence of DM and CVD, with higher disease prevalence among S Asians (DM: 14.6%; CVD: 12.2%), and at a leaner phenotype, while the prevalence of DM was lowest among Europeans (DM: 3.8%; CVD: 8.8%) and CVD among Afro-Caribbeans (DM: 8.6%; CVD: 6.8%). Among Europeans, BMI and WHR had stronger association with both DM and CVD than BF%, while WHR stood out as being strongly associated with DM and CVD among S Asians and Afro-Caribbeans, e.g. DM prevalence among Europeans who were obese only by BF% was 2.55% as compared to obese by BMI only (4.44%) and obese by WHR (4.93%). Among S Asians, obese by WHR only group had DM and CVD prevalence of 20.47% and 15.66% and as compared to obese by BMI only (DM:17.50%, CVD: 12.5%) and obese by BF% only (DM: 12.54%, CVD: 11.31%). Afro-Caribbeans had associations similar as of S Asians, although their prevalence of DM and CVD was lower.

**Conclusion:** Ancestry-level differences in adiposity measures should be taken into consideration when evaluating their risk for DM and CVD.

## POSTER PRESENTATIONS

### Board 6, Poster 22

<b>Abstract Topic Category *</b>	Population Health and Epidemiology
<b>Abstract Title *</b>	Home Environment Factors Associated with Dietary and Physical Activity Behaviors of Low-Income, Overweight and Obese Bronx Youth
<b>Authors *</b>	Conlon, BA,1* Isasi, CR,1 McGinn, AP,1 Lounsbury, D,1 Mossavar-Rahmani, Y, 1 Diamantis, PM, 2 Groisman-Perelstein, AE, 2 Wylie-Rosett, J1
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#### Structured Abstract \*

**Background:** Family-based weight management programs are the most recommended interventions for the treatment of childhood obesity; however, few studies have examined childhood obesity risk factors in the home environments of low-income, urban families.

**Objective:** With the aim of informing interventions, this cross-sectional study examined home environment factors associated with dietary intake and physical activity levels of overweight and obese (BMI  $\geq$ 85th percentile) youth.

**Methods:** Baseline data from 7–12 year old children and their parent or primary caregiver (n=301 parent-child dyads) enrolled in a family weight management program in an urban hospital were analyzed. Children's weight-related outcomes included fruit/vegetable (FV) and sugar-sweetened beverage (SSB) intake measured by the Block Kids Food Frequency Questionnaire, and moderate-vigorous physical activity (MVPA) and sedentary time (ST) derived from accelerometry data. The sociocultural (parenting practices and family meal habits) and physical (food, screen-media, and physical activity resource availability) home environments were assessed using parent-reported responses to validated survey questions. Multivariable logistic regression was used to examine home environment associations with children's weight-related outcomes adjusting for potential confounders.

**Results:** The odds of children consuming  $\geq$ 1 cup of fruit/day was significantly associated with frequency of family meals (OR 1.88, 95% CI 1.02 to 3.46) and frequency of meals in front of the TV meals (OR 0.60, 95% CI 0.37 to 0.99). The odds of children consuming  $\geq$ 1 cup vegetable/day was significantly associated with home fruit/vegetable availability (OR 1.96, 95% CI 1.05 to 3.67) and sugar-sweetened beverage (SSB) availability (OR 0.42, 95% CI 0.20 to 0.92). The odds of children drinking  $\geq$ 5% of calories/day from SSB was associated with parents limit setting of soda/snacks (OR 0.68, 95% CI 0.52 to 0.88). Children's likelihood of engaging in sedentary time was associated with parent monitoring (OR 1.99, 95% CI 1.39 to 2.85) and the frequency of watching TV during meals (OR 2.20, 95% CI 1.17 to 4.12). Children's likelihood of engaging in moderate-vigorous physical activity was associated with owning active video games (OR 0.42, 95% CI 0.20 to 0.90).

**Conclusions:** Parenting practices, family meal habits, food availability, and video game availability may be important components of primary care-based pediatric weight management programs among Bronx families.

## POSTER PRESENTATIONS

### Board 6, Poster 23

<b>Abstract Topic Category *</b>	Population Health and Epidemiology
<b>Abstract Title *</b>	Make Half Your Child's Plate Fruits and Vegetables: Correlations with Food-Related Practices and the Home Food Environment
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#### Structured Abstract \*

**Purpose:** Few studies have examined how often the United States Department of Agriculture's (USDA) MyPlate guidelines are followed including limited methods of how to measure it beyond observation. This study examined the prevalence of parental report of children's adherence to MyPlate guidelines of 'fill ½ your plate with fruits and vegetables (FV)' and associations with parent report of food-related practices and the home food environment.

**Methods:** Baseline data (n=160 parent-child dyads) from the Healthy Home Offerings via the Mealtime Environment (HOME) Plus study were analyzed. HOME Plus was a randomized controlled trial to prevent excess weight gain among 8–12 year-old children. Parents were predominantly female (95%) while children were equally split by gender. Based on Social Cognitive Theory, parent and child surveys assessed food-related personal, behavioral and home environmental factors, including self-efficacy to cook healthy meals, cooking skills, neophobia, family meal frequency and home food availability. Children's height and weight were measured by study staff. Spearman correlations were used to assess associations between a newly created ½ plate FV variable 'During the past seven days how many times was ½ of your child's plate filled with fruits and vegetables at dinner?' (½ plate FV) and personal, behavioral and environmental factors as well as child standardized body mass index (BMIz scores).

**Results:** Parents reported their children had ½ their plate filled with FV at dinner on average 2.6 days per week. Adherence to ½ plate FV was significantly and positively associated with parent self-efficacy to cook healthy meals, parent cooking skills, parent perception of child's cooking skills, family meal frequency and availability of a variety of fruits and vegetables in the home while a significant inverse association was found for child food neophobia. The ½ plate FV variable was not significantly associated with child BMIz.

**Conclusion:** Results suggest that nutrition programs may increase children's adherence to MyPlate guidelines of having ½ their plate filled with FV by promoting healthful meal planning and cooking skills for both parents and children, increasing children's willingness to eat more FV and the availability of FV in the home.

## POSTER PRESENTATIONS

### Board 6, Poster 24

<b>Abstract Topic Category *</b>	Population Health and Epidemiology
<b>Abstract Title *</b>	Epicatechin, Procyanidins, Cocoa and Appetite – a randomized controlled trial.
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#### Structured Abstract \*

**BACKGROUND:** Two recent human randomized controlled trials reported that dark chocolate acutely decreased appetite in human subjects, but did not assess the type or concentration of cocoa compounds needed. Several other studies suggest that the cocoa compounds epicatechin and procyanidins may be involved.

**OBJECTIVE:** To test the hypotheses that compared to placebo (an alkalized cocoa mixture, containing essentially no epicatechin or procyanidins), the following beverages cause a decrease in appetite: 1) a non-alkalized cocoa mixture; 2) epicatechin plus placebo; and 3) procyanidins plus placebo. We measured the concentrations of cocoa compounds in the beverages.

**DESIGN:** We used a four-way randomized crossover placebo-controlled human trial balanced for period and carry-over effects with 28 healthy young-adult male participants. We also conducted a smaller (n=14) parallel secondary randomized trial in which we explored the effects of higher doses of epicatechin and procyanidins. Our primary measure of appetite was ad-libitum pizza intake 150 minutes after beverage ingestion. We used linear mixed models analysis.

**RESULTS:** The beverage with the non-alkalized cocoa mixture containing 0.6 mg epicatechin, 0.2 mg catechin and 2.9 mg monomer-decamer procyanidins per kg of body weight did not decrease pizza intake significantly (p=0.29) compared to placebo. In the smaller secondary trial a combination of epicatechin and the non-alkalized cocoa mixture containing 1.6 mg epicatechin per kg of body weight, did significantly decrease pizza intake by 18.7% (p=0.04).

**CONCLUSIONS:** Our non-alkalized cocoa mixture was only able to cause a significant acute decrease in food intake after being supplemented with epicatechin. It is possible that epicatechin at a dose >1.6 mg per kg of body weight, alone, or in concert with appropriate catalytic cocoa compounds, may be useful for helping people control their food intake; and that other cocoa compounds at higher doses than those in our non-alkalized cocoa mixture may be effective.

## POSTER PRESENTATIONS

### Board 7, Poster 25

<b>Abstract Topic Category *</b>	Population Health and Epidemiology
<b>Abstract Title *</b>	Facilitators and Barriers to Healthy Eating and Disease Management Among Low-Income Seniors Residing in Subsidized Housing: A Case Study
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#### Structured Abstract \*

**Background:** Reducing barriers to food access can help alleviate or eliminate risk factors for nutrition-related chronic illnesses. These barriers may be exacerbated among older adults living in subsidized living communities, who already experience a disproportionate burden of disease. Neighborhoods with poor accessibility to healthful foods and an overabundance of fast food restaurants have been linked to a higher prevalence of chronic disease among low-income seniors. Conversely, increasing access and availability of healthful foods can facilitate primary and secondary disease prevention and management. A clear understanding of the social determinants of health and how food choices and behaviors can be improved is fundamental during nutrition program planning and implementation. The present study evaluated if community-driven nutrition education programming can be implemented within a subsidized living setting to facilitate improvements in dietary intake and self-management of nutrition-related chronic conditions among low-income seniors.

**Methods:** Formative research methods were implemented to collect information using ethnographic and phenomenological techniques. Residents were recruited to participate in monthly food focus groups, which included hands-on cooking activities, taste testing, and informal discussions related to nutrition, chronic illness, and interest in and preference for health-related programming. Recipe development for the focus groups was based on the foods available from the community garden and food pantry, was mindful of cultural sensitivity, clarity, and food cost. The grounded theory approach included a set of techniques for (1) identifying categories and concepts that emerge from focus group text, and (2) relating the concepts into substantive and formal theories.

**Results:** Seven major themes were derived from the NVivo 10 Software data analysis. Themes included: Negative dietary attitudes about nutritional quality, Challenges of change around nutrition and healthy eating, external barriers in the food environment, negative influences in the internal environment, Disconnect between disease state and nutrition recommendations, Difficulties of disease self-management through dietary modifications, Interest for learning new recipes to improve nutrition knowledge base.

**Conclusions:** The themes are considered generalizable to similar populations indicating that community-driven nutrition education programming can be implemented within a subsidized living setting to facilitate improvements in dietary intake and self-management of disease among low-income seniors. This research uncovered two novel concepts; residents were not familiar with healthier food options that were not culturally relevant and community tensions existed among the residents due to a lack of social cohesion. Future research must consider these novel concepts while developing nutrition programming within subsidized housing facilities.

## POSTER PRESENTATIONS

### Board 7, Poster 26

<b>Abstract Topic Category *</b>	Population Health and Epidemiology
<b>Abstract Title *</b>	Evaluation of a school nurse–led severe obesity intervention in New York City schools: Implementation and impact on BMI percentile change, school absences, and school nurse visits
<b>Authors *</b>	Krista Schroeder*, Haomiao Jia, Y. Claire Wang, Arlene Smaldone
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#### Structured Abstract \*

**Background:** The Healthy Options and Physical Activity Program (HOP) is an intervention for kindergarten through fifth grade children with severe obesity who attend New York City schools. The purpose of this study was to evaluate implementation of HOP and examine its impact on BMI percentile change, school absences, and acute illness/injury visits to the school nurse at 1 year follow-up.

**Methods:** This study employed a retrospective cohort design. To examine HOP implementation, participation rate, session frequency and content, and factors associated with participant enrollment were examined. To assess program impact, children who participated in HOP were compared to 1:1 propensity score matched children who were eligible but did not participate. Data analysis included descriptive statistics, Wilcoxon signed rank and McNemar's tests, and logistic regression.

**Results:** During 2012–2013, approximately 5% (n=1,049) of eligible children participated in HOP. Almost one third of participants (32.6%) had  $\geq 1$  chronic illness. Low school nurse workload, low school poverty rate, older age, higher BMI percentile, and presence of a chronic diagnosis were significantly associated with student selection for HOP. Program intensity was low (median 1 session/year). Parental attendance at HOP sessions was rare (3.2% of sessions). There was no decrease in body measures or difference in school absences for participants at 1 year; participants had more acute school nurse visits during the year (5.0 versus 3.7 for boys, 5.9 versus 3.2 for girls,  $p < 0.01$ ).

**Conclusion:** There exists potential for refined and expanded implementation of HOP. Areas of focus for HOP refinement should include increasing frequency and comprehensiveness of HOP sessions, promoting parental involvement, and encouraging selection of younger students for HOP participation.

## POSTER PRESENTATIONS

### Board 7, Poster 27

<b>Abstract Topic Category *</b>	Population Health and Epidemiology
<b>Abstract Title *</b>	Prepregnancy overweight and obesity are associated with impaired child neurodevelopment
<b>Authors *</b>	Elizabeth Widen*, Piera Cirillo, Barbara Cohn, Linda Kahn, Katrina Kezios, Pam Factor-Litvak
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#### Structured Abstract \*

**Background:** Subtle developmental deficits in early childhood may have long-term implications for later educational attainment, occupational achievement, and health. Evidence is mixed regarding the relationship of prepregnancy body mass index (BMI) and pregnancy weight gain with child neurodevelopment. We examined associations between prepregnancy BMI, pregnancy weight gain, and child neurodevelopment at age 9.

**Methods:** Maternal-child dyads were a subgroup (n=1,879) of the Child Health and Development cohort enrolled during pregnancy between 1960 and 1963 at the Kaiser Foundation Health Plan in the Oakland, California, area and followed postpartum. At age 9, children were administered a Peabody Picture Vocabulary Test and the Raven Progressive Matrices. Multivariable linear regression was used to examine the relationship between BMI, pregnancy weight gain, and age-standardized Peabody and Raven scores, adjusting for covariates and evaluating for effect modification by prepregnancy BMI. Covariates included socio-economic status, race, maternal age and parity, gestational age at delivery, and child sex, weight at birth, and weight and height at 9 years.

**Results:** Before pregnancy, a majority of mothers were normal weight (77.2%), while fewer were overweight (11.0%), underweight (8.8%), and obese (3.0%). Compared to normal weight, prepregnancy overweight and obesity were associated with lower child Peabody scores [estimated  $\beta$ : -4.5 (95% CI: -7.7, -1.4),  $p=0.005$  and estimated  $\beta$ : -5.6 (95% CI: -9.8, -1.3),  $p=0.01$ , respectively], but not Raven score. Effects of pregnancy weight gain on child outcomes varied by prepregnancy BMI. Specifically, compared to normal weight women, a 1 kg increase in pregnancy weight gain was associated with 0.30 units higher Peabody score among overweight women [estimated  $\beta$ : 0.30 (95% CI: 0.07, 0.50),  $p=0.01$ ]. Pregnancy weight gain was not associated with child outcomes for women with prepregnancy underweight or obesity [Peabody estimated  $\beta$ : 0.20 (95% CI: -0.13, 0.67),  $p=0.18$  and estimated  $\beta$ : 0.29 (95% CI: -0.09, 0.66),  $p=0.13$ , respectively].

**Conclusions:** Maternal overweight and obesity were associated with lower scores for verbal recognition in mid-childhood. This decrease may not be meaningful on an individual level, but may be important for educational attainment, employment, and earning potential on a population level. There is evidence of effect modification by prepregnancy BMI on the relationship between pregnancy weight gain and child Peabody scores. Specifically, among women with prepregnancy overweight, higher pregnancy weight gain counteracts the detrimental effect of prepregnancy overweight on child age 9 Peabody scores. These findings contribute to evidence linking maternal BMI and pregnancy weight gain with child neurodevelopment.

## POSTER PRESENTATIONS

### Board 7, Poster 28

<b>Abstract Topic Category *</b>	Population Health and Epidemiology
<b>Abstract Title *</b>	Participatory Action Development of a Lifestyle Questionnaire
<b>Authors *</b>	Sarah Martin*, Camille Gonzalez, Judith Wylie-Rosett, Michelle Bouchard, Jean Lim, Suada Fangaj, Giovanni Hall, Josiah Chandler
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#### Structured Abstract \*

**Background:** Items from the Youth Risk Behavior Survey (YRBS) have been used to evaluate the HealthCorps program (Heo et al. J Sch Health 2016). During the 2015–2016 school year, as part of the HealthCorps Building Wellness for Life program, we used an online 34 item lifestyle survey in eight NYC schools to provide individual feedback reports aimed at initiating behavior change. Student evaluations suggested that the survey was complicated, and many students indicated that the results did not reflect their actual health behaviors.

**Methods:** A participatory action process was used to engage teens in revising the questionnaire to make the instrument more relatable and to provide results that teenagers feel more accurately reflect their health behaviors. A 12-item semi-structured survey collected data related to how students (n =34) perceive selected obesity-related categories: sugary beverages, breakfast, fast/junk food, and physical activity. NYC high school students (n=3) helped analyze the results and develop the revised 15-item questionnaire. The revised questionnaire was piloted using a purposive sample of high school students (n=40). The overall categorical classifications obtained using the revised questions were similar to the classification obtained with the corresponding YRBS questions.

**Results:** The revised survey, which was designed to be simpler and more relatable to teenagers, was limited to a total of 15 items. The length of question stems and response choices were also shortened; most questions limited to 4 response choices. The revised questions did not list multiple recall periods (times per day/days per week) and excessive specificity (e.g. serving size descriptions in the response options) was avoided.

**Examples of the revised questions include:**

How often do you exercise hard enough to sweat?

Every day

Most days (4–5 days each week)

Some days (2–3 days each week)

Never

Do you ever drink water?

Yes, I drink a lot

I drink some water

I drink a little water

I don't drink water

**Conclusion:** Obesity-related YRBS questions aimed at quantifying specific behaviors related to energy intake or expenditure may be less useful for identifying behavioral change targets in teens. The revised instrument is designed to be used to evaluate obesity-related behaviors in teens while minimizing barriers such as question burn-out, numeracy and recall challenges, and misinterpretation of terms. Questionnaires using conversational and teen-relevant terminology, while seemingly less sensitive, can provide a more positive user experience and potentially more relevant outcomes.

## POSTER PRESENTATIONS

### Board 8, Poster 29

<b>Abstract Topic Category *</b>	Population Health and Epidemiology
<b>Abstract Title *</b>	Food sources around high schools in the Bronx: unexpected items in unexpected places
<b>Authors *</b>	Brooke Lawrence*, Evans Osei Sarpong Nduro, Salamatu Nurudeen, Sean C. Lucan, MD, MPH, MS*
<b>Institutional Affiliations For Each Author. *</b>	Albert Einstein College of Medicine, Bronx, NY (BL, EN, and SN are summer research students and SL is their faculty advisor)
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#### Structured Abstract \*

**BACKGROUND:** Food sources around schools may be relevant to adolescents' dietary intake and overall health. Studies of food sources around schools have focused mostly on select stores and restaurants. Neglected have been other potential food sources: both storefronts (e.g., various retail outlets) and non-storefronts (e.g., street vendors, farmers' markets, vending machines). This study sought to characterize all the sources of foods and beverages accessible to adolescents around select high schools.

**METHODS:** Researchers selected 10 high schools in demographically distinct areas across the Bronx, NY, and systematically evaluated all streets within a ½ mile of each school for any sources of foods or beverages accessible to adolescents. A distinction was made between 'food businesses' (businesses primarily focused on the provision of foods and beverages like grocery stores and fast food outlets) and 'other businesses' (businesses that might offer foods and beverages but for which such provision was not the primary focus). For foods, a distinction was made between 'healthful' (fruits, vegetables, whole grains, nuts) and 'less-healthful' (e.g., refined sweets, salty snacks). For beverages, categories included 'healthful' (water, milk), 'less-healthful' (sodas, alcohol), and 'other' (diet drinks, juices).

**PRELIMINARY RESULTS:** Assessment of the food sources around school #1 is complete with assessments of food sources around schools #2 and #3 in progress. Around school #1, there were 235 open businesses within a ½ mile by street network. Seventy of these businesses (30%) offered some kind of food or drink. This sum represented the 54 'food businesses' (including 2 street vendors) and 16 of 165 'other businesses' (8.8%). 'Other businesses' that were selling food or drink included outlets such as barber shops, auto repair shops, pharmacies, a car wash, a hardware store, and a gas station. 'Less-healthful' foods and beverages like candy, chips, sugary drinks, and beer were among the items these 'other businesses' offered, but so were some more-'healthful' items like nuts, granola bars, salsa, milk, and water.

**CONCLUSION:** Food sources around schools include businesses beyond just select food stores and restaurants. 'Other businesses' offer foods and beverages—even healthful items in some cases. When data collection is complete we will be able to assess for differences in foods sources by school/school neighborhood. This project is part of broader work to link data about food sources to students' eating behaviors and health measures.

## POSTER PRESENTATIONS

### Board 8, Poster 30

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Leptin does not maintain weight loss in obese mice
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#### Structured Abstract \*

**Background:** Although leptin therapy is not effective in general obesity, robust impact on body weight is observed in rare diseases with leptin deficiency. Clinical data supports that following 10% weight loss (which also creates a relative leptin deficiency), leptin replacement reverses declines in both energy expenditure & satiety associated with weight loss. However, whether leptin therapy prevents weight regain (i.e. weight loss maintenance) has yet to be tested. Therefore, the aim of this study is to evaluate whether leptin therapy is effective for weight loss maintenance using a mouse model of obesity.

**Methods:** Body weight (10%) and plasma leptin ( $\geq 25\%$ ) reduction was achieved via caloric restriction in diet-induced obese (DIO) mice (male C57Bl6N, 60% fat diet from age 6–18 weeks). Two models of weight regain were tested: 1) a weight regain model where mice were transitioned immediately to the weight regain phase after reaching 10% weight loss, and 2) a weight maintenance model where mice were weight stabilized at  $-10\%$  for  $\geq 2$  weeks before entering the weight regain phase, which more closely reflects clinical study design. In both models mice were then switched to ad libitum feeding +/- recombinant leptin treatment during the weight regain phase.

**Results:** The dose of leptin chosen for these studies (2mpk, BID, SC) is comparable to the maximum dose tested for weight loss in human clinical trials, achieving  $\sim 100\text{pM}$  CSF exposure. As expected, this dose caused weight loss (7% over 7 days) in non-obese mice but was attenuated in DIO mice ( $\sim 2\%$  over 7 days). In the weight regain model, leptin treatment (CSF 100pM) did not decrease body weight. Even when leptin was delivered at a much higher concentration (35nM) and continuously via ICV/ minipump application, there was no significant effect. To address concerns related to the relevance of the 60% fat diet, DIO mice were acclimated to a 30% fat diet for three weeks and the weight regain study was repeated. However, dietary fat reduction was not sufficient to uncover leptin (100pM CSF) efficacy. Furthermore, there was no leptin (100pM CSF) benefit in the weight maintenance model.

**Conclusions:** These data suggest that weight reduction & the associated relative leptin deficiency is insufficient to uncover a leptin response for weight maintenance. It is possible that much higher brain exposures ( $> 35\text{nM}$ ) are necessary to drive an effect, however this would be difficult to achieve therapeutically.

## POSTER PRESENTATIONS

### Board 8, Poster 31

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Cyp8b1 ablation prevents western diet-induced weight gain and hepatic steatosis due to impaired fat absorption
<b>Authors *</b>	Enrico Bertaggia <sup>1</sup> , Kristian K. Jensen <sup>2</sup> , Jose Castro-Perez <sup>2</sup> , and Liangsu Wang <sup>2</sup> and Rebecca A. Haeusler <sup>1</sup> .
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#### Structured Abstract \*

**Background and aims:** Bile acids (BAs) are cholesterol derivatives that regulate lipid metabolism, through their dual abilities to promote lipid absorption and activate BA receptors. However, different BA species have varying abilities to carry out these functions. In humans, the levels of the subset of BAs that are 12 $\alpha$ -hydroxylated are negatively correlated with insulin sensitivity. Eliminating 12 $\alpha$ -hydroxy BAs in mice via Cyp8b1 knockout causes low body weight and improved glucose tolerance. The goal of this study was to determine mechanisms of low body weight in Cyp8b1<sup>-/-</sup> mice.

**Methods:** We challenged Cyp8b1<sup>-/-</sup> mice with western type diet for four weeks and assessed body weight and composition. We measured energy expenditure via indirect calorimetry and quantified fecal calories via bomb calorimetry. We carried out lipidomic analyses in intestinal and fecal samples to assess lipid hydrolysis, and performed lipid absorption analysis with radioactive triolein. We used a fat-free diet to assess the requirement for dietary fat in the low body weight phenotype.

**Results:** Cyp8b1<sup>-/-</sup> mice were resistant to western diet-induced body weight gain, hepatic steatosis, and insulin resistance. These changes were associated with increased fecal calories, due to malabsorption of hydrolyzed dietary triglycerides. This was reversed by treating the mice with taurocholic acid, the major 12 $\alpha$ -hydroxylated BA species. The improvements in body weight and steatosis were normalized by feeding mice a fat-free diet.

**Conclusions:** The effects of BA composition on intestinal lipid handling are important for whole-body energy homeostasis. Modulating BA composition is a potential tool for obesity or diabetes therapy.

## POSTER PRESENTATIONS

### Board 8, Poster 32

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Investigating the role of ILDR2 in $\beta$ cell function and diabetes
<b>Authors *</b>	Elizabeth J. Millings*, Charles A. Leduc, Rudolph L. Leibel
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#### Structured Abstract \*

##### Background

ILDR2 (Immunoglobulin-like domain-containing receptor 2) is a single-pass ER transmembrane protein originally identified by our lab as a modifier of diabetes susceptibility in obese mice [1]. Genetic markers with Chr1q23 in which human ILDR2 is located, have been associated with T2D phenotypes [2]. Initial studies of this gene demonstrated that genetically obese (ob/ob) and diet-induced obese B6.DBA congenic mice segregating for a hypomorphic (DBA) allele of *Ildr2* displayed decreased glucose tolerance at 9, 14, and 29 weeks old, reduced glucose-stimulated insulin secretion from isolated islets at 9 and 14 weeks old, and decreased  $\beta$ -cell area at 9 and 21 weeks old [1]. ILDR2 also interacts with ER stress transducers and has a protective role in maintaining hepatic lipid homeostasis [3].

##### Methods

To explore the role of ILDR2 in  $\beta$  cell function, we crossed C57BL/6J mice expressing RIP2-cre to those segregating for a floxed first exon of *Ildr2*. In male progeny, glucose tolerance and hyperglycemic clamps were performed; islet morphology was analyzed by immunohistochemistry.

##### Results

Male,  $\beta$ -cell specific *Ildr2* KO mice had body mass and composition comparable to controls, but displayed decreased glucose tolerance and sustained hyperglycemia by ipGTTs at 8 and 12 weeks old and hyperglycemic clamping at 24 weeks old. These mice exhibited a slight decrease in plasma insulin concentrations during ipGTT but no difference from controls in plasma insulin during hyperglycemic clamping. The insulin sensitivity index (ISI) was slightly decreased KO mice. Immunohistochemical analysis showed enlarged islets and increased  $\beta$  cell area compared to controls.

##### Conclusions

8, 12, and 24 week old, non-obese  $\beta$  cell-specific *Ildr2* KO C57BL/6J male mice display mildly impaired glucose tolerance in association with systemic insulin and  $\beta$  cell phenotypes consistent with insulin resistance. Effects conveyed by other DBA alleles associated with *Ildr2* in the B6.DBA congenic line may have affected the timing and mildness of their  $\beta$  cell failure. The enlarged  $\beta$  cells in the C57BL/6J *Ildr2* KO mice are consistent with cell-autonomous derangements in insulin homeostasis. The molecular bases for these effects are under investigation.

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## POSTER PRESENTATIONS

### Board 9, Poster 33

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	CX3CR1 And CCR2 Synergistically Modulate Inflammatory But Not Metabolic Effects Of High-fat Feeding
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#### Structured Abstract \*

**Backgrounds:** Obesity is associated with a systemic inflammatory reaction that has been associated with the development of type 2 diabetes and atherosclerosis. Substantial evidence points towards the C-C motif chemokine receptor-2 (CCR2) and fractalkine receptor (CX3CR1) as important modulators of metabolic and inflammatory phenotypes in high fat diet (HFD)-induced obesity, but the synergistic effects of dual targeting of CX3CR1 and CCR2 have not been studied. We hypothesize that CX3CR1 and CCR2 exert synergistic effects in HFD-induced obesity.

**Methods:** C57BL/6J wild type mice (WT), Cx3cr1-/-, Ccr2-/- and Cx3cr1-/-Ccr2-/- double knockout mice were fed a 45% HFD (D124551, Research Diets), which is known to promote hypertriglyceridemia and insulin resistance, for up to 6 months starting at 12-wks old (n=10-16 male mice per group).

**Results:** WT, Cx3cr1-/-, Ccr2-/-, and Cx3cr1-/-Ccr2-/- gained weight at a similar rate and developed similar degrees of adiposity and hyperglycemia in response to 45% HFD. All groups demonstrated progressive impairment in glucose tolerance, insulin sensitivity (by Insulin Tolerance Test), and glucose-evoked insulin secretion. A complete blood cell count with differential suggested reduced monocyte count in Ccr2-/- ( $22.2 \pm 10.1\%$  of WT, mean $\pm$ SEM,  $P < 0.05$ ) and Cx3cr1-/-Ccr2-/- ( $10.6 \pm 1.9\%$  of WT,  $P < 0.05$ ), but not in Cx3cr1-/- ( $82.8 \pm 16.3\%$  of WT,  $P = 0.45$ ), consistent with the impaired monocytosis due to Ccr2 deficiency. FACS analysis showed that in stromal vascular cells from epididymal adipose, % of CD45(+)F4/80(+)CD11c(+)MGL1(-) M1-like macrophage was lower while CD45(+)F4/80(+)MGL1(+)CD11c(-) M2-like macrophage was higher in the Cx3cr1-/-Ccr2-/- mice vs. WT mice. In contrast, a single knockout of Cx3cr1 or Ccr2 did not affect macrophage phenotypic switching.

**Conclusion:** A single knockout or double knockout of Cx3cr1 and Ccr2 did not affect weight gain, glucose levels and insulin sensitivity in response to HFD. However, the Cx3cr1-/-Ccr2-/- but not the single knockout of Cx3cr1 or Ccr2 mice, showed reduced adipose macrophage activation. The results indicate that CX3CR1 and CCR2 synergistically modulate inflammatory but not metabolic effects of HFD.

## POSTER PRESENTATIONS

### Board 9, Poster 34

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	The Long Intergenic Non-Coding RNA Landscape in Human Macrophage Activation
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<b>Structured Abstract *</b>	<p><b>Backgrounds:</b> With remarkable plasticity and wide-ranging states of activation in response to environmental challenges, macrophages play a central role in pathogenesis of cardiometabolic diseases (CMDs). However, the long non-coding RNA landscape that regulates macrophage activation is poorly defined. We hypothesize that comprehensive analysis of long intergenic non-coding RNA (lincRNA) expression profiles reveals novel macrophage lincRNA signature.</p> <p><b>Methods:</b> We used deep RNA sequencing to assemble the lincRNA transcriptome in human macrophages (HMDM, N=6 subjects) at rest and also after stimulation with lipopolysaccharide and interferon-gamma for M1-like inflammatory activation, and interleukin-4 for M2-like anti-inflammatory activation (A).</p> <p><b>Results:</b> Through de novo assembly, we identified 2,766 macrophage lincRNAs including 861 previously unannotated novel lincRNAs. The majority (86%) was non-syntenic, or syntenic but not annotated in mouse genomes (B). Many macrophage lincRNAs also demonstrated tissue-enriched transcription patterns (12 %) and enhancer-like chromatin signatures (62 %). Macrophage activation, particularly to the M1 phenotype, markedly altered the lincRNA expression profiles with 96 lincRNAs differentially expressed (fold-change &gt; 2 and FDR &lt; 0.01) (C), suggesting a role for lincRNAs in macrophage inflammatory response. A subset of CMD trait-associated variants in genome-wide association studies tagged lincRNAs that may contribute to macrophage-related human diseases. Induced pluripotent stem cell-derived macrophages (IPSDM) recapitulated lincRNA transcriptome of primary macrophage and provide a high-fidelity model system to study function of lincRNAs in human macrophage biology (D).</p> <p><b>Conclusion:</b> In summary, high-resolution transcriptomics identified 100s of lincRNAs that form part of the cellular response in macrophage activation as well as specific macrophage lincRNAs associated with human CMDs.</p>

## POSTER PRESENTATIONS

### Board 9, Poster 35

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Identification of a GPR171 antagonist that modulates food intake
<b>Authors *</b>	Ivone Gomes <sup>1*</sup> , Jonathan H. Wardman <sup>2</sup> , Erin Bobeck <sup>1</sup> , Abhijeet Kapoor <sup>1</sup> , Jennifer Stockert <sup>1</sup> , Mihaly Mezei <sup>1</sup> , Marta Filizola <sup>1</sup> , Lakshmi A. Devi <sup>1</sup>
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#### Structured Abstract \*

Studies have shown that a number of neuropeptide systems in the hypothalamus are involved in the regulation of food intake and body weight. Among these are peptides derived from proSAAS, a precursor implicated in regulation of body weight. We recently identified GPR171 as a G protein-coupled receptor (GPCR) for BigLEN (b-LEN), a peptide derived from proSAAS. In order to facilitate studies exploring the physiological role of this receptor system, we virtually screened an in-house collection of compounds using a homology model built based on the evolutionarily related P2Y<sub>12</sub> receptor to identify small molecule ligands for GPR171. The hits from the screen were tested in cell-based assays and identified MS0021570\_1 as a GPR171 antagonist. The selectivity of MS0021570\_1 for GPR171 was ascertained using cell lines expressing endogenous receptors. Biochemical characterization verified that MS0021570\_1 binds and exert its effects via GPR171. Examination of the effect of MS0021570\_1 administration to mice showed that chronic administration had no effect on food intake but significantly decreased body weight in wild-type mice; this decrease in body weight was further exacerbated in mice with lentiviral-mediated knockdown of GPR171. Interestingly, in mice with lentiviral-mediated knockdown of GPR171, chronic treatment with MS0021570\_1 significantly decreased the mRNA levels of NPY, a neuropeptide that increases food intake. Together these results suggest that MS0021570\_1 serves as a useful tool to probe the pharmacological and functional properties of GPR171 and could form the basis for therapeutics to treat obesity.

This work was supported by National Institute Health Awards DA008863 and NS026880 to LAD, and DA026434 to MF. JHW was supported by a T32 NIDA training grant DA007135.

## POSTER PRESENTATIONS

### Board 9, Poster 36

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Meal patterns and refeeding recovery following an intermittent fasting protocol for weight loss.
<b>Authors *</b>	Juliet D. Gotthardt* and Nicholas T. Bello
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#### Structured Abstract \*

**Background:** Alternate day, intermittent fasting (IMF) can promote weight loss in obese individuals. However, the persistent effects of IMF on eating behaviors is unknown. We investigated the effects IMF on feeding behavior in diet-induced obese (DIO) mice.

**Methods:** Forty-two C57BL/6 male mice at PND 49 were fed a high-fat diet ad libitum for 8 wks to produce DIO. Mice were placed on one of six dietary protocols (n=6-8/group) for 4 weeks: ad libitum high-fat diet (HFD), IMF of the high-fat diet (IMF-HFD), pair fed to IMF-HFD group (PF-HFD), ad libitum low-fat diet (LFD), IMF of low-fat diet (IMF-LFD), or pair fed to IMF-LFD group (PF-LFD). After which, all groups were refed the high-fat diet for 6 weeks. Meal patterns were recorded with BioDAQ system at the start and end of the diet period and again after the 6 wk re-feeding.

**Results:** On the first day of the diet period, LFD and IMF-LFD ate significantly fewer average number of meals than HFD (~50% for both;  $P < 0.05$ ) and IMF-HFD (~50% for both;  $P < 0.001$ ) groups, though this effect was not observed at the end of the diet period nor after the re-feeding period. On the first day of the diet period, LFD (-45.2%;  $P < 0.05$ ) and IMF-LFD (-64.4%;  $P < 0.01$ ) consumed a significantly smaller average meal sizes (kcal) than IMF-HFD mice. At the end of the diet period, IMF-LFD animals consumed significantly larger average meal sizes than HFD (+53.6%;  $P < 0.01$ ) and LFD (+36.4%;  $P < 0.05$ ) mice. All differences in meals size were abolished after the re-feeding period. Average meal duration (seconds) was significantly higher at the start of diet period in the LFD group than in HFD and IMF-HFD groups (+~82% for both;  $P < 0.05$ ). At the end of diet period, LFD and IMF-LFD mice ate significantly longer meals on average than both HFD and IMF-HFD mice (+~75% for all groups;  $P < 0.001$ ).

**Conclusions:** These findings suggest that meal patterns were transiently altered during the diet period and returned to that of the control (HFD) group after the refeeding period. Moreover, dietary composition served as a greater determinant of feeding behavior than did schedule of access.

## POSTER PRESENTATIONS

### Board 10, Poster 37

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Vitamin D Repletion Reduces Adipose Tissue Fibrosis and Improves Insulin Sensitivity in Humans
<b>Authors *</b>	Kehao Zhang, Akankasha Goyal, Eric Lontchi, Armand Mbanya, Jennifer Ognibene, Raphael Hulkower, Preeti Kishore, Meredith Hawkins
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#### Structured Abstract \*

**Background:** Adipose tissue fibrosis has been implicated as a contributing factor to insulin resistance and adipose inflammation in obesity. Vitamin D has been shown to reduce fibrosis in other tissue types by inhibiting pro-fibrotic processes and collagen synthesis. Thus we hypothesized that vitamin D repletion could reduce adipose tissue fibrosis and improve insulin sensitivity.

**Methods:** Stepped euglycemic, hyperinsulinemic (30 and 80 mU/m<sup>2</sup>/min) clamp studies were performed in 11 obese and insulin resistant human subjects (8M, age 43 ± 4 yr, BMI 33.6 ± 1.4 kg/m<sup>2</sup> and HOMA-IR= 5.1 ± 0.7) to quantify endogenous glucose production and glucose uptake before and after normalizing vitamin D levels (>30ng/ml) with oral vitamin D3.

**Results:** Subcutaneous adipose tissue fibrosis diminished significantly after repletion of vitamin D with oral vitamin D3 supplements, as evidenced by changes in expression of pro-fibrotic genes and by reduced collagen immunofluorescence. Specifically, we observed that the expression of the pro-fibrotic genes HIF1 $\alpha$ , TGF- $\beta$ 1, MMP7, and collagen I, V, and VI in whole fat decreased by 0.42, 0.24, 0.39, 0.47, 0.4, and 0.44-fold, respectively; all results demonstrated statistical significance with p<0.05. Collagen I immunofluorescence decreased by 61% (p=0.04). In addition to this reduction in adipose tissue fibrosis, adipose tissue inflammation also decreased significantly. Vitamin D repletion was associated with 0.37, 0.41, 0.27 and 0.33-fold decreases of expression of the following pro-inflammatory factors: TNF- $\alpha$ , IL-6, iNOS and PAI-1; all p<0.05. Furthermore, the expression of the pro-inflammatory factors TNF- $\alpha$ , IL-6, iNOS and PAI-1 in adipose tissue macrophages also decreased by 0.53, 0.62, 0.54 and 0.46-fold, respectively; all p<0.05. Importantly, these findings were associated with a 34% greater ability of insulin to suppress endogenous glucose production (p= 0.03). Glucose uptake, however, did not show significant change.

**Conclusions:** Vitamin D repletion elicited three beneficial effects in obese, insulin-resistant humans: reduced adipose tissue fibrosis, improved hepatic insulin sensitivity, and decreased adipose tissue inflammation. Thus, correcting vitamin D deficiency in obese, insulin resistant individuals may have favorable metabolic effects by reducing both adipose fibrosis and inflammation, and might therefore have public health benefits in light of the obesity epidemic.

## POSTER PRESENTATIONS

### Board 10, Poster 38

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Serum Excursions of the Putative Anti-Incretin Dopamine are reduced during Mixed Meal Tolerance Testing in Roux-En-Y Gastric Bypass Patients relative to Controls.
<b>Authors *</b>	Gerardo Febres, Antonella Maffei, Sarah Rosen, Judith Korner, and Paul Harris*
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#### Structured Abstract \*

**Background.** Bariatric surgery is an effective treatment for obesity and associated T2DM. Improved  $\beta$ -cell function, as well as improvement in hyperglycemia, independent of weight loss, have been observed when portions of the gastrointestinal tract are bypassed (e.g. Roux-en-Y gastric bypass (RYGB)). Two hypotheses have been developed to explain these observations; the hindgut hypothesis, posits that nutrient delivery to the distal intestine results in the secretion of "incretins," which enhances insulin action (e.g. GLP-1), and the foregut hypothesis, proposes that foregut bypass reduces the secretion of factors that normally defend against hypoglycemia and antagonizes the effects of incretins by decreasing insulin secretion. Recently we demonstrated that; 1) dopamine (DA) mediates a glucose stimulated insulin secretion inhibitory circuit in human  $\beta$ -cells expressing the dopamine receptor, 2)  $\beta$ -cells co-secrete dopamine as well as insulin in response to glucose challenge, and 3)  $\beta$ -cells express the dopamine active transporter (DAT) allowing  $\beta$ -cells to store circulating DA. After ingestion of a standard mixed meal (i.e. mixed meal tolerance testing [MMTT]), healthy human volunteers show significantly increased plasma levels of DA. The kinetics of plasma DA release coincides with the postprandial rise and fall of GLP-1 plasma levels observed after MMTT. These DA excursions might represent "anti-incretins" destined to regulate  $\beta$ -cell insulin secretion, given the ability of  $\beta$ -cells to take-up DA and concentrate DA for vesicular release.

**Methods and Results.** Following IRB approval, we studied 13 subjects enrolled at the Weight Control Center (three obese controls, six after Sleeve Gastrectomy (SG, a foregut sparing metabolic surgery), and four after RYGB (a metabolic surgery which bypasses the foregut). All subjects underwent a standard MMTT with 5 ml blood draws at baseline, 15 minutes, 30 minutes and 60 minutes into EDTA tubes. Plasma samples were prepared and analyzed fresh by HPLC- electrochemical detection following solid phase extraction on alumina oxide. For each subject, the area under the curve (AUC) of the dopamine concentration versus time plot was calculated. We found that the RYGB surgery population had significantly lower plasma dopamine excursions than the combined SG & obese subjects as judged by the AUCs (1740 pg\*min/ml versus 12522 pg\*min/ml, p=0.047)

**Conclusions.** Our results suggest that circulating DA, most likely originating in the gastrointestinal system, satisfies many of the characteristics of the hypothesized anti-incretins and may represent a novel axis of regulation of insulin secretion between the gut and endocrine pancreas.

## POSTER PRESENTATIONS

### Board 10, Poster 39

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	General Control Nonderepressible 2 (GCN2) Kinase Regulates Body Composition and Antioxidant Defenses during Dietary Methionine Restriction.
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#### Structured Abstract \*

**Background:** Dietary methionine restriction (MR) produces physiological responses associated with resistance to metabolic disease and increased lifespan, but the sensing mechanism remains to be established. As a part of the integrated stress response pathway (ISR), the eukaryotic initiation factor 2 (eIF2) kinase, General Control Nonderepressible 2 (GCN2), is a sensor of amino acid insufficiency. We hypothesized that phosphorylation of eIF2 (pEIF2) by GCN2 mediates the metabolic phenotype by dietary MR.

**Methods:** C57Bl/6J wildtype mice (WT) or mice deleted for Gcn2 (GC) were fed an obesity-promoting diet (60% kcal fat) sufficient in methionine (0.86% kcal met, OD) for 1 week. Mice then remained on OD or were switched to an obesity-promoting diet restricted in methionine (0.12% kcal met, MR) for an additional 2 days or 5 weeks (n=6–8 per group). Results were evaluated by 2 factor ANOVA and Tukey post hoc with a significance level set at p<0.05.

**Results:** MR reduced body weight in WT and GC mice similarly (↓22%) even though MR mice consumed more energy (↑13%) than OD mice. WTMR mice also lost a significant amount of body fat (↓15%) as compared to WTOD but surprisingly, GCMR mice lost an insignificant amount of body fat as compared to GCOD (↓4%). Consistent with this difference in body composition, subcutaneous fat weights were decreased ~60% in WTMR as compared to WTOD but unchanged in GCMR as compared to GCOD. In the liver, activation of the ISR was indicated in both WTMR and GCMR via pEIF2. MR also induced ISR genes Atf4 and, Fgf21 and a profile of antioxidant genes including Ho1 and Nqo1 regardless of GCN2 status. On the other hand, MR reduced expression of fatty acid synthesis genes including Scd1 to a greater extent in the liver of WT versus GC mice. Furthermore, expression of the hepatic antioxidant defense gene Sod2 was increased in WTMR but not GCMR.

**Conclusion:** These results indicate that GCN2 contributes to but is not a primary sensor of MR because activation of the ISR in the liver and reduction of body weight occurred largely independent of GCN2. However, certain physiological outcomes such as body composition and mitochondrial oxidative defenses in the liver were influenced by GCN2 status. Our study provides new insights into the GCN2 dependent and independent mechanisms by which MR alters metabolism and cellular defenses.

## POSTER PRESENTATIONS

### Board 10, Poster 40

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Inhibition of Adipocyte Browning and Beiging by Allograft Inflammatory Factor-1 Promotes Obesity and Impairment of Metabolic Health
<b>Authors *</b>	Prameladevi Chinnasamy <sup>1</sup> , Aparna Srinivasan <sup>2</sup> , Isabel Casimiro <sup>3</sup> , Dario F. Riascos-Bernal <sup>1</sup> , Lander Egaña-Gorroño <sup>1</sup> , Dippal Parikh <sup>1</sup> , Vanessa M. Almonte <sup>1</sup> , and Nicholas E.S. Sibinga <sup>1</sup>
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#### Structured Abstract \*

Total body energy expenditure depends in part upon uncoupled respiratory activity of brown adipocytes and beige adipocytes within white adipose tissues, and methods that increase these activities — referred to as browning or beiging, respectively — have therapeutic potential to counter obesity and the metabolic syndrome. Studies in human populations link sequence variants at the allograft inflammatory factor-1 (AIF-1) locus to obesity, adipose inflammation, and diabetes, conditions strongly associated with cardiovascular disease. We assessed a possible causal role of Aif-1 in obesity and diabetes using mouse models. Here we show that genetic inactivation of Aif-1 expression in mice fully blocks high fat diet-induced obesity, limiting expansion of white adipose depots, decreasing lipid accumulation within brown adipose tissues, and improving glucose handling. This protection reflects increased basal metabolic activity, with no significant changes in core body temperature or physical activity. At the tissue level, Aif-1 deficiency promotes brown adipogenic capacity and beiging, with increased expression of key thermogenic genes including UCP1, but does not impair basal white adipogenesis. Mechanistically, brown adipocytes lacking Aif-1 show increased  $\beta$ -adrenergic signaling. Further, the increase in basal metabolism due to loss of Aif-1 improves glucose homeostasis and insulin sensitivity, correlates with reduced inflammatory infiltrates and increased M2 vs. M1 macrophage marker expression in epididymal adipose tissue, and protects against hepatosteatosis. These results describe a novel function for Aif-1, and point to its inhibition as a potential new strategy to prevent obesity and improve metabolic health.

## POSTER PRESENTATIONS

### Board 11, Poster 41

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Bile Acid Synthesis and 12-Hydroxylation are Increased, and Bile Acid Transport is Impaired, in Human Obesity
<b>Authors *</b>	Rebecca A. Haeusler(1)*, Stefania Camastra(2), Monica Nannipieri(2), Brenno Astiarraga(2), Jose Castro-Perez(3), Dan Xie(3), Liangsu Wang(3), Manu Chakravarthy(3), and Ele Ferrannini(2)
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#### Structured Abstract \*

**Background.** Alterations in bile acid (BA) synthesis and transport have the potential to affect multiple metabolic pathways in the pathophysiology of obesity. In this work, we investigated the effects of obesity on serum fluctuations of BAs and markers of BA synthesis.

**Methods.** We measured BA fluctuations in 11 nonobese and 32 obese subjects, and BA transporter expression in liver specimens from 42 individuals, and specimens of duodenum, jejunum, ileum, colon, and pancreas from 9 individuals. We analyzed serum BAs and markers of BA synthesis after overnight fasting, during a hyperinsulinemic-euglycemic clamp, or a mixed meal tolerance test and the association of BA transporter expression with body mass index.

**Results.** BA synthesis markers were twofold higher ( $P < 0.01$ ) and preferentially 12 $\alpha$ -hydroxylated ( $P < 0.05$ ) in obese subjects, and both measures were correlated with clamp-derived insulin sensitivity ( $r = -0.62$ ,  $P < 0.0001$  and  $r = -0.39$ ,  $P = 0.01$ , respectively). Insulin infusion acutely reduced serum BAs in nonobese subjects, but this effect was blunted in obese subjects ( $\Delta$ BAs  $-44.2\%$  versus  $-4.2\%$ ,  $P < 0.05$ ). The rise in serum BAs postprandially was also relatively blunted in obese subjects ( $\Delta$ BAs  $+402\%$  versus  $+133\%$ ,  $P < 0.01$ ). Liver expression of the Na $^{+}$ -taurocholate cotransporting polypeptide (NTCP) and the bile salt export pump (BSEP) were negatively correlated with BMI ( $r = -0.37$ ,  $P = 0.02$  and  $r = -0.48$ ,  $P = 0.001$ , respectively).

**Conclusions.** Obesity is associated with increased BA synthesis, preferential 12 $\alpha$ -hydroxylation, and decreased hepatic BA transport. The findings reveal new pathophysiological aspects of BA action in obesity that may lend themselves to therapeutic targeting in metabolic disease.

## POSTER PRESENTATIONS

### Board 11, Poster 42

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Small animal computed tomography enables longitudinal monitoring of hepatic steatosis in mice with non-alcoholic fatty liver disease
<b>Authors *</b>	Sarah E. Fleet*, Charles A. LeDuc, Christopher B. Damoci, Rudolph L. Leibel
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#### Structured Abstract \*

##### Background

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease and reason for liver transplantation. The hallmark of this disease is lipid accumulation in the liver, which in some individuals can lead to inflammation (NASH) and eventually cirrhosis. Rodent models of NAFLD have been developed, but, as with humans, definitive diagnosis and monitoring of disease progression currently requires liver biopsy. In mouse models this requirement for organ access prohibits monitoring of disease progression in the same animal. Here, we propose to evaluate the utility of small animal computed tomography (CT) to monitor hepatic steatosis in mice.

##### Methods

Both wild type (B6) and obesity-resistant, ApoEKO mice were fed a high fat, high fructose diet (HFHFD) to induce NAFLD. The animals had a baseline CT prior to initiation of HFHFD to serve as a control, and will have CT every 4 weeks for a total of 12 weeks while being fed the provocative diet ad libitum. The fat content of the liver is being assessed using CT and fat-sensitive gating in the image analysis software. The gating has been performed on ex vivo livers and been shown to be a sensitive and reproducible method to determine hepatic fat fraction.

##### Results

Baseline hepatic fat fractions were significantly different between B6 and ApoEKO mice ( $p=0.009$ , data preliminary). Preliminary measurements of hepatic fat content after the first 4 weeks of provocative diet have shown some differences from the baseline scans, and no difference between the wild type and ApoEKO animals.

##### Conclusions

We anticipate that these differences will increase over time (these data will be presented), and that CT will provide a non-invasive means to monitor disease progression in murine models of NAFLD and possibly provide a comparable tool for patients.

## POSTER PRESENTATIONS

### Board 11, Poster 43

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	12-hydroxylated bile acids regulate food intake
<b>Authors *</b>	Sei Higuchi*, Enrico Bertaggia, Kristian Jensen, Liangsu Wang, Rebecca Haeusler
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<b>Structured Abstract *</b>	
<p>Background: Bile acids (BAs) are synthesized from cholesterol in the liver and promote absorption of dietary fat in the intestine. Recent studies show that BAs act as signaling molecules through multiple receptors. There are dozens of types of BAs. Emerging data suggests that the composition of BAs present in an individual affects metabolic regulation. Our recent studies in humans showed that a particular subset of BAs – the 12-hydroxylated BAs (12-OH BAs) – are negatively correlated with insulin sensitivity and positively correlated with BMI.</p> <p>Methods and Results: To determine the direct effects of 12-OH BAs, we evaluated the metabolic function by using genetically modified mice. Deficiency of essential enzyme to produce 12-OH BAs, Cyp8b1, improves insulin sensitivity and reduces body weight in mice. One mechanism by which these occur is that Cyp8b1 deficiency reduces intestinal absorption of hydrolyzed dietary fats in mice. Intestinal lipid induces satiation and inhibition of gastric emptying through activation of intestinal receptors. We hypothesize that Cyp8b1 deficiency causes reduced food intake due to decreased fat absorption and increased fat signaling in the intestine. To evaluate the relationship between food intake and body weight, we performed a pair-feeding experiment. Food intake of Cyp8b1<sup>-/-</sup> mice was lower than WT mice. Body weights of paired-WT mice decreased to the level of the Cyp8b1<sup>-/-</sup> mice. These data indicate that reduced food intake is involved in the low body weight of Cyp8b1<sup>-/-</sup> mice. We evaluated solid and liquid gastric emptying by two methods, and both tests showed that Cyp8b1 deficiency decreased gastric emptying. To test the effect of intestinal lipid, we gave mice a fat-free diet (FFD). On this diet, food intake and gastric emptying were not different between genotypes. However, stimulation with a single fat-rich meal decreased gastric emptying in Cyp8b1<sup>-/-</sup> mice. These data suggest that Cyp8b1<sup>-/-</sup> mice have reduced gastric emptying and increased satiation due to intestinal lipid accumulation.</p> <p>Conclusions: Suppression of Cyp8b1 may be a novel target to reduce gastric emptying and increase satiation for obesity and diabetes treatment.</p>	

## POSTER PRESENTATIONS

### Board 11, Poster 44

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	FoxO Transcription Factors are Required for Hepatic HDL-Cholesterol Clearance
<b>Authors *</b>	Samuel X. Lee*, Markus Heine*, Christian Schlein, Rajasekhar Ramakrishnan, Jing Liu, Ido Haimi, Henry Ginsberg, Joerg Heeren, Franz Rinninger, and Rebecca A. Haeusler
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<b>Structured Abstract *</b>	
<p><b>Background:</b>  Insulin resistance and type 2 diabetes are associated with low levels of high-density lipoprotein-cholesterol (HDL-C). The insulin-repressible FoxO transcription factors are potential mediators of insulin's effect on HDL-C. FoxOs mediate a substantial portion of insulin-regulated transcription, and poor FoxO repression is thought to contribute to the excessive glucose production in diabetes.</p> <p><b>Methods/Results:</b>  In this work, we show that mice with liver-specific triple FoxO knockout (L-FoxO1,3,4), which are known to have reduced hepatic glucose production, also have increased HDL-C. This was associated with decreased expression of HDL-C clearance factors, scavenger receptor class B type I (SR-BI) and hepatic lipase, and defective selective uptake of HDL-cholesteryl ester by the liver. The phenotype could be rescued by re-expression of SR-BI.</p> <p><b>Conclusion:</b>  These findings demonstrate that hepatic FoxOs are required for cholesterol homeostasis and HDL-mediated reverse cholesterol transport to the liver.</p>	

## POSTER PRESENTATIONS

### Board 12, Poster 45

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	High fat diet-induced obesity shifts in the balance of Mmp3 and Timp4 may mediate adipose depot- and sex-dependent adipose expansion in C57BL/6 mice
<b>Authors *</b>	Mi-Jeong Lee*, Yuanyuan Wu, Yasuo Ido and Susan K. Fried
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#### Structured Abstract \*

**Background:** Increased adipocyte size is hypothesized to signal the recruitment of adipose progenitor cells (APC) to expand tissue storage capacity.

**Methods:** To investigate depot- and sex- differences in these processes, male and female C57BL/6J mice (10-weeks-old) were challenged with 14 weeks of high fat (HF) or low fat (LF) diets (D).

**Results:** In females, HFD increased GON depot weight by adipocyte hypertrophy and hyperplasia while in males it was exclusively hypertrophy; in both sexes, inguinal (ING) adipocytes were smaller and depot expansion was due to hypertrophy. Matrix metalloproteinase 3 (Mmp3), an antiadipogenic factor, and its inhibitors, Timps modulate the extracellular matrix remodeling required to recruit adipose progenitor cells (APCs). Mmp3 mRNA was depot different (ING > GON), higher in females than males and mainly expressed in APCs. In males, HFD-induced obesity increased tissue and APC Mmp3 mRNA, and tissue MMP3 protein, but in females it decreased MMP3 protein without affecting its mRNA levels. Timp4 mRNA was mainly expressed in adipocytes. HFD tended to increase Timp 4 expression in females and decreased in males, so the Timp4 to Mmp3 ratio increased in females, consistent with changes Mmp3 activity measured tissue homogenates. Overexpression of Mmp3 in 3T3-L1 adipocytes or exogenous rhMMP3 protein to primary human preadipocytes inhibited differentiation; the effect was attenuated by rhTIMP4.

**Conclusions:** Collectively, these data suggest that Timp4 serves as a signal from adipocytes that inhibits APC Mmp3, triggering their differentiation and hyperplastic expansion in a sex- and depot -dependent manner

## POSTER PRESENTATIONS

### Board 12, Poster 46

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Cephalic-phase insulin release is modulated by dietary carbohydrate content in mice
<b>Authors *</b>	Yonina G. Frim*, John I. Glendinning
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#### Structured Abstract \*

**Background:** Type II diabetes (T2D) is characterized by malfunctions in glucose homeostasis. Because T2D is associated with increased carbohydrate consumption, researchers have been studying how dietary carbohydrate alters sugar processing and insulin release in the body. Insulin release is thought to be elicited by both pre- and post-absorptive mechanisms. Pre-absorptive insulin release is mediated by oral stimulation and is called cephalic-phase insulin release (CPIR). It primes the body for incoming sugar, and enhances glucose tolerance. We focused on CPIR in C57BL/6 (B6) mice.

**Methods:** In Experiment 1, we manipulated the intensity of glucose stimulation by either varying the glucose concentration or the number of licks taken by each mouse. Blood glucose and plasma insulin levels were measured prior to licking and at four time points after initiating licking (5, 15, 30 and 60 min). In Experiment 2, B6 mice were placed on one of three isocaloric diets (2%, 40% or 82% carbohydrate) for two weeks. Afterwards, we compared the magnitude of CPIR across the three dietary treatments. We defined CPIR as a significant increase in plasma insulin (relative to baseline) within 5 min of initiating licking.

**Results:** In Experiment 1, we found that (a) the magnitude of CPIR increased with glucose concentration and number of licks, and (b) 200 licks for a 1 M glucose solution elicited the largest and most reliable CPIR. In Experiment 2, we found that the magnitude of CPIR and the post-absorptive insulin spike increased with carbohydrate content of the diet. Further, maintenance on the 2.2% carbohydrate diet virtually eliminated the CPIR and impaired glucose tolerance.

**Conclusions:** CPIR is a quantitative response that varies as a function of amount of oral stimulation and prior dietary experience.

## POSTER PRESENTATIONS

### Board 12, Poster 47

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Vitamin A and protein kinase C in the regulation of respiration and mitochondrial energy homeostasis
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#### Structured Abstract \*

Obesity and its related disorders, including insulin resistance, are critical public health issues worldwide. Oxidative stress and mitochondrial dysfunctions are among the causes underlying these metabolic diseases, given the central role played by mitochondria in regulating energy metabolism. We identified a novel protein kinase C $\delta$  (PKC $\delta$ ) signaling pathway that requires retinol (vitamin A) as a cofactor and is involved in the regulation of fuel utilization in mitochondria. The mitochondria-localized PKC $\delta$  forms a signaling complex with the adapter p66Shc, cytochrome c and retinol that stimulates the conversion of pyruvate to acetyl-coenzyme A by the pyruvate dehydrogenase complex (PDHC) and regulates glucose flux. We previously demonstrated that excess retinol enhances PKC $\delta$  and PDHC activity and further impairs glucose metabolism in a mouse model of diet-induced insulin resistance.

To unequivocally prove the role of retinol as PKC $\delta$  co-factor in the regulation of mitochondria energy homeostasis and the etiology of the metabolic syndrome, we generated a new mouse strain in which only the retinol-binding site of PKC $\delta$  is mutated (PKC $\delta$ ki-/-). Here we report the first characterization of this strain.

PKC $\delta$ ki-/- mice display a severely reduced Mendelian ratio of PKC $\delta$ ki-/- mice from PKC $\delta$ ki+/- crosses. Given the high-energy requirement during organogenesis, this finding supports the involvement of retinol and PKC $\delta$  as regulator of mitochondrial energy metabolism.

Proliferation assay of mouse embryo fibroblast (MEF) derived from the PKC $\delta$ ki+/+ and PKC $\delta$ ki+/- embryos showed that the percent of metabolically active PKC $\delta$ ki+/+ MEF cells was enhanced upon retinol stimulation. This stimulatory effect was dramatically attenuated in the PKC $\delta$ ki+/- MEF cells. Moreover, the number of metabolically active cells was significantly lower in the PKC $\delta$ ki+/- MEF cells, suggesting that the PKC $\delta$ ki mutation impairs the respiratory capacity of the mitochondria already in heterozygosity.

The T and B cells proliferative capacity was assessed in 8 weeks old PKC $\delta$ ki+/+, PKC $\delta$ ki+/- and PKC $\delta$ ki-/- mice and was diminished in a gene dosage-dependent manner. However, the proliferative response of T and B cells to phorbol ester was similar among genotypes, further supporting our hypothesis that the compromised mitochondrial energy metabolism of the mutant cells is dependent on the inactivation of the PKC $\delta$  retinol-binding site.

Overall, our preliminary findings suggest that vitamin A and PKC $\delta$  have an important role in regulating respiration and energy homeostasis and, potentially, in a number of pathological conditions linked to mitochondrial dysfunctions. This novel knock-in mouse model constitutes an important tool to further understand the role of the mitochondria-localized PKC $\delta$  in human health.

## POSTER PRESENTATIONS

### Board 12, Poster 48

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Dach1: A Liver Transcriptional Co-Repressor that Contributes to Defective Fibrinolysis in Obesity
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#### Structured Abstract \*

Increased risk of thrombosis and impaired fibrinolytic activity are critical pathophysiologic consequences of obesity, but the molecular-cellular mechanisms are poorly understood. We recently showed that a transcriptional co-repressor, DACH1, is elevated in human liver as a function of BMI. In obese mice, elevated hepatocyte DACH1, by suppressing the transcription factor ATF6, activates an ER stress response and causes defective insulin signaling. Here we reveal that another consequence of DACH1-mediated ATF6 suppression in hepatocytes in obesity is decreased hepatic expression of tissue plasminogen activator (tPA), which is a transcriptional target of ATF6. We hypothesized that DACH1-mediated tPA suppression in obesity would disturb the tPA/PAI1 balance in such a manner as to affect bleeding and thrombosis. In support of this hypothesis, we found that genetic knockout of DACH1 in hepatocytes in obese mice (a) raised hepatic tPA (Plat) mRNA and protein in the liver; (b) increased tPA levels, tPA enzymatic activity, tPA:PAI1 ratio, and fibrin-degradation products in the blood; and (c) lengthened both tail bleeding time and the time to occlusion in the FeCl<sub>3</sub>-induced carotid arterial thrombosis model. Moreover silencing of the Plat gene in hepatocytes in hepatocyte-DACH-knockout mice reversed these effects. These data provide new molecular and pathophysiological insight into hepatocyte-mediated mechanisms linking obesity with defective fibrinolysis. Moreover, the findings reveal that regulation of tPA in hepatocytes, a cell type not previously appreciated as playing a major role in tPA biology, is a key determinant of the tPA/PAI1 balance in blood and its effects on bleeding and thrombosis.

## POSTER PRESENTATIONS

### Board 13, Poster 49

<b>Abstract Topic Category *</b>	Metabolism and Integrative Physiology
<b>Abstract Title *</b>	Effect of a dopamine agonist on food reinforcement and autonomic response to binge food cues in those with and without BED.
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#### Structured Abstract \*

**Background:** The role of low dopamine (DA) tone to eating behavior differences between obese binge eaters (B, n = 9) and non-binge eaters (C, n = 6) is not established. We assessed the relationship of dopamine to food reinforcement under three doses of methylphenidate (MPH), a dopamine agonist, and the correlation of self-reported eating behavior with autonomic nervous system response to binge food exposure under the same MPH dosing conditions. We hypothesized 1) that food reinforcement would decrease under MPH dosing compared to placebo, 2) that heart rate (HR) in response to food exposure under placebo dosing would correlate with B status, and 3) that dosing with MPH would disrupt the positive correlation between HR and B status.

**Methods:** Ss took part in four separate 2-hr sessions in which they consumed 600 kcal of a liquid meal 30 minutes before eating an ad libitum meal (0 MPH), or performing an operant task to choose food or non-food gifts under 0, 20 or 40 mg MPH. HR was monitored continuously during all sessions. The main outcome measures were ad libitum food intake, food break point (FBP; the highest ratio of computer responses completed in the operant task when choosing the food category) and HR.

**Results:** Dosing with 20 mg and 40 mg MPH produced a 39% decrease in FBP ( $F = 8.6$ ,  $p = .012$ , power = .77) but no significant difference between B and C. Fat grams of operant task food choices were significantly reduced by 43% ( $F = 8.6$ ,  $p = .013$ , power = .77) by 20 mg MPH. B status was correlated with heart rate (HR) response measured 120 minutes after binge food exposure under 0 mg MPH ( $r = 0.67$ ,  $p = 0.009$ ). Additionally, HR, measured at baseline, correlated positively with kcal of ad libitum food intake ( $r = 0.67$ ,  $p = 0.009$ ). Dosing with 20 and 40 mg of MPH eliminated the correlations between HR, B status and ad libitum food intake.

**Conclusions:** Our data suggest that differences in eating behavior between B and C are not due to DA transporter function. The data also suggests that B status is accompanied by physiological responses that predict binge eating. Dosing with a DA reuptake inhibitor may be useful in reducing intake of high fat foods independent of binge eating status, and through disruption of physiological responses to binge foods may provide a method for reducing cue-induced bingeing.

## POSTER PRESENTATIONS

### Board 13, Poster 50

<b>Abstract Topic Category *</b>	Neurological
<b>Abstract Title *</b>	Changes in neural activity of the prefrontal cortex during eating in humans.
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#### Structured Abstract \*

**Background:** Functional neuroimaging shows reduced post-ingestive lateral prefrontal cortex (IPFC) activity in people with obesity. Technical limitations have not allowed for the exploration of the neurofunctional response during eating.

**Methods:** Using functional near infrared spectroscopy (fNIRS) we measured changes in neural activity in the IPFC and the medial PFC (mPFC) in 29 healthy males (BMI <25 n = 14; BMI > 25 n = 15) before and during eating to test the hypothesis that loss of control overeating is associated with a greater increase of activity in the mPFC vs. IPFC.

Participants underwent two ten minute, ad libitum eating sessions: one in which they ate a preferred food (PF) and one in which they ate a less preferred food (NP) presented in random order. LOC status was based on the EDE-Q.

**Results:** While IPFC and mPFC neural activity did not differ before eating, during eating mPFC activity was greater than IPFC activity in 15 subjects [irrespective of BMI group] and this was associated with increased intake (grams) of both PF and NP ( $235 \pm 90$  vs.  $163 \pm 19$ ,  $p = 0.026$  PF;  $217 \pm 155$  vs.  $132 \pm 73$  NP,  $p = 0.054$ ).

**Conclusion:** These results suggest that a greater mPFC vs. IPFC neural activity during eating may be a marker of overeating.

## POSTER PRESENTATIONS

### Board 13, Poster 51

<b>Abstract Topic Category *</b>	Neurological
<b>Abstract Title *</b>	Attention bias and emotional dysregulation in response to food stimuli may lead to dietary disinhibition and blunted somatosensory awareness in obese adults with binge eating disorder
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<b>Corresponding Author Email *</b>	ra2211@columbia.edu; Aviram.f.roni@gmail.com
<b>Structured Abstract *</b>	<p>Binge eating disorder (BED) is prevalent in obese adults, but its bio-behavioral markers are not completely understood. Purpose: The current project sought to identify psycho-neurobiological markers in 42 adults: 'obese with BED' (n = 13) and 'obese' controls (n = 29), who following a meal, were brain scanned while shown images of food or control items (i.e. office supplies). Their disinhibition, behavioral approach, and anxiety were assessed using questionnaires. Methods: Two BOLD signal contrast maps were examined: 1/"food versus nonfood", and 2/"high energy processed food (HEPF) versus low energy unprocessed food (LEUF)". Psycho-behavioral group differences were correlated with BOLD signal, and regression was used to test the strength of these relationships. RESULTS: analysis of "food versus nonfood" (<math>p \leq 0.005</math>; <math>k \geq 88</math>) showed group differences in the right insula, ACC, lingual gyrus, BAs 19 &amp; 32, IPL, left MFG and postcentral gyrus, as well as in the PCC and cuneate gyrus (both bi-laterally). In response to "HEPF versus LEUF", the groups differed in the left MFG, BA 6, and SFG (<math>p &lt; 0.01</math> ; <math>K \geq 119</math>). Furthermore, the groups differed in the relationships between 'disinhibition' and BOLD signal in both the left postcentral gyrus (<math>p = 0.04</math>) and the ACC &amp; BA 32 (<math>p = 0.02</math>). 'Disinhibition' was higher in the 'obese with BED', and negatively associated with BOLD signal in the left postcentral gyrus (<math>p = 0.01</math>). 'Disinhibition' scores predicted weaker BOLD signal in the left postcentral gyrus for all participants as one group (<math>p = 0.04</math>). DISCUSSION: when faced with binge-triggers, obese with BED showed neural markers associated with attention bias, emotional dysregulation, and disinhibition. Greater 'disinhibition' in obese with BED may be linked with dysfunctional left postcentral gyrus.</p>

## POSTER PRESENTATIONS

### Board 13, Poster 52

<b>Abstract Topic Category *</b>	Neurological
<b>Abstract Title *</b>	The FTO locus: obesity and the primary cilium
<b>Authors *</b>	George Stratigopoulos+*, Lisa C. Burnett+, Ross Tanis++, Rudolph L. Leibel+
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<b>Structured Abstract *</b>	
<p><b>Background</b> Common intronic single nucleotide polymorphisms (SNPs) in the fat mass and obesity-associated (FTO) gene are highly associated with per-risk-allele increased body weight in adults. Previous studies have suggested that SNPs embedded in CUX1 regulatory elements in intronic FTO affect the expression of FTO and the nearby ciliary gene, RPGRIP1L.</p> <p><b>Methods</b> We employed in vivo murine gene-deletion models and in vitro genome editing.</p> <p><b>Results</b> We show allele-dose-dependent co-regulation of FTO/RPGRIP1L expression in iPSC-derived human hypothalamic neurons. We also demonstrate the synergistic contributions of hypothalamic Fto and Rpgrip1l to obesity susceptibility, and the role of the primary cilium in leptin sensitivity and the development of the feeding neurocircuitry.</p> <p><b>Conclusions</b> Our findings suggest a mechanism by which apparently functional polymorphisms in intron 1 of FTO affect hypothalamic FTO and RPGRIP1L expression and thereby influence energy homeostasis.</p>	

## POSTER PRESENTATIONS

### Board 14, Poster 53

<b>Abstract Topic Category *</b>	Neurological
<b>Abstract Title *</b>	Neuroimaging to Predict Bariatric Surgery Outcomes.
<b>Authors *</b>	Julia Lushing*, Allan Geliebter
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#### Structured Abstract \*

Bariatric surgery is currently the most effective intervention to promote durable weight loss in obese individuals. There is still uncertainty, however, which mechanisms are responsible for weight loss after bariatric surgery and what factors make patients more likely to succeed. Previous studies using brain imaging to predict weight change outcomes with non surgical interventions have shown a relationship between increased reward sensitivity to the anticipation of food and future weight gain. With this in mind, we sought to test the relationship between baseline neural correlates with food related reward and future amount of weight loss in bariatric surgery patients. Functional magnetic resonance imaging and verbal ratings were used to assess brain activation to high and low calorie foods and non food stimuli in 20 patients seeking bariatric surgery and 20 obese controls. Findings suggest that baseline activation in the amygdala and anterior cingulate cortex are correlated with weight loss outcomes after bariatric surgery. Additionally, baseline activation in the insula predicted weight changes in the control group who lost weight from non-surgical means. These findings are consistent with previous literature, which suggest that neural correlates of reward related areas are predictive of future weight changes.