4th Annual NYC Regional Obesity Forum

Co-hosted by:

NYU Langone Comprehensive Program on Obesity
NYU Langone Division of Endocrinology

Farkas Auditorium, NYU Langone Health
550 First Ave,
New York, NY 10016

Keynote Speakers

Marion Nestle, Ph.D., M.P.H
Paulette Goddard Professor of Nutrition, Food Studies, and Public Health, Emerita
New York University

Steven Smith, M.D.
Senior Vice President & Chief Scientific Officer
AdventHealth Orlando Research Services

Thursday, September 26th, 2019
9:00 am – 4:30 pm

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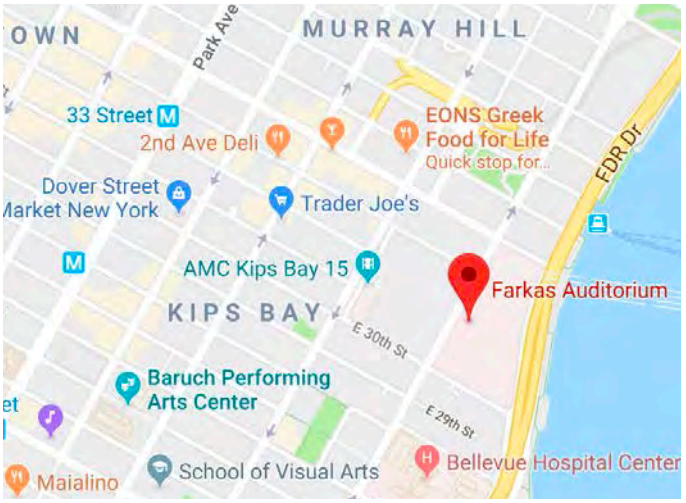
Visiting NYU Langone Medical Center

The NYU Langone Health campus stretches from East 30th St. to East 34th St along First Ave on Manhattan's East Side.

The 2018 NYCROF meeting will be held in the Farkas Auditorium. The main entrance to the campus is at:

NYU Langone Health
550 First Avenue
New York, NY 10016



Directions to NYU Langone Medical Center

By Public Transportation

By Train or Bus

Trains to New York arrive at Grand Central Station or Pennsylvania Station; buses stop at the Port Authority Bus Terminal. Visitors arriving at these stations can take either public transportation or a taxi to the campus.

Buses: Coming from downtown, the M15 bus runs the length of First Avenue in Manhattan and stops at 32nd Street and First Avenue. Coming from uptown, the M15 bus runs along Second Avenue and stops at 34th and 2nd. The M34 bus runs the length of 34th Street in Manhattan and stops directly in front of the north entrance to NYU Langone Medical Center on 34th Street, East of First Avenue. The M16 bus directly connects nationwide bus service at the Port Authority Bus Terminal (42nd Street and 8th Avenue) with the NYU Langone Medical Center 34th Street entrance bus stop. Bus fare is $2.75. A MetroCard or coins are required.

By New York City Subway

The subway costs $2.75 and you must purchase a MetroCard. The stops closest to the NYU Langone Medical Center are:
33rd Street stop (at Park Avenue) on the Number 6 line.
Grand Central Terminal at 42nd Street between Lexington Avenue and Park Avenue (4,5,6).
Maps of bus and subway routes are available on the Metropolitan Transportation Authority website:
http://web.mta.info/nyct/maps/subwaymap.pdf

By Car

If you are travelling top Manhattan by car, please use the following GPS address:
NYU Langone Health, 550 First Avenue New York, NY 10016

*MTA bridges and tunnels do not accept cash for tolls. For more information on how to pay visit:
http://web.mta.info/bandt/cashless/

Parking Options

Metered and non-metered parking is available on New York City streets. See parking information and traffic advisories on the New York City Department of Transportation website: http://www.nyc.gov/html/dot/html/motorist/motorist.shtml

Metered parking spots are available along First Avenue in the NYULMC area and street parking can be found on the side streets. Please be sure to check posted signs for street cleaning and alternate-side parking rules.

There are also several parking garages located near the Medical Center. The following is a partial list. Please check with each individual service provider for rates and hours.

West Plaza Garage - 460 Second Avenue at 26th Street
350 E. 30th Parking - 30th Street between First and Second Avenues
Imperial Parking - 25th Street at Second Avenue
Central Parking System - 530 First Avenue at 30th Street (under NYU Langone Medical Center)

Because parking is limited at the Manhattan VA Medical Center, taking public transportation is recommended. There are, however, a small number of spaces available for cars with handicapped stickers. There are public parking garages on 23rd Street between 2nd & 3rd Avenues and on 1st Avenue which also serve Bellevue and NYU.

Main Campus Map

NYU Langone MEDICAL CENTER

Welcome

Welcome to NYU Langone's new wayfinding system. The **colored pathways, named elevators** and **interactive signs** are designed to help patients, visitors and staff find their way around the medical center campus. The system is being introduced in phases over the months and years ahead. Please bear with us as we work to improve your NYU Langone experience!

Floor 1 Destinations

- Skirball Elevators was D
- Information
- Parking (temporarily closed)
- Restrooms

Blue Pathway

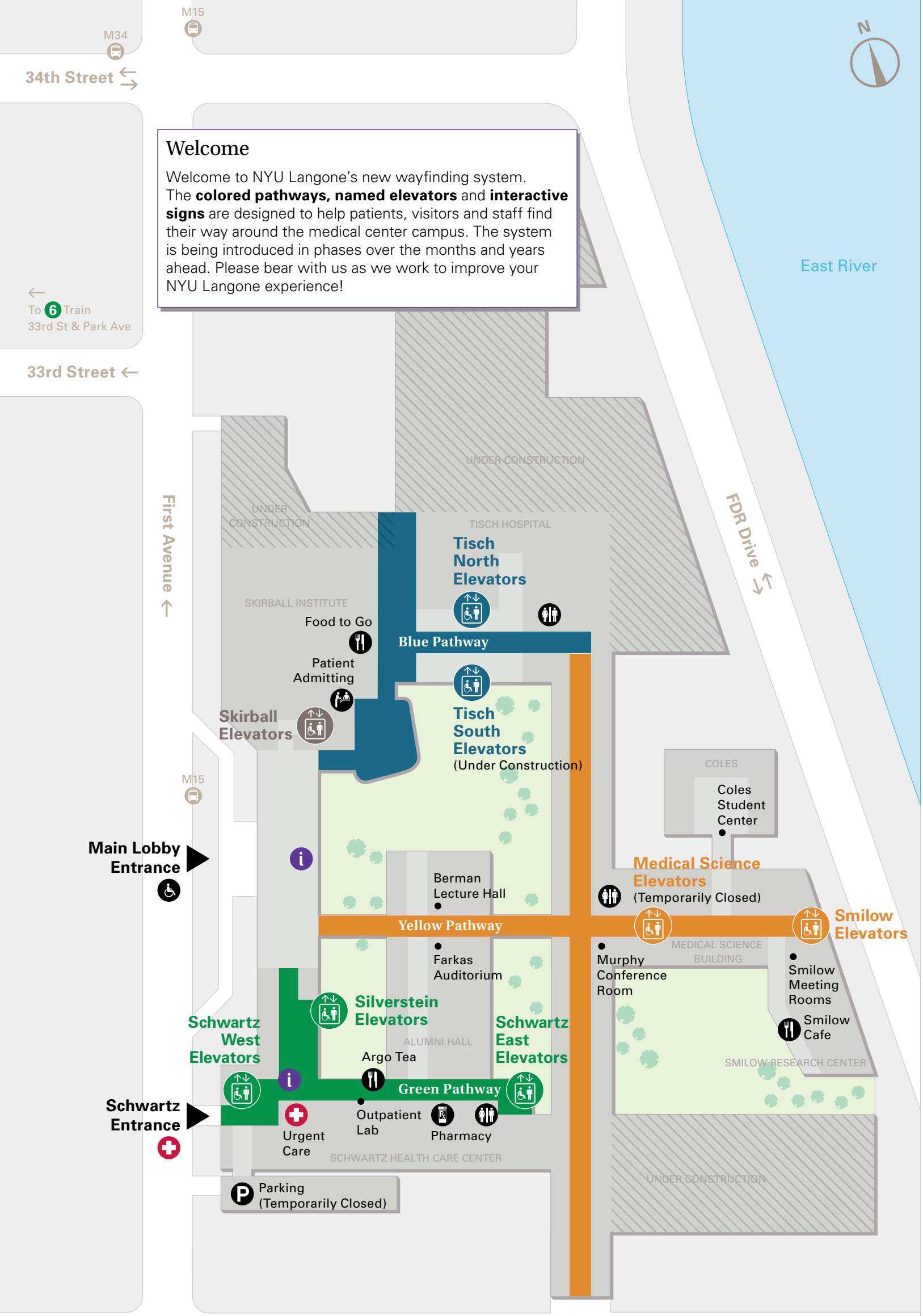
- **Tisch North Elevators** was A (under construction)
- **Tisch South Elevators** new
- Food to Go
- Patient Admitting

Yellow Pathway

- **Medical Science Elevators** was B (temporarily closed)
- **Smilow Elevators** was S
- Berman Lecture Hall
- Coles Student Center
- Farkas Auditorium
- Murphy Conference Room
- Smilow Cafe
- Smilow Meeting Rooms – Goldstein Conference Center

Green Pathway

- **Schwartz East Elevators** was H
- **Schwartz West Elevators** was G
- **Silverstein Elevators** was F
- Urgent Care
- Argo Tea
- Outpatient Lab
- Pharmacy



New York City Regional Obesity Forum

Wednesday, September 26, 2018

NYU Langone Health

Farkas Auditorium, 550 First Ave, New York

8:15-9:00	45min	Arrive, coffee, poster set-up
9:00-9:10	10min	Welcome remarks
		Chair:
9:10-9:30	20min	**Short talk 1** - Kenichi Sakamoto (Mount Sinai) - The role of the sympathetic nervous system in metabolic disease and adipose dysfunction in Obesity and Aging
9:30-9:50	20min	**Short talk 2** - Yanjun Xu (Columbia University) - Role of TBX3 in human stem cell-derived hypothalanic neurons
9:50-10:40	**5 intro+45min**	**Keynote 1: Marion Nestle - TBD**
10:40-11:10	30min	Coffee/Networking/Poster viewing
		Chair:
11:10-11:30	20min	**Short talk 3** - Damaskini Valvi (Mount Sinai) - Environmental chemical burden in metabolic tissues and systemic biological response in bariatric surgery patients using innovative –omics technologies
11:30-11:50	20min	**Short talk 4** - Lakshmi Arivazhagan (NYU Langone) - Myeloid RAGE Protects from Insulin Resistance in Mice Fed High Fat Diet
11:50-12:10	20min	**Short talk 5** - Victor J. Pai (Albert Einstein) Inhibiting the prostaglandin transporter PGT induces non-canonical thermogenesis at thermoneutrality
12:10-2:00	110min	Lunch/Networking/Poster viewing and presentations (between 1pm and 2pm)
		Chair:
2:00-2:20	20min	**Short talk 6** - Nathalie Chami (Mount Sinai) - Low polygenic risk attenuates the obesity-increasing effects of pathogenic mutations in MC4R
2:20-2:40	20min	**Short talk 7** - Rachel Arakawa (Columbia University) - Gut Hormone Changes After Roux-en-Y Gastric Bypass and Laparoscopic Sleeve Gastrectomy
2:40-3:00	20min	**Short talk 8** - Botija Picatoste (Cornell University) - Disruption of insulin stimulated Glut4 translocation in brown adipose tissue induces systemic insulin resistance
3:00-3:30	30min	Coffee/Networking/Poster viewing
		Chair:
3:30-4:20	**5 intro+45min**	**Keynote 2: Steven Smith (AdventHealth, Orlando, FL) - Epigenetic regulation of adipose tissue patterning**
4:20-4:30	10min	Closing remarks, poster awards

Short Talk 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	The role of the sympathetic nervous system in metabolic disease and adipose dysfunction in Obesity and Aging
Authors *	Kenichi Sakamoto*, Chunxue Zhou, Giulia Maurizi, Amesh Sarecha, Henry H. Ruiz, Christoph Buettner
Institutional Affiliations For Each Author. *	Department of Medicine, Diabetes, Obesity, and Metabolism Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA
Corresponding Author Email *	kenichi.sakamoto@mssm.edu

Structured Abstract *

Introduction
Both obesity and aging increase susceptibility to metabolic disease and type 2 diabetes. In both conditions, impaired autonomic control, specifically sympathetic tone has been described. However, the role of catecholaminergic signaling in metabolic disease and adipose tissue dysfunction associated with obesity and aging has not been well defined in large part due to a lack of suitable animal models. Abrogation of catecholamine (CA) synthesis in the whole body due to genetic deletion of the gene for tyrosine hydroxylase (th), that encodes a key enzyme in CA synthesis results in embryonic lethality, possibly due to the lack of dopamine and norepinephrine in the CNS that serve as key neurotransmitters. Surgical denervation is not specific to the SNS and chemical sympathectomy through 6-hydroxydopamine causes inflammation due to toxic effects as we have found in an unpublished study. Here we studied a novel model of peripherally restricted, inducible th deletion that does not involve the brain and results in markedly reduced peripheral catecholamine levels. We are testing whether the reduction in catecholaminergic signaling improves metabolic control both after HFD feeding and aging.
Method
Peripherally restricted TH KO mice were created by crossing a strain of mice in which Cre expression is under the control of the Rosa26 locus that is induced upon tamoxifen administration, with a strain harboring floxed alleles of th. 8weeks after th deletion, Blood glucose, insulin, and lipid were measured. De novo lipogenic capacity and lipolysis in white adipose tissue (WAT) were assessed by western blot.
Result
CA levels in peripheral tissues were reduced more than 90% in TH KO mice. TH KO mice are cold intolerant consistent with functional sympathectomy. Interestingly, TH KO mice are protected from HFD feeding induced glucose intolerance. Furthermore, glucose tolerance was improved and fasting blood glucose levels reduced in 20 months old TH KO mice. Insulin level are higher in these mice, while insulin tolerance tests did not show marked differences. Both obesity and aging are characterized by impaired adipose tissue function for which reduced lipogenic capacity is a hallmark. We find that TH KO mice exhibit increased WAT de novo lipogenesis and decreased lipolysis, suggesting that the SNS is a major culprit for the impaired lipogenic capacity in adipose tissue.
Conclusion
Our data provides support for the paradigm that impaired SNS function plays an important role in the dysmetabolic states of obesity and aging.

Short Talk 2

Abstract Topic Category *	Neurological
Abstract Title *	ROLE OF TBX3 IN HUMAN STEM CELL-DERIVED HYPOTHALAMIC NEURONS
Authors *	Yanjun Xu1,2, Maria Caterina De Rosa3, Carmelo Quarta4,5, Alexandre Fisette1,2, Richard Rausch3, Matthias H. Tschöp1,2,6, Cristina García-Cáceres1,2, Vidhu V. Thaker7, Claudia A. Doege8
Institutional Affiliations For Each Author. *	Yanjun Xu1,2, Maria Caterina De Rosa3, Carmelo Quarta4,5, Alexandre Fisette1,2, Richard Rausch3, Matthias H. Tschöp1,2,6, Cristina García-Cáceres1,2, Vidhu V. Thaker7, Claudia A. Doege8
Corresponding Author Email *	cad2114@cumc.columbia.edu

Structured Abstract *

The leptin-melanocortin pathway of the hypothalamus is a master regulator of body weight. Thus, it is no surprise that mutations in genes expressed in hypothalamic pro-opiomelanocortin (POMC) neurons have been identified as monogenic causes of human obesity. So far, the functional relevance of novel variants identified in sequencing studies of obese humans has been tested mostly in non-human models and human non-neuronal cell lines. Here, we use human stem cell-derived hypothalamic neurons as a model to dissect the role of novel variants associated with human obesity. Mutations in the transcription factor T-box 3 (TBX3) have been associated with obesity in humans, but the molecular mechanism underlying this association remains unknown. We have recently shown that loss-of-function of TBX3 homolog in Drosophila causes excessive fat accumulation, while hypothalamic loss-of-function of Tbx3 in mice disrupts peptidergic identity and maturation of POMC-expressing neurons. Based on these findings from non-human models, we further investigated the role of TBX3 in the differentiation of human stem cells into hypothalamic neurons to establish a functional and causal link between TBX3 mutations and the development of obesity in humans. Loss-of-function models were created using CRISPR/Cas9 and their cellular and molecular phenotypes were obtained at several time points during the course of differentiation from stem cells into hypothalamic neurons. These studies revealed the critical role of TBX3 in the maturation of hypothalamic progenitors into POMC-expressing neurons. These results also suggest that the role of TBX3 in the regulation of energy homeostasis is conserved across species.

Key words: human iPSC, human ESC, hypothalamic neurons, POMC, TBX3, obesity

ORAL PRESENTATIONS

Short Talk 3

Abstract Topic Category *	Population Health and Epidemiology
Abstract Title *	Environmental chemical burden in metabolic tissues and systemic biological response in bariatric surgery patients using innovative -omics technologies
Authors *	Damaskini Valvi (1)*, Douglas I. Walker (1), Thomas Inge (2), Todd Jenkins (3), Michael Helmrath (3), Thomas R. Ziegler (4), Michelle La Merrill (5), Scott M Bartell (6), Sandrah P. Eckel (7), David Conti (7), Yongliang Liang (8), Dean P. Jones (8), Rob McConnell (7), Leda Chatzi (7)

Institutional Affiliations For Each Author. *

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(6) Program in Public Health and Department of Statistics, University of California, Irvine, CA,
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Structured Abstract *

Background: Growing evidence from experimental and epidemiological studies shows that a wide list of environmental chemicals can disrupt the endocrine and metabolic systems and act as obesogens. Recent advances in untargeted metabolomic technologies have great potential for insight into the mechanisms of metabolic toxicity that are not yet fully understood. However, important challenges need to be addressed, including how biological response corresponds to the environmental chemical burden in different target tissues.
Aim: We performed a pilot study using state-of-the-art ultra-high-resolution mass spectrometry (UHRMS) to characterize the burden of lipophilic persistent organic pollutants (POPs) in metabolic tissues and associated alterations in the plasma metabolome.
Methods: We studied 11 adolescents with severe obesity at the time of bariatric surgery. We measured 18 POPs that can act as endocrine and metabolic disruptors (i.e. 2 dioxins, 11 organochlorine compounds [OCs] and 5 polybrominated diphenyl ethers [PBDEs]) in visceral and subcutaneous adipose tissue (vAT and sAT), and liver samples using gas chromatography with UHRMS. Biological response was evaluated by measuring the plasma metabolome using high-resolution metabolomics. Network and pathway enrichment analysis assessed correlations between the tissue-specific burden of three frequently detected POPs (i.e. p,p'-dichlorodiphenyldichloroethene [DDE], hexachlorobenzene [HCB] and PBDE-47) and plasma high-resolution metabolomics pathways.
Results: Concentrations of 4 OCs and 3 PBDEs were quantifiable in at least one metabolic tissue for >80% of participants. All POP had the highest median concentrations in adipose tissue, and especially sAT, except for PBDE-154 which had comparable concentrations across all tissues. Pathway analysis showed high correlations between tissue-specific POP and metabolic alterations in pathways of amino acid metabolism, fatty acid biosynthesis and metabolism, glycolysis and glyconeogenesis and lipid signaling.
Conclusions: Most of the measured POPs appear to accumulate preferentially in adipose tissue compared to liver. Findings of plasma metabolic pathways potentially associated with tissue-specific POPs concentrations merit further investigation in larger populations. The potential impact of exposure to environmental chemicals on metabolic improvement after bariatric surgery deserves attention in future investigations.

Short Talk 4

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Myeloid RAGE Protects from Insulin Resistance in Mice Fed High Fat Diet
Authors *	Lakshmi Arivazhagan1*, Evelyn MS Litwinoff1, Henry R. Ruiz1, Laura Frye1, Jason Kim2, Ravichandran Ramasamy1 and Ann Marie Schmidt1
Institutional Affiliations For Each Author. *	1Diabetes Research Program, Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, NYU School of Medicine, New York, NY, United States 10016 2Program in Molecular Medicine and Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Massachusetts Medical School, Worcester, MA
Corresponding Author Email *	annmarie.schmidt@nyulangone.org

Structured Abstract *

Background:
Obesity is a major global health problem, with over one third of adults in the US alone classified as obese. Obesity, partially attributed to "western" diets which are high in fats and carbohydrates, coupled with a sedentary lifestyle, often leads to a state of insulin resistance (IR), type 2 diabetes and its complications. We previously showed that the receptor for advanced glycation end products (RAGE) and its ligands contribute to the pathogenesis of obesity and IR, as whole body and adipocyte-specific Ager (gene encoding RAGE) deleted mice fed a high fat diet (HFD) showed protection from weight gain and IR. Bone marrow transplanted from Ager-deleted into wild type mice fed HFD partially protected them from weight gain and IR. Here, we hypothesize that myeloid RAGE contributed to IR upon HFD feeding.

Methods:
We generated mice with myeloid-specific (MDR) LyzMCre(+/+).Agerflox/flox and adipocyte and myeloid-specific (Double Knockouts) AdipoQCre(-/+)LyzMCre(+/+).Agerflox/flox deletion of Ager. Controls were considered the mice bearing Flox and Cre alone. Mice were fed either standard chow (LFD) or HFD (60% kcal/fat) for 3 months starting at 6 weeks of age. The mice were assessed for body mass and composition, glucose and insulin sensitivity, food consumption, energy expenditure, physical activity, whole body glucose metabolism by hyperinsulinemic-euglycemic clamp studies and hepatic triglycerides.

Results:
After 3 months on LFD or HFD, there were no significant differences observed in body mass, body composition, food intake, energy expenditure and physical activity of the MDR mice vs. controls. However, surprisingly, insulin tolerance tests and hyperinsulinemic-euglycemic clamp studies showed decreased insulin sensitivity and insulin action in the livers of MDR mice vs. controls, respectively, indicating that the MDR mice were more insulin resistant. MDR mice demonstrated elevated levels of triglycerides in the liver vs. controls, suggesting poorer lipid metabolism in the liver, leading to liver steatosis and increased IR. In the case of Double Knockouts, the Cre (+) mice were more glucose tolerant and insulin sensitive compared to MDR mice, showing that deletion of Ager in the adipocytes rescued the adverse effects of deletion of Ager in myeloid cells.

Conclusion:
Myeloid-specific deletion of Ager mediates IR in the absence of changes in body weight in mice fed HFD. Furthermore, adipocyte-specific deletion of Ager rescues the effects of myeloid-specific Ager deletion and plays a major role in exerting protection from weight gain and IR upon HFD feeding. The mechanisms underlying these findings are under active investigation.

Short Talk 5

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Inhibiting the prostaglandin transporter PGT induces non-canonical thermogenesis at thermoneutrality
Authors *	Victor J. Pai*, Run Lu, Licheng Wu, Marina Garcia Macia, Wade R. Koba, Yuling Chi, Rajat Singh, Gary J. Schwartz, Victor L. Schuster
Institutional Affiliations For Each Author. *	Albert Einstein College of Medicine
Corresponding Author Email *	victor.schuster@einstein.yu.edu

Structured Abstract *

Background: Prostaglandins (PGs) are released into the extracellular fluid by adipocytes to effect autocrine and paracrine signaling. In white adipose tissue (WAT), PGF2α inhibits lipogenesis and adipocyte differentiation, whereas PGE2 induces a beige phenotype comprised of UCP1 expression and thermogenesis. Because the rate-limiting step in PGF2α and PGE2 inactivation is uptake by the prostaglandin transporter PGT (SLCO2a1), we hypothesized that inhibiting PGT would increase PGF2α and PGE2 and therefore both inhibit white adipogenesis and increase UCP1-mediated beige thermogenesis.

Method: We performed a thorough and physiological analysis of primary thermogenesis on PGT global knockout (PGT-KO) mice and wildtype mice (WT) housed at thermoneutrality. Indirect calorimetry chambers were used to measure mice energy expenditure and activity. Thermopreference, acute cold exposure, and Scholander assays were used to determine whether thermogenesis was primary or secondary. Tissue glucose uptake was measured by F18-fluorodeoxyglucose uptake. Inguinal WAT (iWAT) oxygen consumption rate and mitochondrial function were measured by Seahorse and citrate synthase activity. iWAT gene expression was measured through qPCR. iWAT stromal vascular fraction (SVF) were cultured and differentiated into primary adipocytes and analyzed by seahorse and qPCR. To determine the underlying mechanism of primary thermogenesis in the PGT-KO mice, we assayed thermoneutral UCP1-KO mice given a high affinity PGT inhibitor or vehicle control. The underlying futile cycle mechanism was interrogated using FP (PGF2α) receptor antagonists and creatine transporter inhibitors.

Results: PGT-KO mice housed at thermoneutrality exhibited both a lean phenotype and increased primary thermogenesis that could not be accounted for by changes in energy intake, mouse activity, or heat loss. UCP1 expression in PGT-KO iWAT adipocytes was strongly suppressed by PGF2α through its FP receptor. Despite UCP1 suppression, iWAT tissue explants from these mice exhibited increased glucose uptake, mitochondrial mass, O2 consumption, and expression of genes implicated in mitochondrial biogenesis and beige conversion. Inhibiting PGT pharmacologically in UCP1-KO mice similarly induced thermogenesis and beige conversion of iWAT. O2 consumption by adipocytes derived from iWAT of PGT-KO mice was enhanced, and was coupled to ATP synthesis, accompanied by induction of components of the creatine shuttle, and normalized by an inhibitor of the creatine importer Slc6a8.

Conclusions: Inhibiting PGT induces non-canonical beige induction and thermogenesis of iWAT at thermoneutrality. PGT may be a useful pharmacological target for inducing non-UCP1 mediated thermogenesis.

Short Talk 6

Abstract Topic Category *	Genetics/Epigenetics/Early Determinants of Obesity
Abstract Title *	Low polygenic risk attenuates the obesity-increasing effects of pathogenic mutations in MC4R
Authors *	Nathalie Chami*, Ph.D, Michael Preuss, Ph.D, Ryan W. Walker, Ph.D, Arden Moscati, Ph.D, Ruth J.F Loos, Ph.D
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Structured Abstract *

Background: Melanocortin 4 receptor (MC4R) deficiency, due to protein-altering mutations, is the most common cause of severe and early onset obesity. We examine why some carriers of pathogenic mutations that result in MC4R deficiency remain of normal weight, to gain insight into the mechanisms that control body weight.

Methods: We identified 69 obesity-increasing mutations (MAF<0.1%) in MC4R reported in the human gene mutation database (HGMD) and Clinvar that were available in ~450,000 individuals of the UK Biobank and calculated their penetrance and effect on obesity (BMI ≥ 30 kg/m2). We then focused on the most penetrant mutations with the largest effect on obesity and examined differences between normal weight and obese carriers. We calculated a genome-wide polygenic risk score for BMI (PRSBMI) to assess the polygenic contribution to body weight in normal weight and obese carriers.

Results: Of the 69 mutations, only 11 mutations had moderate to high penetrance (≥30%) and increased the odds of obesity by more than twofold. Twenty-nine of the 183 carriers of these 11 mutations were of normal weight. Body composition of normal weight carriers was similar to non-carriers, whereas obese carriers had a somewhat higher BMI (P=0.034) than obese non-carriers, due to greater lean mass (P=0.002). Normal weight carriers more often reported that, already at age 10y, they were thinner/average (72%) compared to obese carriers (48%) (P=0.02). The PRSBMI of normal weight carriers (PRSBMI=-0.66±0.18) was significantly lower than of obese carriers (0.40±0.12; P=8x10-6), and also lower than that of normal weight non-carriers (-0.28±0.003; P=0.04). Further, among MC4R mutation carriers, those with a low PRSBMI (bottom quartile) have ~5 kg/m2 lower BMI (~14 kg of body weight for a 1.7m-tall person) than those with a high PRSBMI (top quartile).

Conclusions: Only 11 (16%) out of 69 previously reported MC4R mutations had high penetrance and increased risk of obesity, highlighting the importance of large-scale data to validate the impact of mutations observed in small-scale and case-focused studies. Furthermore, our results show that despite the key role of MC4R in obesity, the obesity-increasing effects of pathogenic MC4R mutations can be countered, at least in part, by a low polygenic risk, potentially representing other innate mechanisms implicated in body weight regulation.

Short Talk 7

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Gut Hormone Changes After Roux-en-Y Gastric Bypass and Laparoscopic Sleeve Gastrectomy
Authors *	Rachel Arakawa, MD* Judith Korner, MD PhD
Institutional Affiliations For Each Author. *	Columbia University Medical Center, Division of Endocrinology
Corresponding Author Email *	rya2103@cumc.columbia.edu

Structured Abstract *

Background
Laparoscopic sleeve gastrectomy (LSG) has surpassed Roux-en-Y gastric bypass (RYGB) as the most prevalent bariatric procedure worldwide. While LSG and RYGB demonstrate equivalent short-term weight loss, long-term weight loss tends to be greater after RYGB. Differences in the effect of these procedures on gut hormones that regulate energy homeostasis are felt to partially underlie differences in outcomes. The objective of this study was to quantify blood levels of GI tract hormones of energy homeostasis at one year follow up to delineate possible reasons for greater efficacy of RYGB over LSG in achieving weight loss.

Methods
Patients undergoing LSG (n=19) and RYGB (n=40) were studied before surgery and at 2,12, 26, and 52 weeks postoperatively. Fasting and postprandial blood samples were assayed at baseline, 26, and 52 weeks for PYY, ghrelin and GLP-1. Fasting and postprandial appetitive sensations were assessed by visual analog scale.

Results
At 1 year there was greater weight loss in RYGB compared with LSG patients (30% vs 27%; p=0.03). At 52 weeks area under the curve (AUC) for PYY was greater in RYGB patients (p=.0008). RYGB patients had significant increases in GLP-1 AUC compared to baseline (p=.002). Ghrelin levels decreased only after LSG compared to baseline (p<.001) but were not significantly different from RYGB. There was a trend toward decreased sweet cravings in RYGB patients (p=.056).

Conclusions
Differences in GI-tract hormones that regulate energy homeostasis and changes in sweet cravings are possible mechanisms for greater efficacy of RYGB compared to LSG.

Short Talk 8

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Disruption of insulin stimulated Glut4 translocation in brown adipose tissue induces systemic insulin resistance
Authors *	Picatoste B*, Soares D, Cohen P, McGraw TE.
Institutional Affiliations For Each Author. *	Picatoste B. Weill Cornell Medicine, New York, N.Y. Soares D. Weill Cornell Medicine, New York, N.Y. Cohen P. Rockefeller University, New York, NY. McGraw TE. Weill Cornell Medicine, New York, N.Y.
Corresponding Author Email *	MAP2094@MED.CORNELL.EDU

Structured Abstract *

Background:
Defective GLUT4 translocation to the plasma membrane is a hallmark of insulin resistance and type 2 diabetes. We have shown that knockout of Rab10 severely inhibits translocation of GLUT4 to the plasma membrane of white and brown adipocytes, resulting in a blunting of insulin-stimulated glucose uptake. Our studies of an adipose-specific (white and brown fat) Rab10 knockout mouse (aRab10KO) revealed systemic insulin resistance on a normal chow diet, primarily due to hepatic insulin resistance (Vazirani R et al, Diabetes 2016). Although the main function of brown adipose tissue (BAT) is to dissipate energy in the form of heat, numerous studies support a role for BAT in metabolic regulation beyond thermogenesis.
Methods:
To determine the impact on whole body metabolism of solely silencing Rab10 in BAT, we have created a BAT-specific Rab10 knockout mouse using CRE driven by UCP-1 promotor (BRab10KO mouse).
Results:
Rab10 protein expression was lost in brown adipose tissues of BRab10KO mice, while remaining unchanged in white adipose tissue. The BRab10KO mice are insulin resistant and glucose intolerant on a normal chow diet and have elevated plasma insulin levels during a glucose tolerance test compared to control mice. However, fasting blood glucose and plasma insulin levels are unchanged. BAT lacking Rab10 shows a dramatically decreased in lipogenic-related gene (FASN, Elovl6, ACC1) and in Carbohydrate Response Element Binding Protein β expression, suggesting that a decrease in glucose uptake by BAT induces the defect in de novo lipogenesis. BRab10KO mice show tolerance to acute cold exposure.
Conclusion:
Disruption of insulin stimulated Glut4 translocation in brown adipose tissue induces systemic insulin resistance. Analyses of BRab10KO mouse demonstrate the importance of the insulin-regulated glucose flux into BAT for whole body metabolic regulation.

Board 1, Poster 1

Abstract Topic Category *	Genetics/Epigenetics/Early Determinants of Obesity
Abstract Title *	Integrative analysis of GWAS and tissue-specific gene expression identifies candidate causal genes underlying obesity risk
Authors *	Daiane Hemerich*, Arden Moscati, Michael Preuss, Ruth J.F. Loos
Institutional Affiliations For Each Author. *	The Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, New York, USA
Corresponding Author Email *	daiane.hemerich@mssm.edu

Structured Abstract *

Obesity, as assessed by body mass index (BMI), is a heritable risk factor for several diseases, affecting >2 billion people worldwide. Genome-wide association studies (GWAS) have identified hundreds of genetic variants influencing obesity risk, mostly in non-coding regions, enriched in the central nervous system. One way to prioritize genes in each locus is to assess whether any of the identified variants are associated with gene expression levels (eQTL). However, the subsequent link from gene expression to disease is rarely made. Summary statistics Mendelian Randomization (MR), or SMR, is an MR approach that integrates GWAS loci with eQTL, and has been used to assess the causal relationship between expression of genes and diseases, such as obesity, using eQTL on whole blood. Tissue-specific information increases power for eQTLs with tissue-specific effects.

Here, we used SMR to prioritize genes within 536 obesity-associated loci by assessing whether observed eQTLs are causally associated with BMI. We integrated brain eQTL from CommonMind Consortium (n=467), ROSMAP (n=494) and GTEx (n=72), and blood eQTL from eQTLGen (n=14,115). We sought further confirmation using other gene-prioritization approaches (DEPICT) and examining the presence of predicted damaging coding variants via Mutation Significance Cutoff (MSC) in each locus.

We identified 119 candidate genes whose expression in blood appear to be causally associated with BMI, and find similar evidence for 163 genes in brain eQTL data (significantly more than in blood, FET $p<0.0001$), with 20 genes shared in both sets. In addition, 249 genes were prioritized by DEPICT (FDR<0.05). Finally, 371 genes contain coding variants with predicted damaging effect, 20 of which are rare (MAF<1%). In total, we identified 756 candidate genes in 351 of the 536 BMI-associated loci, 35 of which were prioritized by more than one line of evidence, e.g. SLC35E2, LUZP1, NUCKS1, MACF1, IPP, FAF1, NEGR1, GPR88 and ADCY3. Some of these genes have already been established as obesity genes (NEGR1, ADCY3, FAF1), and others are supported by evidence from animal models (MACF1, GRP88, NRXN1, NUCKS1). With additional prioritization tools, we will provide further candidate genes and additional evidence.

The prioritization of likely causal genes is a critical step in the translation of GWAS results into functional follow-up studies to increase our understanding of the underlying biology and, in time, develop better therapeutics for obesity.

Board 1, Poster 2

Abstract Topic Category *	Genetics/Epigenetics/Early Determinants of Obesity
Abstract Title *	Large scale meta-analysis of genome-wide association studies for physical activity highlights shared genetic factors with education and obesity
Authors *	Zhe Wang1*, Marylin C. Cornelis2, Søren Brage3, Ulf Ekelund4, Nick Wareham3, Ruth J.F. Loos1,5, Marcel den Hoed6, Genome Wide Association of Physical Activity (GWAPA) Consortium

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Structured Abstract *

Background: Low levels of physical activity (PA) and a sedentary lifestyle (SL) are well-established, modifiable risk factors for human health. Despite being moderately heritable (h2~40%), our understanding of genetic factors influencing PA and SL are limited.

Methods: We performed the largest meta-analysis of genome-wide association studies (GWAS) to date, including up to 641,692 individuals of European (94%), African (2%), East Asian (1%), South Asian (1%), and Hispanic (2%) ancestries. We studied self-reported moderate-to-vigorously intensity leisure time PA (MVPA); leisure screen time (LST); sedentary behavior at work and commuting. Sex- and ancestry-specific associations were adjusted for age and study-specific covariates. Summary statistics were meta-analyzed using a fixed-effect, inverse-variance weighted approach.

Results: We identified 123 PA and SL associated loci (p<5□10-9); 95 in European ancestry individuals and 28 additional loci in all ancestries combined. In total, 98 loci had not been identified for PA/SL traits before, 87 of which were previously associated with educational attainment (EA, n=81) and/or obesity traits (n=77). Genetic correlations between MVPA and LST were modest-to-high (r=-0.49), as were their correlations with EA (r [0.43, 0.65]) and obesity traits (r [-0.41, -0.23]). We also observed genetic correlations with mental health, cancer and aging (r [-0.48, 0.45]). Using uni- and multivariable Mendelian Randomization (MR), we found that a 1SD genetically higher LST caused a 0.27SD higher BMI (p=3.09□10-9). Conversely, a 1SD genetically higher BMI only caused a 0.09SD higher LST (p=7.26□10-10). Multivariable MR showed that the bidirectional causal effects between LST and BMI were independent of EA. However, higher LST caused lower EA through an effect on BMI (univariable □=-0.48, p=3.76□10-30; multivariable □=-0.07, p=0.24), while higher EA caused lower LST independently of BMI (univariable □=-0.29, p=5.55□10-17; multivariable □=-0.31, p=4.52□10-17). Tissue and pathway analyses showed enrichment of gene expression in the central nervous system, especially in reward-related areas, such as basal ganglia, cerebellum, hippocampus and the limbic system. In addition, variants of known relevance for muscle performance in ACTN3 showed suggestive associations with MVPA and LST (p=4.25□10-8).

Conclusions: Genes in loci identified in our study point to the brain as a key player in PA regulation. Furthermore, we confirm that lower LST has a causal effect on higher BMI.

Board 2, Poster 1

Abstract Topic Category *	Genetics/Epigenetics/Early Determinants of Obesity
Abstract Title *	Resilience to obesity in genetically at-risk individuals: a study on the underlying mechanisms
Authors *	R.A.J. Smit*1,2, M. Graff3, R.W. Walker1,4, A.R. Wood5, M. Preuss1, K.L. Young3, E. Marouli6, C.M. Lindgren7,8, K.E. North3, T.M. Frayling5, J.N. Hirschhorn9,10,11, R.J.F. Loos1,12,13, on behalf of the Genetic Investigation of ANthropometric Traits (GIANT) Consortium.

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Structured Abstract *

Background: Obesity is a major risk factor for chronic disease. Besides an obesogenic lifestyle, genetic factors also determine susceptibility to obesity. Using a polygenic risk score (PRS) for obesity, those in the top 10% were shown 25x more likely to be severely obese compared to the bottom 10%. Interestingly, 17% of the top 10% were of normal weight. To gain insight into the mechanisms that determine resilience to genetic predisposition to obesity, we characterized normal weight and obese individuals with an extremely high or low PRS within the UK Biobank.

Methods: Using PRSice, we built a PRS with BMI association summary statistics of 2.1 million variants (Locke 2015) that we tested in 372,584 unrelated UKB participants of European ancestry. We defined 6 groups: by PRS [bottom 5%, middle 35-65%, top 5%) and BMI-category (under/normal weight [BMI<25kg/m2, NW] and obese [BMI≥30, OB]), and compared demographics, body composition, clinical history, and measures of the obesogenic environment. All analyses were adjusted for age, sex, center, and the first ten PCs.

Results: In the top 5% of the PRS (N=18,630), 44.5% were OB, whereas 17% were NW. In the bottom 5% PRS (N=18,628), the discrepancy was more pronounced; 53.9% were NW, and only 9% were OB. Among NW individuals, those in the top 5% PRS had (P<1e-3) somewhat higher adiposity, lower energy intake, more sedentary time, were more often smokers, were less educated, and had more often diabetes, compared to those in the bottom 5%, though material deprivation and birth weight were similar. Among OB individuals, we saw similar differences. In the high-PRS group, 84% of the NW reported to be thinner or of average body size at age 10, compared to 59% of the OB (P<2e-16). Conversely, in the low-PRS group, 27% of OB reported to be "plumper" at age 10, compared to 6% of NW (P<2e-16). Among the high-PRS group, NW were (P<1e-3) more physically active and educated, less sedentary and materially deprived, fewer had diabetes, but more were smokers, than OB. Inverse trends were observed in the low-PRS group.

Conclusions: Taken together, body size tracks across the life course, which seems to be largely driven by a genetic predisposition (PRS), but also by (non-)genetic factors not captured by the PRS. Moreover, material deprivation, education and lifestyle may counteract one's genetic predisposition to obesity. Understanding the genetic and non-genetic contributors to body size can help define the scope and timing of prevention.

Board 2, Poster 2

Abstract Topic Category *	Genetics/Epigenetics/Early Determinants of Obesity
Abstract Title *	The Effect of Choline on DNA Methylation in the Hippocampus of the Offspring of Gestational Diabetes Mellitus (GDM) Mice
Authors *	Kaydine Edwards, Hunter Korsmo, Xinyin Jiang
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Structured Abstract *

DNA Methylation is an epigenetic modification that changes the expression of genes without altering the genomic sequence. Maternal nutrition exposures and health status, such as maternal overnutrition and gestational diabetes mellitus (GDM), have permanent influence on DNA methylation of offspring. Choline is a water-soluble vitamin-like nutrient that is essential for healthy brain development and provides the methyl group for DNA methylation. The objective of this project is to determine the effects of choline supplementation on DNA methylation in the hippocampus of the offspring from mouse dams with GDM. In this study, female mice were divided into four groups: high fat (HF) feeding (to induce GDM), HF with choline supplementation, normal fat (NF) control and NF with choline supplementation. The experimental groups followed their diets and supplements for 4 weeks before timed-mating and throughout gestation. Thereafter, they were fed the NF diet during lactation. After weaning, the offspring were fed the HF diet for 6 weeks before dissection. Brain hippocampus was then dissected for DNA extraction and global DNA methylation analysis. Global DNA methylation was increased in the NF choline supplemented group versus the NF control group ($P = 0.056$); however, there were no differences between the HF choline versus the HF or NF control groups ($P = 0.992$). In summary, there was an interaction between maternal HF feeding and choline supplementation in influencing global DNA methylation. Maternal HF feeding eliminated the increase in offspring hippocampal DNA methylation by choline supplementation observed under the NF feeding condition.

Board 3, Poster 1

Abstract Topic Category *	Genetics/Epigenetics/Early Determinants of Obesity
Abstract Title *	mRNA decay factor AUF1 controls adipogenesis through the targeted degradation of mitochondrial proton pump protein UCP1 AU-rich mRNA, a regulator of adipose fate determination.
Authors *	Melanie Mahe, Abilash Gadi, Dounia Abbadi, John J. Andrews and Robert J. Schneider
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Structured Abstract *

Adipose tissue plays a critical role in the regulation of metabolic function. It can be categorized into three types: white adipose tissue (WAT, white fat), beige adipose tissue and brown adipose tissue (brown fat, BAT). BAT and beige adipose tissues are involved in thermogenesis (production of body heat) through the activity of the protein UCP1 (uncoupling protein 1, thermogenin). UCP1 is a transmembrane protein activated by fatty acids that increases proton translocation to the mitochondrial matrix, promoting more rapid oxidation with low ATP production. Moreover, subcutaneous and inguinal WAT is in a physiologically dynamic state, and can become beige adipose tissue that physiologically resembles brown fat (BAT) for periods of time for adaptive thermogenesis, such as increasing heat generation during winter. However, WAT cannot turn into authentic brown fat because WAT and BAT are derived from different stem cell progenitors.

Here we report that KO mice deficient in AU-rich factor 1 (AUF1), which targets certain mRNAs with AU-rich element (ARE) 3' untranslated regions (3' UTRs) for rapid decay, display abnormal adipogenesis and are significantly skewed in their development of WAT. Using AUF1 knockout mice, adipocyte cell cultures and adipogenesis lineage determination studies, we show that in the absence of AUF1 there is strong development of "beiging" subcutaneaous and inguinal WAT that has taken on brown fat characteristics, that are not observed in wild-type mice. Reduction in WAT and increased beige fat has been shown to reduce propensity for obesity and onset of type 2 diabetes in experimental animals and is similarly associated in humans. Our findings that UCP1 protein and mRNA are strongly increased in the subcutaneous and inguinal adipose tissue with AUF1 inactivation leading to conversion of WAT to beige fat, indicates that AUF1 mediated mRNA decay is a key regulator of white versus beige fat development and WAT-specific inhibition of AUF1 might be a therapeutic target in the management of obesity.

Board 3, Poster 2

Abstract Topic Category *	Genetics/Epigenetics/Early Determinants of Obesity
Abstract Title *	Perinatal Depressive Symptoms and Maternal Locus of Control over Child Weight at 2 Years
Authors *	Celia Lenarz-Geisen*, Michelle Katzow, Mary Jo Messito, Rachel S Gross
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Structured Abstract *

Background: Perinatal depressive symptoms adversely impact parenting and subsequent child health outcomes, such as child obesity. How maternal depressive symptoms impact child weight, whether the timing and duration of these symptoms are important, and the mechanisms through which they operate are less clear. Since depressive symptoms are related to decreased internal locus of control, and lower internal locus of control is associated with less healthy feeding practices, this may represent a mechanism between maternal depression and child weight outcomes.

Objective: To determine if persistent perinatal depressive symptoms are independently associated with a low internal locus of control over child weight at age 2 years.

Design/Methods: We analyzed longitudinal data collected from low-income, Hispanic mothers participating in the Starting Early Program, a randomized controlled trial at a New York urban public hospital. Depressive symptoms were assessed during the 3rd trimester and 3 months postpartum using the Patient Health Questionnaire (PHQ-9) and defined as present if the score was ≥ 5 and absent if <5. Patterns of depressive symptoms were categorized into 4 groups: 1) no depressive symptoms (absent at prenatal and postpartum assessments); used as the reference group; 2) prenatal depressive symptoms (present at prenatal, absent at postpartum assessment); 3) Postpartum depressive symptoms (absent at prenatal, present postpartum assessment); 4) persistent perinatal depressive symptoms (present at prenatal and postpartum assessments). Locus of control over child weight was assessed using questions adapted from the Parental Health Belief Scale at child age 2 years, with the lowest quartile of responses categorized as low locus of control. Chi squares and logistic regression analyses controlling for potential confounders (intervention group, parity, mother's age, US born, education, 3-month locus of control, 19-month depressive symptoms) were used.

Results: 369 mothers were included in the analyses. Mothers with persistent perinatal depressive symptoms were 2.6 times more likely to have low internal locus of control over child weight at 2 years as compared to those with no depressive symptoms (aOR 2.6, p=0.048). Those with depressive symptoms present only at one of the two time points did not have significantly higher rates of low locus of control (aOR 1.4, p=0.353 and aOR 1.0, p=0.985).

Conclusion: Persistent perinatal depressive symptoms may have a unique detrimental effect on maternal locus of control over child weight at 2 years. Further study on locus of control as a potential mediator between depression and child weight is warranted.

Board 4, Poster 1

Abstract Topic Category *	Genetics/Epigenetics/Early Determinants of Obesity
Abstract Title *	Neuro-cellular mechanisms for the association of obesity and Alzheimer's disease
Authors *	Zhangji Dong 1, Maria Caterina De Rosa 1, Vidhu V. Thaker 1, Daniele Neri 1, George Stratigopoulos 1, Rick Rausch 1, Alicja Skowronski 1, Charles LeDuc 1, Qi Su2, Yurong Xin 2, Judith Altarejos 2, Rudolph L. Leibel 1, Claudia A. Doege 1
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Structured Abstract *

Background: Epidemiological studies have found that two of the major health concerns in the U.S. – obesity and Alzheimer's disease (AD) – are clinically associated. Hypothalamic nuclei comprising the melanocortin pathway (such as the paraventricular nucleus [PVH]) have been implicated in the control of body weight. Lateral entorhinal cortex (LEC) as well as locus coeruleus (LC) in the brain stem have been implicated in the early stages of AD. We hypothesized that the clinical association of cognitive dysfunction and disturbed energy homeostasis might be due to actions of genes that are expressed in both of these anatomic regions. We hypothesized specifically that the melanocortin-4 receptor (MC4R) and amyloid beta precursor protein (APP) and presenilin 1 (PSEN1) would be highly expressed in PVH, LEC and LC.
Methods / Results: Single-cell RNA sequencing analysis of the PVH region and a publicly available data set of the LEC (by McCarroll and colleagues) of mice showed expression of App and Psen1 in the Mc4r neurons of the PVH as well as throughout the neuronal populations of the LEC. We confirmed the co-localization of Mc4r, App and Psen1 in PVH and LEC of 5-weeks old mice using single-molecule fluorescence in situ hybridization (RNAscope) followed by confocal imaging. In mouse PVH, 54% of the Mc4r positive neurons also express both App and Psen1. In LEC, more than 90% of cells co-express Mc4r, App and Psen1. Furthermore, in the LC, 61% of Dbh (marker for LC neurons) neurons co-express Mc4r, App and Psen1.
Conclusions / Ongoing Studies: The co-expression of Mc4r, App and Psen1 in PVH, LC and LEC supports our working hypothesis that the cell-autonomous interaction between the melanocortin and AD-associated signaling pathways could be a molecular basis for the association between obesity and AD. To test whether these pathways functionally interact we are performing genetic analyses in human stem cell-derived hypothalamic and cortical neurons. Allelic series of cells carrying obesity (MC4R) or AD-associated (APP and PSEN1) mutations are generated using CRISPR. Readout for the MC4R pathway will be cAMP signaling upon stimulation with the endogenous agonist alpha-melanocyte-stimulating hormone (□-MSH), and readouts for AD pathways will be APP processing and tau phosphorylation.

Board 4, Poster 2

Abstract Topic Category *	Genetics/Epigenetics/Early Determinants of Obesity
Abstract Title *	Identifying novel candidate genes for obesity by study of extreme and rare phenotypes.
Authors *	Vidhu Thaker*, Ellie Seaby, Radha Sathanayagam, Nia Ebrahim, Jane Kim, Casie Genetti, Farrah Rajabi, John Schreiber, Joel Hirschhorn, Pankaj Agrawal
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Structured Abstract *

Introduction: Rapid Onset Obesity, Hypothalamic Dysfunction, Hypoventilation and Autonomic Dysfunction (ROHHAD) syndrome is a rare disease named in 2007 based on the clinical characteristics. Approximately 140 children have been described in the literature with prominent features of severe obesity, neurobehavioral phenotype and a neuroendocrine tumor in about 30% of the cases. This study seeks to investigate the genetic bases of the disease.

Methods: We are undertaking genetic analyses in trios or families of children with ROHHAD syndrome. Whole exome sequencing (WES) and data processing were performed by the Genomics Platform at the Broad Institute of Harvard and MIT. The WES pipeline consists of standard hybrid capture and library preparation followed by sequencing of short paired reads performed on an Illumina platform with a mean coverage of ~100X (> 90% targets 20x). Bioinformatic pipeline includes mapping to hg19 build using BWA aligner, joint calling with GATK and variant annotation using VEP. The variant callset are uploaded to seqr and analyses are focused on recessive and de novo inheritance patterns.

Results: The current cohort comprises of 21 families. We have completed analyses in 10 families and identified 4 genes of interest. 1) ARNT2 is a basic helix-loop-helix transcription factor that is an obligate heterodimeric partner for SIM1. A novel, pathogenic de novo variant in a girl likely explains extreme obesity (BMIz +3.5) and the neurobehavioral phenotype. Through Genematcher, we identified another patient with epilepsy and obesity harboring a biallelic variant. 2) NSD1 is a histone methyltransferase that controls normal growth and development and known to be associated with overgrowth, neurobehavioral changes and certain type of cancers. The de novo pathogenic variant seen in this patient explains her physical/neurobehavioral phenotype and the neuroendocrine tumor. 3) MAPKAPK5 is a tumor suppressor serine/threonine-protein kinase involved in mTORC1 signaling and post-transcriptional regulation. The de novo variant seen in a girl with a neuroendocrine tumor, severe obesity (BMIz +3) and hypoventilation is a candidate gene requiring elucidation of role in the weight regulation pathway. 4) OCRL is a ciliary gene known to cause Lowe's syndrome. The frameshift variant in this X-linked recessive gene explains the neurobehavioral phenotype, short stature and renal tubular dysfunction, and may be implicated in obesity given its high expression in the areas of hypothalamus involved in weight regulation.

Conclusions: The family genetic study has identified interesting candidate genes in some patients, without a unified etiology so far.

Board 5, Poster 1

Abstract Topic Category *	Genetics/Epigenetics/Early Determinants of Obesity
Abstract Title *	Longitudinal changes in measured caloric intake in children without obesity by FTO genotype
Authors *	Simon P.K. Liebling*, Laurel E.S. Mayer, Lisa M. Ranzenhofer, Michael Rosenbaum
Institutional Affiliations For Each Author. *	Columbia University Vagelos College of Physicians and Surgeons, Columbia University Department of Psychiatry and New York State Psychiatric Institute, Columbia University Department of Pediatrics
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Structured Abstract *

Background:
The rs9939609 single-nucleotide polymorphism in the first intron of the FTO gene is associated with an increased risk of obesity. Our initial laboratory meal studies conducted with 5- to 10-year-old children without obesity demonstrate a significant dose-dependent effect of FTO SNP rs9939609 on total caloric intake adjusted for body weight during laboratory lunch meals, with children consuming 64 more calories per copy of the obesity-risk allele at baseline. In order to determine whether the FTO obesity-risk allele is associated with increasingly divergent caloric intake over time, we measured total caloric intake during subsequent laboratory meals one year and two years after the participants' original laboratory meals.

Methods:
122 child participants without obesity between 5 and 10 years old were genotyped for FTO SNP rs9939609. After an overnight fast, participants were served a standardized breakfast with portion size adjusted for their estimated daily energy requirements. Participants were instructed to refrain from consuming anything but water for the subsequent 3.5 hours, after which they were served a laboratory lunch meal. Total caloric intake during the meal was determined by weighing all individual food and beverage items before and after the meal. Linear regressions were used to assess the association between FTO genotype and total caloric intake during the baseline meal adjusted for body weight. Participants repeated the laboratory meal procedure one year and two years after the baseline meal. Linear mixed models were used to assess the association between FTO genotype and changes in total caloric intake during the laboratory meal over time.

Results:
Of the 122 children who participated in the baseline laboratory meal, 22% were homozygous for the obesity-risk allele (AA), 44% were heterozygous (AT), and 37% were homozygous for the non-risk allele (TT). 90 participants completed the one-year meal, and 64 participants completed the two-year meal. There was a significant association between FTO genotype and the rate of change of total caloric intake between annual meals, with the AA genotype associated with an additional 120 kilocalories of increase in intake per year.

Conclusions:
These findings demonstrate that the FTO SNP rs9939609 is associated not only with greater total caloric intake by children without obesity during laboratory test meals but also with a greater rate of change of caloric intake over time.

Board 5, Poster 2

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Weight Loss Maintenance in Medically Managed Patients with Obesity
Authors *	Beverly G. Tchang*, MD; Mohini Aras, MD; Lindsay Mandel, BA; Leon I. Igel, MD; Rekha Kumar, MD; Katherine H. Saunders, MD; Jonathan Waitman, MD; Louis J. Aronne, MD; Alpana P. Shukla, MD
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Structured Abstract *

OBJECTIVE: To investigate the real-world effectiveness of FDA-approved and off label anti-obesity medications (AOMs) with respect to weight loss and weight loss maintenance at 1 and 2 years. BACKGROUND: The efficacy of AOMs in combination with lifestyle modification is robustly supported by randomized clinical trials, but there is a paucity of data on their effectiveness for weight loss maintenance in clinical practice. Data on polypharmacotherapy is also poorly reported. METHODS: This retrospective chart review included 1775 patients age 18-75 who established care at an academic weight management center between April 2014 and April 2016. Three independent reviewers evaluated demographic, medication, and weight data from patients who had both 1-year and 2-year follow up appointments. Patients were excluded as detailed in flowchart below. RESULTS: The mean weight loss at year 1 and year 2 were similar (-9.9+7.7% vs. -10.3+8.7%, p=0.44). There was no statistically significant difference in weight loss between the T2DM and non-DM cohorts at 2 years (-8.3+8.7% vs. -10.5+8.7%, p=0.07). The average BMI change at 2 years was -10.6+9.4% (p<0.001). At 1 year, 75.3% of patients achieved >5% weight loss and 46.3% achieved >10% weight loss. Of these cohorts, 87.4% maintained >5% weight loss and 76.9% maintained >10% weight loss at 2 years. At 2 years, 96.2% of patients were taking >1 weight loss medication, and 79.3% of patients were taking 2 or more AOMs, with an average of 2.5+1.2 AOMs per patient. The most commonly prescribed weight loss pharmacotherapies were metformin, phentermine, and topiramate. CONCLUSIONS: Clinically significant weight loss is achievable and maintainable over 2 years with the use of combined AOMs in an academic weight management center.

Board 6, Poster 1

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Feasibility of a Standard Behavioral Weight Loss Intervention in a Diverse Urban Population
Authors *	Kristie Rupp* and Ciarán P. Friel
Institutional Affiliations For Each Author. *	1. Department of Health and Movement Sciences, Southern Connecticut State University, New Haven, CT 2. Center for Behavioral Cardiovascular Health, Columbia University Medical Center, New York, NY
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Structured Abstract *

Background: Standard behavioral weight loss interventions (SBWLI) are effective at reducing body weight by approximately 10% in 6 months. SBWLIs are comprised of weekly group behavioral intervention sessions designed to help participants meet prescriptions for reduced caloric intake and increased physical activity, however, the feasibility of SBWLIs in a diverse urban population is not well understood. The purpose of this pilot study was to examine the feasibility of this approach in a diverse urban environment.

Methods: Participants (N=23) with obesity (body mass index (BMI) of 34.6 ± 3.2 kg/m2) were 47.8% non-Hispanic black, 17.4% Hispanic, 95.7% female, and reported engaging in < 60 mins per week of structured physical activity at baseline. Participants were recruited through flyers posted throughout Brooklyn College and the surrounding communities, as well as through online classifieds (Craigslist). Assessments at baseline and following the 6 month SBWLI included: height; weight; resting blood pressure; waist circumference; body composition; fitness (time to 85% age-predicted HRmax); and physical activity (via accelerometry). Participants were divided into small cohorts, which met weekly throughout the intervention. The SBWLI was comprised of a prescription to reduce caloric intake by ~500 kcal/day and 200 mins/week of moderate to vigorous physical activity (MVPA).

Results: A total of n=16 completed the 6-month SBWLI. Participants who completed the study had significant reductions in body weight (-7.8 ± 6.6 kg), BMI (-2.8 ± 2.7 kg/m2), waist circumference (-6.6 ± 5.2 cm), and significantly increased fitness (1.3 ± 2.1 mins) and MVPA (17.5 ± 16.8 mins/day) (p's <0.01). Participants who completed the study were significantly older in comparison to non-completers at baseline, (31.5±10.7 vs. 20.6 ± 3.3 years, respectively [p<0.05]), but were no other differences with respect to BMI, fitness, MVPA, race/ethnicity, gender, income, or educational attainment.

Conclusions: SBWLI's are efficacious in reducing body weight and increasing MVPA among a diverse urban population who complete a 6-month program. However, high drop-out rates in our study suggest that the current SBWLI format may not be the most effective weight loss approach when targeting younger adults with obesity in a diverse urban environment.

Board 6, Poster 2

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Trial of Restarting and Tolerating Metformin (TreatMet)
Authors *	1) Jeremy N. Orloff 2) Samir Touhamy II* 3) James H. Flory M.D. 4) Leon Igel M.D.
Institutional Affiliations For Each Author. *	1) Researcher, Weill Cornell Medicine Comprehensive Weight Control Center 2) Student, Weill Cornell Medical College 3) Assistant Attending, Endocrine Service Memorial Sloan Kettering Cancer Center 4) Assistant Professor of Clinical Medicine, Division of Endocrinology
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Structured Abstract *

Background:
Metformin is a safe, effective first-line medication for T2DM and is also used for weight loss and diabetes prevention. Gastrointestinal and other side effects prevent its use in 10-20% of patients and may limit dosage in others (Flory J, Lipska K. Metformin in 2019. JAMA. 2019 Apr 22). But, side effects in chronic medications are not always reproducible. A study of patients who discontinued statins due to subjective myopathy found that participants could not distinguish between statin and placebo, and half were able to adhere to therapy after trial completion (Joy et al, Ann Intern Med. 2014 Mar 4;160(5):301-10). We aimed to assess whether these results generalize to metformin by exposing previously metformin-intolerant participants to alternating metformin and placebo. The primary hypotheses are that satisfaction and side effects will be the same for placebo and metformin, and that at least 30% of participants will adhere to a higher-dose 6 months after completion.
Methods:
13 metformin-intolerant participants were recruited. 'Intolerant' meant either unable to take metformin at all, or to increase the dose past 1,000 mg. Participants continued their baseline medications with escalating doses of metformin in 250mg increments, alternating with placebo in a randomized, double-blinded fashion. After each two-week period, participants completed questionnaires on satisfaction, symptoms, adherence, and the participant's assessment of whether they had just been taking metformin or placebo. Follow-up at six months will determine if they are continuing metformin and at what dose.
Results:
3/13 participants were lost to follow-up and not included in analysis. Of the others, at time of enrollment, 3/10 were not taking any metformin while 7/10 were taking metformin but unable to increase their dose past 1000 mg. Common reasons for intolerance at baseline were nausea (5/10) and diarrhea (5/10). 3/10 participants were able to complete the full protocol. 7/10 stopped early due to side effects.
Conclusions:
The rate of protocol cessation due to intolerance suggests that metformin intolerance is relatively reproducible, but that approximately 1/3 of these patients will be able to resume metformin or increase its dosing at a later date. This contrasts to statins, for which other investigators found intolerance was not reproducible. These findings highlight metformin's side effects as a major, insufficiently studied, barrier to use. They also allow providers to counsel patients that a rechallenge with metformin is not futile, although the probability of success is likely less than 50%. Further interpretation awaits unblinding

Board 7, Poster 1

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Magnetic Resonance Methodologies to Assess Change in Hepatic Fat Fraction in Adolescents After Sleeve Gastrectomy
Authors *	Elizabeth A. Berg, MD*, Jennifer Woo Baidal, MD, MPH, Jeffrey Zitsman, MD, Ilene Fennoy, MD, Joel Lavine, MD, PhD, Wei Shen, MD, MPH
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Structured Abstract *

Background:
Weight loss above 7-10% reduces histologic hepatic steatosis (Promrat, 2017) yet few approved treatments exist for pediatric obesity and nonalcoholic fatty liver disease (NAFLD). Metabolic bariatric surgery (MBS) treats weight loss most effectively (Ryder, 2018); its impact on pediatric NAFLD remains unknown. MRI with spectroscopy (MRS) provides a validated, reproducible means to evaluate hepatic steatosis and avoids repeated liver biopsies. This study assesses whether MRI and MRS can quantify hepatic steatosis changes in adolescents with severe obesity after MBS and correlates MRI/MRS with liver histology and serum markers.

Methods:
This observational cohort study recruited adolescents with severe obesity undergoing sleeve gastrectomy (SG) from a multidisciplinary MBS program in Manhattan. MRI and MRS were performed to quantify hepatic fat fraction (HFF) 2-10 weeks pre-operatively and 12-24 weeks post-operatively. Paired t-tests evaluated HFF and ALT changes after SG. Pearson correlations were calculated between MRI-determined HFF (MRI-HFF), MRS-determined HFF (MRS-HFF), ALT and intra-operative liver biopsy.

Results:
20 participants have enrolled in this ongoing study. 12 have completed pre- and post-operative MRI, serum markers for metabolic syndrome (ALT, lipid profile, fasting glucose and insulin), and intraoperative needle biopsy of the liver. All completers were female, 73% were Hispanic, mean age was 16.7 years (range 14-18), mean BMI was 44.1kg/m2 (range 36.4-59.8). 7 biopsies detected hepatic steatosis but only 4 participants had elevated pre-operative ALT >22U/L (Schwimmer, 2010). Mean pre-operative MRS-HFF was 9.1%±10.2% and mean post-operative MRS-HFF was 2.8%±1.8%. MRS-HFF decreased significantly (-6.3%±9.9%, $p<0.05$) and the decrease in MRI-HFF trended to significance (-5.4% ±9.8%, $p=0.10$). Pre-operative ALT correlated with pre-operative MRS-HFF ($r=0.69$, $p<0.05$) and MRI-HFF ($r=0.65$, $p<0.05$). ALT decreased post-operatively (-5.9±7.7 units/L, $p=0.04$) and correlated with post-operative MRS-HFF ($r=0.64$, $p<0.05$).

Conclusions:
This study demonstrates that MR methodologies detect changes in hepatic steatosis associated with SG, which has not yet been shown in adolescents. HFF decreases after SG and correlates with a decrease in ALT. When all data collection has been finalized, MR results will be correlated with metabolomics profiles from banked plasma collected at the time of the MRI.

References:
1. Promrat K et al. Randomized controlled trial testing the effects of weight loss on nonalcoholic steatohepatitis. Hepatology. 2010;51(1):121-129.
2. Ryder JR et al. Treatment options for severe obesity in the pediatric population: Current limitations and future opportunities. Obesity. 2018;26(6):951-960.
3. Schwimmer JB et al. SAFETY study: Alanine aminotransferase cutoff values are set too high for reliable detection of pediatric chronic liver disease. Gastroenterology. 2010;138(4):1357-1364.e2.

Board 7, Poster 2

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Time Restricted Eating Administered via a Smartphone Application in Adults with Overweight and Obesity: A Feasibility Study
Authors *	Abigail Jawahar, Malini Prasad*, Nandini Nair, Emily Manoogian, Satchin Panda, Blandine Laferrère
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Structured Abstract *

Background:
Adults with obesity have an increased risk for developing diabetes and cardiovascular disease. Achievement of modest weight loss can decrease these risks. Long-term caloric restriction is difficult and novel interventions, such as time restricted eating (TRE), may be more sustainable. TRE, or restricting the food intake interval, improves metabolism via weight loss and circadian realignment, i.e. aligning internal clocks with the feeding/fasting pattern. Smartphone applications (apps) are promising affordable tools to monitor behavior and improve adherence to lifestyle interventions.

Our goal is to study the effect of a TRE intervention, administered via the app My CircadianClock, on weight loss, in metabolically unhealthy ethnically diverse adults with obesity. This open labeled study will assess: 1) The recruitment potential; 2) The percentage of individuals eating ≥14 h/d; 2) The effectiveness of TRE to 10 h/d, administered via the study app, on weight loss; 3) Whether adherence to TRE and self-efficacy score predict 3-month weight loss.

Methods:
Recruitment occurs in 3 phases: a phone screen to assess eligibility; an in-person screen for medical history, anthropometrics measurement and instruction on how to use the study app; a 2-week run-in period to establish eating pattern and duration. The intervention consists of one baseline education session about healthy lifestyle, followed by educational and motivational text messages about healthy lifestyle, diet and benefit of weight loss, administered via the app, several times a week, for 3 months. Adherence is defined as 2 or more login events, occurring at least 5 hours apart, and reduction of eating duration by ≥4h.

Results:
35 participants, 86% women, were phone-screened: age 55.0±9.5y [39-72], BMI 31.8±6.0 kg/m2 [24.1-46.2]. 15 participants underwent in-person screening; results from the 2-week run-in period show a 15.0±0.5 h [14.2-15.56] mean eating duration. The main reason for the attrition during the 2-week run-in period is concern about effort needed keep accurate food logs. During the active TRE intervention, login occurred >95% of days, with 4.26 login events/d; adherence to the TRE schedule was good with average reduction of eating duration by 3.37 h ± 1.75 h/d.

Conclusion:
These preliminary data show that recruitment for a TRE weight loss intervention administered via the smartphone app My CircadianClock is feasible; the majority of screened individuals eat > 14h/d and could benefit from TRE intervention; the intervention is effective at reducing eating duration. Its effect on weight loss will be assessed.

Board 8, Poster 1

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Underdiagnoses of dyslipidemia in children by use of adult reference ranges
Authors *	Michael Ohene-Adjei*, Shuliang Deng, Martina Pavlicova, Thomas Starc, Vidhu Thaker
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Structured Abstract *

Background: Cardiovascular disease (CVD) commences during childhood, and the National Heart Lung and Blood Institute (NHLBI) provided guidelines for pediatric specific reference ranges for lipoproteins in 2012. After 7 years, many laboratories serving children have failed to adopt these reference ranges. This study seeks to identify the prevalence of underdiagnoses of dyslipidemia in 4 different pediatric cohorts due to incongruent lipid reference ranges seen across laboratories in metropolitan New York.

Methods: We extracted lipoprotein values and reference ranges from the laboratory reports of children referred to the pediatric lipid clinic at Columbia University Medical Center (CUMC) from Jan-Dec 2018. The unique lipoprotein reference ranges were compared to the NHLBI reference ranges. Lipoprotein levels were obtained from 3 additional pediatric cohorts: i) NHANES population-based data, ii) pediatric clinics at CUMC, and iii) pediatric clinic at Boston Children's Hospital (BCH) between 2009-17. Using the NHLBI and laboratory reference ranges, 2x2 matrices were constructed to identify the subjects who were underdiagnosed for abnormal levels of total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL-C) and high-density cholesterol (HDL-C) to identify the sensitivity (Sen) and negative predictive values (NPV). Linear temporal trends were analyzed using multivariable regression models using age and sex as covariates. All analyses were conducted in R v3.4.

Results: We identified 8 unique normal cut off levels from 11 different laboratories in metropolitan NYC, of which 2 were aligned with the NHLBI guidelines. In these pediatric cohorts, the use of these reference ranges results in low sensitivity and NPVs for each of the lipoproteins: TC: Sen 0.02-0.2, NPV 0.75; HDL-C: Sen 0.1-0.5, NPV 0.78; LDL-C: Sen 0.05-0.3, NPV 0.86; TG: Sen 0.1-0.5 NPV 0.88. This will result in underdiagnoses of dyslipidemia in children: TC: 22-27% (CI: 21-29), HDL-C 12-23% (CI: 11-25), LDL-C 11-15% (CI: 8-19), TG: 8-15% (CI 6-19). While the NHANES data showed a falling temporal trend in the proportion of underdiagnoses, the two hospital-based cohorts showed a rising trend over time. The children seen with the higher lipoprotein levels in the lipid clinic had lower rates of underdiagnoses, regardless of the reference ranges.

Conclusions: The incongruent lipoprotein reference ranges for children compared to NHLBI recommendations misleads clinicians with underdiagnoses preventing much needed counseling for dyslipidemia at the primary care level, ultimately resulting in a higher burden of atherogenic diseases in our future generations.

Board 8, Poster 2

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Offspring body composition at 59 weeks: No sustained effects of gestational weight gain intervention
Authors *	K Whyte*, J Thornton, FX Pi-Sunyer, D Gallagher
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Structured Abstract *

Background: LIFT (Lifestyle Intervention for Two) trial found that intervening in women with overweight and obesity through behaviors promoting healthy diet and physical activity to control gestational weight gain (GWG) resulted in neonates with similar fat and greater lean mass at birth. Whether these neonate measureable effects are sustained though 1-year was the focus of this investigation.

Methods: Neonatal body composition was assessed by Infant QMR at birth (n=169), 14 weeks (n=136) and 59 weeks (n=139). Between group (Lifestyle Intervention, LI and Usual Care, UC) differences in fat and lean mass were investigated using ANCOVA adjusting for maternal age and BMI in early pregnancy, GWG, offspring sex, ethnicity, and age.

Results: Retention at 59 wks was 82.2% (N=139). At birth, compared to UC, LI had greater weight (131±59g p=0.03), head circumference (0.38±0.17mm; p=0.003), and lean mass (105±38g; p=0.006). At 14 wks, compared to UC, LI infants had similar weight (112±131 g p=0.395), fat mass (14±80 g; p=0.86), lean mass (100±63g; p=0.117), and at 59 wks, had similar weight (168±183 g p=0.36), fat mass (148±124 g; p=0.237), lean mass (117±92g; p=0.205). Head circumference was greater in LI at 59 wks (0.46±0.21mm; p=0.003).

Conclusions: The intervention effects on body composition observed at birth were not sustained into and beyond the post-natal period. Unmeasured early life factors that influence growth and body composition, not limited to nutrition and diet as examples, strongly impact post-natal growth and composition.

Board 9, Poster 1

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Lifestyle Modifications and Weight Loss Surgery Outcomes in Ethnically Diverse Adolescents
Authors *	Gabrielle M. Estevez-Inoa, BS 1 Jeffrey Zitsman, MD 2
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Structured Abstract *

Background - Bariatric surgery has emerged as a safe and effective treatment for severe obesity and obesity-related comorbidities in adolescents. However, most research studies evaluating the efficacy of bariatric surgery in adolescents lack a representative sample of certain ethnic subpopulations with distinct eating choices as well as a higher prevalence of childhood obesity. Furthermore, no study to-date has assessed the impact of dietary habits on weight loss outcomes in adolescents who undergo bariatric surgery.

Methods - In this retrospective analysis, we performed a medical chart review of all Hispanic and Orthodox Jewish adolescents who underwent sleeve gastrectomy (SG) at the Morgan Stanley Children's Hospital. Dietary habits and anthropometrics were collected at two time periods (i.e. at baseline and at a follow-up visit 6 months+/-3 months after surgery). Dietary habits of interest included 'consumption of sugar-sweetened beverages (SSBs)', 'skipping meals', 'eating large portions', and 'exercise', each with dichotomized responses (i.e. healthy or unhealthy). Outcomes of interest included change in body mass index (delta_BMI), percent of total weight loss (%TWL), and percent of excess BMI loss (%EBMIL). To determine the relationship between dietary/lifestyle changes and weight loss outcomes, the ethnic groups were analyzed separately using unpaired t tests or Wilcoxon rank-sum test, depending on normality of the outcome variable.

Results - The study included 72 Hispanic and 30 Orthodox Jewish adolescents, with a median age of 15 years old (interquartile range [IQ]: 14-16 year old). Dietary habits related to 'skipping meals', 'eating large portions', and 'exercising' differed significantly at baseline between Hispanic and Orthodox Jewish subgroups (p=0.004, p=0.011, p=0.013, respectively), but only 'skipping meals' differed significantly postoperatively (p=0.024). The delta_BMI was 9.75+/-4.19 kg/m^2 for the Hispanic subgroup and 9.47+/-4.52 kg/m^2 for the Orthodox Jewish subgroup. In the Hispanic subgroup, the median %TWL was 20.2% (IQ: 16.2-24.3%) and the median %EBMIL was 43.1% (IQ: 34.2-58.5%). In the Orthodox Jewish subgroup, the %TWL was 20.8+/-9.48% and the %EBMIL was 53.5+/-23.4%. In this study, weight loss outcomes at the 6-month postoperative period did not differ between healthy and unhealthy dietary/lifestyle changes, except for significant differences seen in delta_BMI (p=0.035) and %TWL (p=0.048) between Orthodox Jewish adolescents who reported exercising vs those who reported not exercising.

Conclusion - Our findings report comparable weight loss outcomes after SG in Hispanic and Orthodox Jewish adolescents relative to results from national cohort studies. Additionally, only exercise modifications in Orthodox Jewish adolescents resulted in greater weight loss.

Board 9, Poster 2

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Associations Between Chronic Pain and Perceived Racial and Weight Discrimination In Participants Enrolled in a Primary Care Based Weight Management Clinical Trial: A Secondary Analysis
Authors *	Ericka N. Merriwether, PT, DPT, PhD (1,2)* Sandra Wittleder, PhD (2) Gawon Cho, MS (3) Eushavia Bogan (2) Binhuan Wang, PhD (4) Stephanie Orstad, PhD (2) Joseph Ravenell, MD (2,4) Melanie R. Jay, MD, MS (2,4)
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Structured Abstract *

Background: Over 40% of American adults have a BMI in the overweight or obese range, with a higher prevalence in Latinx/Hispanics (47.0%) and non-Hispanic Black/African-Americans (46.8%). Chronic pain is highly prevalent in adults with obesity (>70%). Perceived discrimination is the reported denial of access to resources based on race and weight, is associated with disparities in pain management, weight loss, and other health outcomes. This study aimed to characterize participant experiences of chronic pain and perceived racial and weight discrimination, and to explore the relationships in adults classified as overweight or having obesity.

Methods: Baseline data was obtained from an ethnically diverse sample of participants enrolled in a dual-site clinical trial of a behavioral weight management intervention called the Goals for Eating and Moving (GEM) Study (n=325). Eligible participants are English and Spanish-speaking adults aged 18-69 years with obesity or who are overweight with a medical comorbidity. Pain intensity and pain interference were assessed using the PROMIS-29. Perceived racial and weight discrimination were assessed using the Experience of Discrimination (EOD) and the NESARC assessments. Frequencies of perceived racial and weight discrimination were determined using the Chi-square test. Differences in pain intensity and pain interference between discrimination groups were compared by Wilson Rank Sum test. Associations between continuous variables were quantified by Spearman's rho correlation coefficient.

Results: Participants reported racial discrimination only (n=175), weight discrimination only (n=6), both racial and weight discrimination (n=55), and no discrimination (n=89). The perceived weight discrimination group (n=61) had higher pain intensity (M=5.2, SD=2.8 vs. M=4.0, SD=3.1; p=.003) and pain interference (M=57.38, SD=9.83 vs. M=52.06, SD=9.88; p<.001) compared with those who did not report weight discrimination. The perceived racial discrimination group (n=230) had higher pain intensity (M=4.4, SD=3.2 vs. M=3.7, SD=3.1; p=.04) and pain interference (M=53.9, SD=9.9 vs. M=50.9, SD=10.2; p<.001) compared with those who did not report racial discrimination. Perceived racial discrimination was associated with higher pain intensity (r=.15, p=.005) and pain interference (r=.22, p=<.001). Perceived weight discrimination was not significantly associated with pain intensity.

Conclusions: These findings show that chronic pain and perceived racial and weight discrimination are highly prevalent in a sample of adults with higher BMIs, and that both types of discrimination are experientially distinct. Future studies should determine how to best mitigate the adverse effects of perceived racial and weight discrimination on pain and general health.

Board 10, Poster 1

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Baseline characteristics and financial incentive preferences of low-income primary care patients with obesity enrolled in the Financial Incentives foR Weight Reduction (FIReWoRk) Study
Authors *	Stephanie L. Orstad, PhD*; Joseph A. Ladapo, MD, PhD; Christina Hernandez, MPH; Susan Parraga, BA; Zuheir Diab, BA; Ololade Afolayan, BS; Miguel A. Cuevas, BS; Victoria Sweat, MA; Melanie Jay, MD, MS
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Structured Abstract *

Background: Obesity is a major public health challenge and may exacerbate economic disparities. Financial incentives for weight management may intensify low-income individuals' utilization of evidence-based behavioral strategies. The objective of this research was to describe the baseline demographic and health-related characteristics, technology use, financial incentive preferences, and residential neighborhoods of patients enrolled in the FIReWoRk Study, a randomized controlled trial to test the effectiveness of goal-directed vs. outcome-based financial incentives for weight loss, as compared to the provision of health behavior change resources alone.

Methods: Patients 18-70 years of age who had a body mass index (BMI) ≥30 kg/m2 were recruited from three primary care clinics serving residents of socioeconomically disadvantaged NYC and LA neighborhoods. All participants received a one-year commercial weight loss program membership, self-monitoring tools (scale, food journal, and Fitbit Alta HR), health education, and monthly in-clinic check-in visits. In addition, intervention group participants earned up to $750 over 6 months for 1) attending the weight management program, self-monitoring weight and diet, and meeting physical activity guidelines (goal-directed arm); or 2) a ≥1.5% to ≥5% reduction in baseline weight (outcome-based arm). Survey items were adapted from the ACS to assess participants' demographic profile and technology use, from NHANES to assess health history, height and weight, and from our prior studies to assess financial incentive preferences. Neighborhood income data from the US Census was mapped using Tableau to each participant's tract of residence. We calculated the number and proportion of participants represented within each categorical variable, and means, standard deviations, and ranges for each continuous variable.

Results: Participants' (N=243) mean age was 46.9±12.8 and mean BMI was 37.6±5.9. Eighty-four percent were female and 97.7% identified as a race/ethnicity other than non-Hispanic white. Two in three participants spoke Spanish at home and 9 in 10 used a smartphone. Participants resided in census tracts with a median household income averaging $33,229±$10,169. The majority (57.6%) preferred to receive goal-directed rather than outcome-based financial incentives.

Conclusions: If FIReWoRk effectively reduces weight by ≥5%, such financial incentive programs may be scaled to benefit similar underrepresented patient populations in public and private health systems.

Board 10, Poster 2

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Parent-child relationship quality and child self-regulation moderate impacts of a primary care-based early child obesity prevention program
Authors *	Rachel S. Gross*, Alan L. Mendelsohn, Mary Jo Messito.
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Structured Abstract *

Background: Starting Early Program (StEP) is a comprehensive prenatal and pediatric primary care-based early child obesity prevention program designed for low-income, Hispanic families, which improves infant feeding, activity and weight. However, variability in weight impacts exists, highlighting the need to explore moderators that could be targeted in future program adaptations. Broader aspects of the parent-child relationship and child self-regulation may represent potential moderators of impact, given their known associations with early child obesity in the literature.

Methods: The StEP randomized controlled trial enrolled pregnant women at a third trimester visit. Women were randomized to standard care or an intervention with prenatal/postpartum individual nutrition counseling and nutrition and parenting support groups coordinated with pediatric visits. We used independent samples t-tests to determine associations between intervention group status and child weight outcomes at 24 months. We used subgroup analyses to explore if parent-child relationship quality (Parenting Stress Index-Dysfunctional Interactions; StimQ survey-verbal responsivity during reading and play) and child self-regulation (Early Child Behavior Questionnaire) moderated intervention impact.

Results: 533 pregnant women randomized (67% high school grads; 87% WIC participants; 29% pre-pregnancy BMI>30). No group differences at baseline (birth weight 3.4kg vs. 3.4kg, p=.30). StEP intervention children had lower mean weight for age z-scores at 24 months compared to controls (0.56 vs. 0.81, Cohen's d -0.25, p=.03). Subgroup analyses revealed reduced child weight impacts for pairs with lower relationship quality (Cohen's d: -0.16, p=.45 vs. -0.31, p=.04) and with lower positive parenting practices (0.08, p=.77 vs. -0.37, p=.01). Subgroup analyses revealed reduced impacts for children with high hyperactivity (-0.08, p=.65 vs. -0.45, p=.01) and low inhibitory control (-0.14, p=.39 vs. -0.41, p=.03).

Conclusions: Although StEP has positive impacts on weight similar to other effective programs, parent-child relationships and child self-regulation moderate effects. Specifically, lower quality interactions and reduced positive parenting practices, together with high child energy and low inhibitory control, are associated with decreased StEP weight impacts. Next steps include the integration of strategies that target general parent-child relationships and child self-regulation within an early obesity prevention program. This integration could represent a novel pregnancy-through-toddlerhood model to increase weight impacts. USDA AFRI 2011-68001-30207; NICHD K23HD081077.

Board 11, Poster 1

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	The effects of a personalized weight loss diet on glycemia in individuals with prediabetes and type 2 diabetes
Authors *	Margaret A. Curran*, David E. St-Jules, Collin J. Popp, Paige Illiano, Mary Ann Sevick
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Structured Abstract *

Background: For overweight and obese individuals with prediabetes and type 2 diabetes (T2D), weight loss is a usual recommendation. However, dysglycemia may make weight loss difficult for these individuals. A diet personalized to reduce postprandial glycemic response (PPGR) may be particularly useful for weight loss in this patient population. The Personal Diet Study is a randomized clinical trial comparing two weight loss approaches: a personalized diet (PD) and a standard low-fat diet (LFD). In this preliminary report we examine the impact of these different approaches on dysglycemia in terms of daily glycemic variability (GV) and hemoglobin A1c (HbA1c).

Methods: Personal Diet involves 6 months of intervention followed by 6 months of observation. Preliminary data on the first 36 participants enrolled (n=21 in PD, n=15 in LFD) and completed 3-month assessments are included in this report. HbA1c was assessed with in-person measurement. GV was assessed from continuous glucose monitoring (CGM) using the Abbott Freestyle Libre Pro. Within-group and between-group changes over time were evaluated.

Results: The majority of participants (71.4%) were female, with a mean age of 58.7 (10.6SD) years and mean BMI of 32.3 kg/m2 (4.5SD). An average of 5.7 (2.3SD) days of CGM data were available. The mean within-group changes in mean amplitude of glycemic excursions (MAGE) were -10.6 (SD 13.1, $p<0.01$) and 2.9 (SD 13.2, $p=0.44$) in PD and LFD groups respectively, and a significant between-group difference ($p<0.01$) was observed. Although a similar within-group trend was seen for HbA1c (-0.08% vs 0.03%, respectively), the between-group difference did not reach significance ($p=0.18$).

Discussion: Our preliminary results indicate that a personalized diet reduces GV but not HbA1c in those with prediabetes and T2D. As the trial is ongoing and weight (the primary outcome) is blinded, it remains unclear whether a difference in diet or weight were the main driver of changes in GV. Regardless, the potential for personalized nutrition to improve glycemic control warrants further investigation.

Board 11, Poster 2

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Visceral Adipose Tissue (VAT) Mass is not Accurately Quantified by CoreScanTM at Pre- and Post-Bariatric Surgery
Authors *	Maxine Ashby-Thompson*, Rosalie Zurlo, John Thornton, Dympna Gallagher
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Structured Abstract *

Background
Elevated VAT is an established metabolic risk factor. The CoreScanTM (GE) software estimates VAT from a specified region on a whole-body DXA scan and has not been validate in persons with severe obesity or longitudinally after rapid weight loss. The purpose of this study was investigate the level of agreement in VAT by DXA and the criterion MRI method.

Methods
Patients (20 women, 2 men; 91% Caucasian) who had DXA and whole-body MRI before surgery (T0) and twelve months (T12) after bariatric surgery were evaluated. Descriptive statistics and scatter plots compared VAT pre- and post-surgery and Bland-Altman plots measured agreement.

Results
At T0, (mean±SD [range]) age 42.0±10.0 years (22-58 years), weight 114.0±12.5 kg (86.2-135.3 kg) and BMI 41.4±3.5 kg/m2 (35.5-51.5 kg/m2). At T12, (mean±SD [range]) BMI 27.5±4.0 kg/m2 (19.3-35.7 kg/m2) and weight change from T0 was 37.0±13.6 kg [9.8-63.4 kg]. Measures of VAT by DXA and MRI were correlated at p=0.01, r=.89 (T0), r=.86 (T12), r=.84 (T12-T0).

At T0, mean (±SD) VAT mass by DXA was 2.05 (±.87kg) compared with 4.58 (±1.80kg) by MRI. On average, DXA estimated 45% of total VAT by MRI. The bias by DXA was -2.53kg (95% CI=-2.04, -3.02kg). At T12, mean DXA VAT mass was 0.69 (±.46kg), and estimated 65% of total VAT by MRI (1.60±1.46kg). DXA bias was -0.91kg (95% CI=-0.42,-1.40kg). Bland-Altman Plot showed between method VAT differences were dependent on VAT mass. Between-method differences were greater: at T0 when VAT was <0.5 and >4.5kg and at T12 when VAT was <0.5 and >1.5.

Conclusions
CoreScanTM VAT estimates are influenced by level of adiposity and by amount of VAT lost following weight reduction surgery, which are associated with error.

Board 12, Poster 1

Abstract Topic Category *	Interventions and Clinical
Abstract Title *	Madre, Niños y Microbioma (MNM) Study: A pilot prospective birth cohort to understand establishment and development of the infant gut microbiome
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Structured Abstract *

Maternal nutrition and feeding practice may influence the infant gut microbiota, potentially due to vertical transmission in utero, during delivery and/or via breastfeeding. These early-life microbiota alterations might influence child health in the long term. We aim to determine how pre- and postnatal nutrition influence infant gut microbiome delevopment.

We enrolled 40 pregnant women in their 3rd trimester (Barcelona, Spain). Stool samples were collected from family triads pre- (fathers, mothers) and postnatally (mothers, infants) on days D0, 7, 14, 30, 60, 90, 120, 270, 365. Samples were sequenced for the 16S rRNA V3-4 region and quantitative taxonomic profiling was performed using QIIME2.

Mean infant species diversity remained stable through D120 and significantly increased thereafter until D365 (Shannon index 2.75 vs. 4.18, p=8.25 x 10-5), but remained lower than that of adults (Shannon index 6.8). Infant microbial composition (mean distance, unifracunweighted) was consistently more similar between infants than to adults through D120 (0.57□0.09 vs. 0.85□0.04, PPERMANOVA=0.001), but on D270 and D365 became more similar to adults (0.78□0.05 to 0.71□0.06; PPERMANOVA=0.001). Infants exhibited inter-individual variability in relative frequency of taxa. Mean infant Gammaproteobacteria and Streptococcus abundance declined from D7 to D365 (12-3% and 14-2%). Bifidobacterium abundance increased from D7 to D120 (33-64%) with a decline at D270 (42%) accompanied by an expansion of Firmicutes (13-28%).

Observed temporal changes in infant taxa suggest breastfeeding and complimentary feeding impact the microbiome and are consistent with development of the infant gut microbiota. Future analyses of breastmilk and dietary data will clarify these preliminary findings.

Board 12, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Effect of unsaturated fat type on carbohydrate-stimulated lipogenic gene expression in rats
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Structured Abstract *

Background. Polyunsaturated fatty acids (PUFA) have been reported to decrease levels of active SREBP1c, a major regulator of fat synthesis. Carbohydrate stimulates hepatic lipogenesis mainly through the SREBP1c pathway. Therefore, high intakes of unsaturated fat may diminish stimulation of de novo lipogenesis (DNL) in the liver by carbohydrate. However, it is unclear whether this effect is specific to n-6 PUFA, and whether it is an acute effect requiring the presence of PUFA in the test meal. For these reasons, we investigated the effects of several different high-fat (HF) diets on carbohydrate-stimulated expression of genes involved in lipogenesis.

Methods. Male Sprague-Dawley rats (N=80) consumed four different HF diets (55% of energy as fat) comprised of menhaden oil (n-3 PUFA), safflower oil (n-6 PUFA), olive oil (cis-MUFA) or high trans-MUFA, or a low-fat (LF, 15%) control diet, for 1 week or 8 weeks. Hepatic levels of mRNA for proteins related to lipogenesis were measured both in the fasting state and 16 hr after refeeding with a fat-free, high-carbohydrate (HC, 85%) meal that elevated insulin levels.

Results. After 1 week, hepatic gene expression in the n-3 PUFA group failed to respond to the HC meal, and n-3 PUFA rats showed lower fasting expression of most genes studied vs. LF or other HF groups; most responses in the other HF groups were similar to LF controls at this time. After 8 weeks, the n-6 PUFA group had lost mRNA responses to the HC meal for INSIG2, SREBP1c and its targets FAS and SCD1, but retained responses for LPK. The trans-MUFA group also lost responses to the HC meal for INSIG2 and SREBP1c, but retained responses for FAS, SCD1 and LPK, suggesting continuation of ChREBP-mediated regulation of those genes in this group. In contrast, rats on the cis-MUFA diet retained mRNA responses that were at least as strong as those of LF controls, and was the only group to develop a fatty liver by week 8.

Conclusions: Impaired responses of lipogenic gene expression to a high-carbohydrate meal was observed after 1 week's intake of n-3 PUFA, or after 8 weeks' intake of n-6 PUFA or trans-MUFA, but not cis- MUFA HF diets. These effects did not require the presence of the fat in the test meal. These findings demonstrate that high chronic intakes of different types of unsaturated fat produce markedly different effects on hepatic lipogenic gene expression in response to carbohydrate in rats.

Board 13, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Bile acid composition regulates GPR119-dependent intestinal lipid sensing and food intake regulation
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Structured Abstract *

Background & Aims:
Excessive food intake is an important risk factor for obesity. Feeding behavior is governed partly by lipid mediators in the gastrointestinal tract, which regulate satiation and satiety. Lipid mediators in the gastrointestinal tract regulate satiation and satiety. Bile acids (BAs) regulate the absorption and metabolism of dietary lipid in the intestine, but their effects on lipid-regulated satiation and satiety are completely unknown. Investigating this is challenging, because introducing excessive BAs or eliminating BAs strongly impacts gastrointestinal functions. We used a mouse model (Cyp8b1-/- mice) with normal total BA levels, but alterations in the composition of the BA pool that impact multiple aspects of intestinal lipid metabolism. We tested two hypotheses: BAs affect food intake by (1) regulating the production of the bioactive lipid oleoylethanolamide (OEA), which enhances satiety; or (2) regulating the quantity and localization of hydrolyzed fat in the small intestine, which controls gastric emptying and satiation.
Methods: To determine the direct effects of 12-OH BAs, we used Cyp8b1 null mice. We evaluated OEA levels, gastric emptying and food intake in wild-type and Cyp8b1-/- mice. We assessed the role of the fat receptor GPR119 in these effects using Gpr119-/- mice.

Results:
Cyp8b1-/- mice on a chow diet showed mild hypophagia. Jejunal OEA production was blunted in Cyp8b1-/- mice, thus these data do not support a role for this pathway in the hypophagia of Cyp8b1-/- mice. On the other hand, Cyp8b1 deficiency decreased gastric emptying, and this was dependent on dietary fat. GPR119 deficiency normalized the gastric emptying, gut hormone levels, food intake, and body weight of Cyp8b1-/- mice.

Conclusions:
These data demonstrate that eliminating 12-OH BAs slows gastric emptying and induces satiation by allowing hydrolyzed fats to access the distal small intestine, where they activate GPR119. This suggests that enhanced satiation signaling by GPR119 overrides OEA signaling in food intake suppression.

Board 13, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Adipsin from bone marrow fat as a regulator of bone remodeling
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Structured Abstract *

Introduction: The sustained rise in prevalence of obesity is associated with an increased risk for the development of osteoporosis, age-related bone loss, and other bone disorders. This expansion of adiposity, especially within the bone marrow niche, is directly linked to an altered metabolic environment that may contribute to skeletal fragility. Adipsin is the first bona-fide identified adipokine and the most abundantly produced protein by adipocytes. Its function remains mysterious except as Complement Factor D in the alternative complement pathway of the immune system. Given the well documented inverse correlation between bone mineral density (BMD) and marrow adipose tissue (MAT), as well as the endocrine function of adipose tissue, we hypothesized that adipsin is an unrecognized adipokine that regulates bone remodeling.

Methods: Using C57BL/6 mice as a model, we employed the bone-protective PPARγ constitutive deacetylation mice (2KR), adipsin and its downstream effector, C3, knockout mice. These mice were challenged to insulin-sensitizer thiazolidine (TZD) treatment or calorie restriction (CR) in order to induce bone loss and expansion of MAT. Analysis of bone density and marrow adiposity of femurs was performed using the Quantum FX μCT Scanner (Perkin Elmer). Tibias were utilized for RNA analysis of adipogenesis and osteoblastogenesis. Mesenchymal stem cells (MSCs) were isolated from the bone marrow of Adipsin-/- and C3-/- mice and subjected to osteoblastogenic or adipogenic differentiation medium followed by morphological and molecular analyses.

Results: Adipsin is more significantly induced than other adipokines of MAT in various bone loss models. The bone-protective 2KR mice were accompanied by a dramatic downregulation of adipsin expression and circulation levels. Adipsin-/- mice were protected from TZD- and CR-induced bone loss. The complement-deficient C3-/- mice displayed denser bones and less MAT following TZD treatment. Moreover, both Adipsin-/- and C3-/- bone marrow-derived MSCs preferentially differentiated into osteoblasts over adipocytes.

Conclusion: Our study has identified a novel function of adipsin in bone remodeling. The bone-protective effect of PPARγ deacetylation is mediated, at least partially, through repression of adipsin. Furthermore, complement activity plays a crucial role in skeletal remodeling and MAT expansion, suggesting that adipsin works through the complement system to regulate bone homeostasis. A further understanding of the cellular connection between adipocytes and osteoblasts through adipsin could improve the treatment for obesity and diabetes-associated bone loss.

Board 14, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Metabolic impact of low-calorie sweeteners in mice
Authors *	John I. Glendinning* (1), Stephanie Hart (1,2), Hyunseo Lee (1), Jennifer Maleh (1), Gabriella Ortiz (1), Young Sang Ryu (1,2), Abdias Sanchez (1), Sarah Shelling (1) and Niki Williams (1)
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Structured Abstract *

Background

There are widespread concerns that low calorie sweeteners (LCSs) cause metabolic derangement. These concerns stem in part from prior studies linking LCS consumption to glucose intolerance in humans and rodents. Here, we examined this linkage in mice.

Methods

In Experiment 1, we provided mice with ad lib access to chow, water and an LCS-sweetened solution (saccharin, sucralose or acesulfame K) for 28 days, and measured glucose tolerance before and after LCS exposure. In Experiment 2, we provided mice with ad lib access to chow, water and a solution containing saccharin (Sacc), glucose (Gluc), or the binary mixture of Sacc + Gluc for 28 days and made more detailed metabolic assessments.

Results

In Experiment 1, the mice did not develop any impairments in glucose tolerance. In fact, exposure to sucralose slightly improved glucose tolerance. In Experiment 2, exposure to saccharin enhanced insulinemic responses to the glucose tolerance test (GTT), while exposure to the binary mixture of saccharin and glucose increased the rate of glucose uptake during the GTT. However, neither of the LCS-containing solutions caused any changes in glucose tolerance, insulin sensitivity, plasma triglycerides or % body fat. Exposure to the glucose solution, in contrast, enhanced glucose tolerance, cephalic-phase insulin release, insulin sensitivity and % body fat.

Conclusions

The metabolic changes induced by the LCS-containing solutions were rather limited in comparison to those induced by the glucose solution. An ability to increase glucose tolerance in response to repeated carbohydrate challenges should be adaptive for an opportunistic omnivore like the house mouse.

Board 14, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Hepatic Y box binding protein 1 (Ybx1) inhibits systemic insulin signaling by exosome-mediated organ crosstalk
Authors *	Samer Azab*, Jixuan Qiao, and Baran A. Ersoy
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Structured Abstract *

Background: Obesity-induced hepatic stress is a primary risk factor for insulin resistance. Y box binding protein 1 (Ybx1) is a stress-activated transcription factor, which also shuttles miRNA into exosomes, especially miR-223 and miR-144. Hepatic Ybx1 expression and circulating levels of miR-223 and miR-144 increase in the setting of liver disease and diabetes in obese patients. Our preliminary studies in mice indicated that the knockdown of Ybx1 expression solely in the liver did not only improve insulin sensitivity in the liver but also in the white and brown adipose tissue of mice without affecting Ybx1 expression in these tissues.

Aim: Based on these observations, this study aimed to establish the metabolic role of Ybx1 in exosome-mediated organ crosstalk.

Methods: Ybx1 was knocked down in HEK-293E cells using siRNA or adenovirus expressing shRNA against Ybx1 or control. 48h following knockdown, cells were incubated with exosome-free media for 12h prior to the collection of conditioned media. Conditioned media was centrifuged (80 x g) to remove cell debris or ultra-centrifuged (100,000 x g) to discard exosomes, then transferred onto untreated HEK-293E cells for 6h prior to insulin stimulation. Exosomal RNA was extracted from livers of mice following Ybx1 knockdown and transfected into HEK-293E cells.

Results: The Loss of Ybx1 activated basal insulin signaling in the absence of insulin as evidenced by increased phosphorylation of Akt and S6K1. Conditioned media that was collected from these cells activated insulin signaling and sensitivity in recipient cells without reducing Ybx1 expression. Basal S6K1 activation by the conditioned media was so robust that the treatment with insulin did not induce further activation. When exosomes were discarded by centrifugation, the remaining media failed to activate insulin signaling in recipient cells. Treatment of cells with the mTOR inhibitor rapamycin completely reversed the activation of S6K1, confirming the role of mTOR in mediating the effects of the conditioned media. To complement modulation by shRNA, treatment of cells with an siRNA that targeted a different sequence on the Ybx1 mRNA, yielded similar results. Liver Exosomal RNA that was packaged in the presence of Ybx1 inhibited basal insulin signaling in cultured cells.

Conclusion: These findings support the exosome-mediated regulation of insulin signaling by Ybx1, which could underlie the improved insulin sensitivity in the adipose tissue of mice following the knockdown of Ybx1 only in the liver. Therefore, Ybx1 represents a promising novel target in the treatment of insulin resistance due to obesity-induced hepatic stress.

Board 15, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Lipoprotein Insulin Resistance Score, but not Traditional Measures, Discriminates Patients with Pre-operative Metabolic Syndrome at up to One Year Following Bariatric Surgery
Authors *	Ruina Zhang*, BingXue Lin, Manish Parikh, Edward A. Fisher, Jeffrey S. Berger, Jose O. Aleman, Sean P. Heffron

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Structured Abstract *

Lipoprotein insulin resistance (LPIR) is a composite biomarker representative of atherogenic dyslipidemia characteristic of early insulin resistance. Clinically, it is elevated in obesity and may provide information not captured in HbA1c and HOMA-IR. Although bariatric surgery is the most effective intervention for severe obesity, reduces diabetes incidence, and resolves the metabolic syndrome, the effect of bariatric surgery on LPIR is untested. We sought to assess the effects of Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) on LPIR in severely obese, non-diabetic women.

Anthropometric measures and blood sampling were performed preoperatively and at six, and 12 months postoperatively. LPIR was measured by NMR spectroscopy.

Among 53 women (RYGB, n=22; SG, n=31), mean age was 32±7 years and BMI 44.1±6.4 kg/m2. LPIR was reduced by 35±4% and 46±4% at six and 12 months after surgery, respectively, with no difference by surgical procedure. 27 of 53 subjects met IDF criteria for the metabolic syndrome prior to surgery and exhibited higher HOMA-IR, HbA1c, nonHDL-C and LPIR preoperatively. Twenty-five of 27 subjects experienced resolution of the metabolic syndrome diagnosis postoperatively. Concordantly, the preoperative differences in HOMA-IR, HbA1c and nonHDL-C between those with and without metabolic syndrome resolved at six and 12 months. In contrast, subjects with the metabolic syndrome prior to surgery show persistent elevated LPIR scores at six and 12 months post-operatively, suggestive of potentially unappreciated residual dyslipidemic risk.

We are the first to demonstrate improvement in insulin resistance, as measured by LPIR, following bariatric surgery. Importantly, we also show that this measure discriminates those with a preoperative metabolic syndrome diagnosis at up to one year post-operatively. Larger prospective studies are needed to determine the additive value of LPIR in characterizing cardiometabolic risk in severely obese patients.

Board 15, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Acot9 induces hepatic steatosis by trafficking fatty acids towards lipid and glucose biosynthesis
Authors *	Sandra Steensels, Jixuan Qiao, Nourhan Kika and Baran A. Ersoy
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Structured Abstract *

Background: Pathogenesis of obesity-related disorders such as non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus are associated with increased lipotoxicity. Acyl-CoA thioesterase 9 (Acot9) is an enzyme that deactivates fatty acyl-CoAs by hydrolyzing them into free fatty acids and CoA. Acot9 expression is low in the livers of chow-fed mice but increases in response to obesity in mice and is associated with NAFLD in obese patients. In support of a maladaptive role for increased Acot9 activity, the loss of Acot9 in mice (Acot9-/-) protects against diet-induced obesity, steatosis and excessive hepatic glucose production (HGP).

Aim: This study was designed to determine the molecular mechanism by which Acot9 thioesterase activity promotes HGP and steatosis.

Methods: Acot9-/- and wild type littermates (Acot9+/+) were weaned to a high fat diet (HFD, 60% kcal) (n=10-12) for 11 weeks. Acot9 subcellular localization was determined in immunoblots, and substrate specificity was elucidated using an in vitro thioesterase activity assay. Radiolabeled substrates were used to assess the role of Acot9 in hepatic β-oxidation, and metabolomics analysis of livers from Acot9-/- and Acot9+/+ mice was performed by mass spectrometry.

Results: Acot9 localized to the inner mitochondrial membrane where it specifically deactivated short-chain fatty acids (acetyl-CoA, butyryl-CoA and propionyl-CoA), but not long-chain fatty acyl-CoA. Immunoblots and metabolomics analysis indicated that the unique localization of Acot9 directs acetyl-CoA away from protein lysine acetylation and towards the TCA cycle, which in turn provides substrates for lipid and glucose biosynthesis. Because β-oxidation and ketone body production mostly depend on long-chain fatty acids, these functions were not affected by the activity of Acot9.

Conclusions: Taken together, our findings suggest that Acot9 traffics acyl-CoAs towards increased steatosis and HGP under the pathophysiology of obesity. Therefore, Acot9 represents a novel target for the management of NAFLD.

Board 16, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Transcriptional regulation of ZNF638 by thermogenic signals via the cAMP response element binding protein CREB
Authors *	Luce Perie*, Narendra Verma and Elisabetta Mueller
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Structured Abstract *

Background: Zinc finger factors are implicated in a variety of cellular processes, including adipose tissue differentiation and thermogenesis. A number of them, including Prdm16 and ZFP516, have been recently shown to play major roles in brown fat tissues by regulating differentiation, thermogenesis and energy expenditure. We have previously demonstrated that the zinc finger protein ZNF638 is a transcriptional coactivator acting as an early regulator of adipogenesis in vitro, but whether ZNF638 is expressed in fat tissues in vivo and how it is regulated in adipocytes is currently unknown. Methods: We performed RNA analysis to assess the levels of ZNF638 expression in mouse fat depots such as brown adipose tissue (BAT), subcutaneous (scWAT) and epididymal (eWAT) white adipose tissue and investigated whether ZNF638 is induced by stimuli that regulate brown fat functionality and thermogenesis. In addition we determined the mechanisms by which ZNF638 is regulated by performing in silico screen of the ZNF638 promoter and molecular analysis involving luciferase and ChIP assays and gain- and loss-of-function studies. Results: Our data we show for the first time that ZNF638 is highly expressed selectively in mature brown and subcutaneous fat tissues and in fully differentiated thermogenic adipocytes. Furthermore, gene expression studies revealed that ZNF638 is upregulated by cAMP modulators in vitro and by cold exposure and pharmacological stimulation of □-adrenergic signaling in vivo. In silico analysis of the upstream regulatory region of the ZNF638 gene identified two putative cAMP response elements within 500 base pairs of ZNF638 transcription start site and ChIP assay and functional studies revealed that CREB is necessary and sufficient to regulate ZNF638 mRNA levels. Conclusion: Taken together, these results demonstrate that ZNF638 is selectively expressed in mature thermogenic adipocytes and tissues and that its induction in response to classic stimuli that promote heat generation is mediated via CREB, pointing to a possible novel role of ZNF638 in brown and beige fat tissues.

Board 16, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	The effect of obesity on DNA damage and repair in BRCA mutant breast epithelial cells
Authors *	Priya Bhardwaj*, Neil M. Iyengar, Sofya Oshchepkova, Rohan Bareja, Andrew J. Dannenberg, Olivier Elemento, Monica Morrow, Jason A. Spector, Kristy A. Brown
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Structured Abstract *

Background: Obese women who carry a mutation in the DNA repair enzymes BRCA1/2 have a greater risk of developing breast cancer compared with lean BRCA1/2 mutation carriers. Previously, we showed that BMI was positively correlated with DNA damage in breast epithelium of BRCA mutation carriers. We hypothesized that obesity-associated dysfunctional adipose tissue causes DNA damage in neighboring breast epithelial cells and/or decreases their capacity for DNA repair. If true, this would provide evidence for the initial insults associated with increased risk of tumor formation in obese women.

Methods: Conditioned media (CM) was collected from breast adipose explants obtained from lean and obese women. Immunofluorescence staining of the DNA damage marker γH2AX was carried out on CM-treated breast epithelial cells (WT or BRCA1+/-). Cell line findings were validated in primary breast epithelial organoids isolated from breast tissue. Additionally, RNA-Seq was conducted on primary breast epithelial organoids isolated from lean and obese women to identify gene expression patterns associated with drivers of DNA damage and alterations in repair machinery.

Results: Obese CM stimulated DNA damage in BRCA mutant breast epithelial cells, while lean CM did not. Similar findings were made in primary breast epithelial organoids. Ingenuity Pathway Analysis of RNA-Seq data from lean and obese breast organoids identified several upstream regulators of gene expression differences, including signaling by estradiol and pro-inflammatory cytokines. Additionally, expression of several genes involved in DNA repair were downregulated in organoids from obese women.

Conclusions: These data show for the first time that local factors produced by obese breast adipose tissue induce breast epithelial cell DNA damage and potentially impact their capacity for DNA repair. Our results suggest that therapies targeting weight or dysfunctional breast adipose tissue may reduce the DNA damage observed in obese BRCA mutation carriers and thereby decrease tumor formation in this high-risk population of women.

Board 17, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Postmenopausal Obese Women with Low Triglyceride Levels have a Favorable Metabolic Profile
Authors *	Marianna Pavlyha, Anastasiya Matveyenko, Steve Holleran, Rajasekhar Ramakrishnan, Henry Ginsberg, Gissette Reyes-Soffer
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Structured Abstract *

Background: It is well known that obesity has a strong association with Type II Diabetes Mellitus and dyslipidemia, which are important risk factors in the development of cardiovascular disease. Obesity has a strong correlation with liver steatosis, which defines nonalcoholic fatty liver disease. There is a group of individuals that, despite increased body fat, are protected from the development of these metabolic disturbances. Our aim was to examine lipid metabolic pathways that protect obese individuals from dyslipidemia. Methods: In an effort to better understand this protected group, we performed a pilot study in 8 BMI>30, postmenopausal women (PMW) with High triglycerides (HTG) (>175mg/dl less than 400mg/dl) or Low TG (LTG) (<100mg/dl) on no lipid-altering drugs. We examined the effects of baseline TG levels on lipoprotein metabolism (using stable isotopes); body fat distribution; liver and muscle fat content; abdominal adipose tissue size and apolipoproteinC3 (apoC3) plasma measurements. Results: We enrolled 5 LTG (mean TG: 97± 24.5) and 3 HTG (mean TG: 232 ± 30.5) PMW. As expected, subjects with LTG were more insulin sensitive when compared to subjects with HTG levels (HOMA index 1.53±0.17 and 3.8±2.1 respectively). This was driven by baseline insulin levels, as plasma levels of glucose and HbA1c were similar between the two groups. Subjects with low TG levels had lower VLDL-TG levels. Subjects with LTG levels had lower production rates (PR-pools/day) of VLDL-TG and VLDL apoB100 (8.69±2.46 and 7.83±3.23) compared to those in HTG (24.8±7.68 and 10.61±5.09). In addition, LTG subjects cleared VLDL-TG and VLDL-apoB at higher rates (0.31±0.13 and 4.37±1.13 pools/day) when compared to the HTG group (0.22±0.05 and 2.13±1.02 pools/day). Total body fat, subcutaneous fat and waist/hip ratios by MRI were similar in the two groups. However, visceral fat % by MRI (5.98±1.64 LTG vs. 9.91±1.75 HTG) and both intrahepatic fat (2.85±1.83 in LTG vs. 4.5±2.61 in HTG) and intramyocellular fat 3.47±3.67 LTG vs. 5.2±2.80 HTG) by MRS were lower in LTG. Adipose tissue biopsies showed no significant difference in adipocyte size (average areas in 9175±2970 in LGT and 9448±2420 HGT with index of roundness as 1.5±0.1 and 1.4±0.1 respectively) and number (400±108 in LGT vs 430±140 in HGT), but LTG had less macrophage infiltration (%) than HTG(6.22 vs.11.57). ApoC3 levels in plasma were lower in LTG versus HTG subjects (94.85±6.93 vs. 147.67±17.02 ug/ml respectively) p=<.005. Conclusion: In obese individuals, low TG levels predict metabolic health

Board 17, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Lipolysis-derived fatty acids are a key driver of meta- and hypothalamic inflammation.
Authors *	Claudia G. Liberini, Giulia Maurizi, Henri Ruiz, Chunxue Zhou, Kenichi Sakamoto, Claudia Lindtner, Petra Kotzbeck, Wilson Hsueh, Thomas Scherer, Rudi Zechner and Christoph Buettner.
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Structured Abstract *

Background: Obesity, diabetes and other metabolic diseases are characterized by low-grade systemic meta-inflammation, particularly prominent in white adipose tissue (WAT), but also hypothalamic inflammation. WAT function plays a pivotal role in metabolic homeostasis as it is the designated organ to store and release lipids. The key driver of lipolysis in WAT is adrenergic signaling through the sympathetic nervous system (SNS), while the key anti-lipolytic hormone is insulin that antagonizes adrenergic signaling in adipocytes, and in the brain dampens SNS outflow to WAT. A hallmark of obesity is impaired insulin action in WAT. Here we asked if brain insulin resistance is sufficient to induce WAT dysfunction and if the resultant unrestrained lipolysis is an essential driver of both meta- and hypothalamic inflammation.

Methods/Results: We first investigated whether the obliteration of brain insulin signaling can induce WAT inflammation by studying an inducible mouse model of either peripheral or whole body (periphery and central nervous system) insulin receptor deficiency. Loss of brain insulin signaling promotes macrophages infiltration and elevates pro-inflammatory cytokine levels while peripheral insulin receptor deficiency. Next, we investigated whether a reduction in WAT lipolysis is able to reduce meta-inflammation in an adipose-triglyceride- lipase (ATGL) knock out mouse model fed a high-fat diet. A reduction of WAT lipolysis in ATGL-KO mice protected against meta- and hypothalamic inflammation. Conversely, pharmacological activation of lipolysis through the administration of a beta-3 agonist markedly induces hypothalamic and WAT inflammation. Importantly, beta-3 agonist induced meta- and hypothalamic inflammation can be prevented through the administration of a lipolysis inhibitor. Conclusions: In summary, our results suggest that WAT dysfunction is a key driver of hypothalamic and meta- inflammation.

Board 18, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Hypothalamic inflammation and microglial cell activation in acute and chronic hyperglycemia
Authors *	Giulia Maurizi, Vitaly Ryu, Chunxue Zhou, Claudia Liberini, Kenichi Sakamoto, Christoph Buettner.
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Structured Abstract *

Background: Microglia activation in the hypothalamus is well documented in rodent models of metabolic disease induced by high-fat or high sugar feeding. Of note, depression and changes in mood are common in obesity and brain inflammation could play an important role in the link between depression and obesity. While sugar feeding induces hyperglycemia and hyperinsulinemia, the relative contributions of hyperglycemia, hyperinsulinemia versus hyperlipidemia/elevated free fatty acids have not been studied. The purpose of this study is to investigate the role of acute and chronic hyperglycemia on microglial cell activation and if the amelioration of hyperglycemia through the treatment with an SGLT2 inhibitor prevents brain inflammation, depression and anxiety.

Methods: Acute hyperglycemia was induced through a hyperglycemic clamp of either 2 or 4 hrs duration, with an n= 6 compared to saline infused 10 week old male Sprague Dawley rats. Plasma glucose levels were raised and maintained at 400 to 500 mg/dl by infusing a variable glucose infusion rate. Chronic hyperglycemia was induced by streptozotocin (STZ) treatment (60mg/kg) and control rats were injected with the vehicle sodium citrate. One week after STZ injection, STZ-treated (diabetic) with an average blood glucose level at 540 mg/dl and vehicle injected (non-diabetic) groups were randomly allocated to either placebo or the SGLT2 inhibitor (dapagliflozin) to ameliorate hyperglycemia which reduced average blood glucose level. 4 weeks after the induction of diabetes rats were sacrificed. Hypothalamic inflammation was assessed by qPCR and microglial activation through IHC of brain sections with IBA1. Depressive behavior was assessed through the splash test.

Results: Acute hyperglycemia induced hyperinsulinemia and suppressed circulating free fatty acids. Acute hyperglycemia induced hypothalamic inflammation by activating microglia in several brain regions and increasing the expression of IFNg and IFNg-target genes such as CXCL9, CXCL10 and CXCL11. In addition, acute hyperglycemia also induced IFNg-driven adipose tissue inflammation and decreased de novo lipogenesis, suggesting that acute hyperglycemia rapidly impairs adipose tissue functions. Similarly, chronic hyperglycemia due to STZ induced insulin-deficiency activated microglial, although the gene expression of cytokines was much less marked. STGL2 inhibitor treatment decreased microgliosis while restoring euglycemia indicating that both acute and chronic glucose toxicity can drive an IFNg driven brain inflammation.

Treatment with an STGL2 inhibitor ameliorated the anxiety compared with STZ treated animals. These data suggest that acute and chronic hyperglycemia can induce brain inflammation and that treatment with an SGLT2 inhibitor prevents the brain inflammation and improves anxiety and depression.

Board 18, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	A high fat diet suppresses body weight defense mechanisms through post-ingestive effects
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Structured Abstract *

Background: Body weight is defended in mammals so that increases or decreases in weight elicit responses favoring a return to the initial weight. However, obesity rates and average body weight have been rising over the past several decades. Multiple factors are implicated in this rise in body weight, including increased consumption of highly palatable, calorically dense foods. We hypothesize that consumption of palatable, high fat foods suppresses body weight defense mechanisms allowing weight gain to occur.

Methods: We have created an intragastric feeding paradigm in mice whereby we can rapidly induce weight gain of roughly 40% of the initial body weight (Ravussin et al., Cell Met 28, 289-299.e285, 2018). This paradigm allows us to study the physiologic system that defends against weight gain and to test whether a palatable diet can suppress this system. To test which diets were more palatable to mice, we used a series of preference tests where mice were concurrently offered two diets for 12 days. Daily caloric intake and body weight measures were taken allowing us to assess the preference and caloric intake of high fat diets and diets sweetened with 30% kcals from sucrose or 3mM sucralose. Finally, using an intragastric infusion, we delivered food directly to the stomach thereby bypassing oral taste allowing us to test the post-ingestive effects of a high fat diet.

Results: We found that sweetened diets are more palatable to C57BL/6J male mice than unsweetened diets, yet the preference for sweet taste was not sufficient to increase caloric intake or body weight. However, we found that increasing the fat content of a diet increases both palatability and consumption leading to weight gain. Moreover, we found that a high fat diet suppresses the hypophagic response which normally facilitates a return to initial body weight following overfeeding leading to a new, higher body weight. Finally, we observed that intragastric infusion of a high fat diet induced ad-libitum caloric intake.

Conclusions: Preference for a sweetened diet was not sufficient to increase caloric intake over a 12-day period suggesting that other factors beyond diet palatability may contribute to increasing caloric intake. Our observation that intragastric infusion of a high fat diet induced caloric intake suggests that post-ingestive effects of a high fat diet are at least partially responsible for the ability of a high fat diet to increase caloric intake and suppress body weight defense mechanisms leading to weight gain.

Board 19, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Effect of hypoxia on cancer cell viability in an in vitro adipose-associated breast cancer cell model
Authors *	Asal Hejazi* Sarah Ackerman Paul Cohen
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Structured Abstract *

Background: In the United States, two-thirds of women are overweight or obese, placing them at an increased relative risk of breast-cancer. New therapies to combat obesity-associated breast cancer are needed and require models to accurately represent the evolution of tumor growth within the mammary fat tissue microenvironment in the obese setting. Previous studies have demonstrated both proliferating tumor cells and obese adipose tissue exist in hypoxic environments, however, hypoxia is rarely incorporated into in vitro models. Thus, to better recapitulate human biology, we modified an in vitro model commonly used in the investigation of a relatively new theory that proposes the obese adipose microenvironment is driving increased tumor progression, and study the effect of hypoxia on murine breast cancer cell viability when treated with adipocyte-conditioned medium (CM).
Methods: Subcutaneous adipose tissue was resected from C57BL/6 female mice and adipocyte precursors were isolated and differentiated into primary adipocytes, which were then incubated under hypoxic conditions using dialyzed Roswell Park Memorial Institute (RPMI) medium. After 30 h, the adipocyte-CM was snap frozen and stored at −80°C. E0771 murine breast cancer cells were cultured in RPMI medium in both normoxic and hypoxic environments for 24 h. The cancer cells were then plated in 96-well plates and treated with either normoxic or hypoxic adipocyte-CM for 48 h. Cell viability was subsequently measured using the Cell Titer-Glo luminescence assay. An incubator set at 37°C with 5% CO2 was used for normoxic environment and a hypoxic chamber with 1% O2 was used for hypoxia. Untreated breast cancer cells, incubated with only RPMI standard media, were used as controls in hypoxic and normoxic environments.
Results: The viability of hypoxic E0771 breast cancer cells increased by 152% when treated with normoxic adipocyte-CM treatment and by 209% when treated with hypoxic adipocyte-CM compared with untreated hypoxic breast cancer cells.
Conclusion: Treatment of hypoxic E0771 breast cancer cells with hypoxic adipocyte-CM was used in our model to simulate the hypoxic environment of obese adipose in humans, and interestingly, it yielded the greatest viability of cancer cells. While studies have shown hypoxic stress induces tumor cell adaptation and subsequent survival mechanisms, our findings suggest these processes may be induced by the hypoxic microenvironment of adipose tissue. Moreover, given that cultured adipocytes are not obese, our study identifies a role for the use of hypoxia with conditioned medium as a possible in vitro simulation of the obese state in humans.

Board 19, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Body shape and adipose tissue expansion in women: potential role of testosterone
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Structured Abstract *

Background: Lower body, gluteal-femoral subcutaneous (GFSAT) vs. abdominal subcutaneous (ASAT) adipose tissue are metabolically protective (e.g. lower risk for type 2 diabetes), independent of total body fat. Limited evidence indicates that GFSAT has a higher capacity to expand via hyperplasia, permitting the 'safe' storage of fatty acids as triglyceride. Testosterone (T) inhibits the differentiation of human adipose progenitors so may limit expansion capacity. AKR1C3, encodes an enzyme that can locally synthesize T from inactive androstenedione. The objective of this study was to assess associations of circulating and bioavailable T and depot differences in AKR1C3 expression in women with an upper body (UB) vs lower body (LB) fat distribution.
Methods: We recruited two groups of Caucasian females (BMI 25-34 kg/m2) with normal menses and a clear UB vs LB fat distribution based on waist to hip ratio (WHR) [0.88 ± 0.04 (n=10, UB) vs 0.73±0.03 (n=9, LB)]. Fat distribution in legs vs trunk was measured by DXA. Bioavailable T was calculated using formulas that account for binding to sex steroid binding globulin (SHBG) and albumin. Gene expression was measured by qPCR in aspirations of ASAT and GFSAT.
Results: The groups had similar average BMIs but differed in body fat distribution [%leg fat: 0.37 ±0.05 (UB) vs 0.46 ±0.05 (LB) (mean±SD)]. Fasting glucose was higher in UB group (91 vs 83 mg/dL). Circulating levels of total and calculated bioavailable T were on average similar but varied over an ~8-fold range in each group. ASAT AKR1C3 mRNA levels were 52% higher in the UB than LB fat distribution group. Further, only in women with an UB fat distribution there was a depot difference in AKR1C3 mRNA levels (ASAT > GFSAT by 23%). Stepwise regression indicated that ASAT AKR1C3 mRNA levels were positively associated with BMI and negatively associated with % leg fat, while in GFSAT AKR1C3 mRNA levels were positively associated with circulating bioavailable T. Further, preliminary results indicate that AKR1C3 protein was higher in GSAT than ASAT of women with LB- but not UB- fat distribution. Expression of androgen receptor mRNA was 47% higher in ASAT than GFSAT independent of body shape.
Conclusion: Data are consistent with the hypothesis that higher circulating bioavailable T and local T production via AKR1C3 may exert depot-dependent actions to restrain adipogenesis. The resulting limited capacity for healthy adipose remodeling or expansion may contribute to their metabolic dysfunction in women, especially those with UB fat distribution

Board 20, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	A naturally occurring coding variant in the GIPR receptor disrupts glucose-stimulated insulin secretion.
Authors *	Lucie Yammine*, Nazish Abdullah, David Soares, Adolfo Garcia-Ocaña, Timothy E. McGraw
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Structured Abstract *

Background: The Glucose-dependent insulinotropic polypeptide receptor (GIPR) activation by GIP in pancreatic β cells is involved in enhanced Glucose Stimulated Insulin Secretion. Carriers of the homozygous GIPR variant GIPR-E354Q (rs1800437) have been shown to exhibit glucose intolerance and BMI lowering. In adipocytes, we have previously described that GIPR-E354Q undergoes enhanced desensitization due to a slower post-GIP-stimulation recycling through the TransGolgi-Network (TGN) as compared to GIPR-WT. Here we demonstrate the effects of altered GIPR trafficking on metabolic regulation in an in vivo model.

Methods: 8 to 12 weeks old GIPR-WT and GIPR-E354Q mice were monitored for weight, blood glucose, GIP and GLP-1 secretion on normal chow. After 16h fasting, an intraperitoneal glucose tolerance test (IP-GTT) was conducted by co-injecting 2mg/kg Glucose and 20nmole/kg GIP. IP insulin tolerance test (ITT) was performed after 6h fasting by injecting the mice with 0.75 IU/kg Insulin. Electron microscopy images of isolated islets from fasted and refed mice were taken and analyzed.

Results: We generated a mouse model of the GIPR-E354Q human variant. First, we show no differences in weight gain or incretins secretion on normal chow diet between the two variants regardless of gender. GIPR-WT and GIPR-E354Q also have the same insulin sensitivity when challenged with an ITT, showing a normal responsiveness to insulin in terms of glucose uptake. However, we demonstrate a sexual dimorphism in the GIPR-E354Q mice in response to an IP-GTT. Indeed, we show that compared to their WT counterparts, GIPR-E354Q males are GIP hypersensitive when co-injected with glucose and GIP. The GIPR-E354Q females on the other hand were more glucose tolerant than the GIPR-WT females and because of this increased glucose tolerance had a blunted response to GIP. By electron microscopy we show that fasted GIPR-E354Q males have the same number of docked insulin granules to the β cell membrane as GIPR-WT mice, but tend to have more docked granules than their counterpart after a 1h refeed period. GIPR-E354Q mice also show reduced average mitochondria area in β cells.

Conclusions: This study is the first in vivo analysis of the GIPR-E354Q naturally occurring variant. We find an altered metabolic response of the GIPR-E354Q mice. These mice provide a model to further define at the molecular level how the GIPR-variant impacts β cell function.

Board 20, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Hepatocyte Notch induces energy expenditure to prevent diet-induced obesity
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Structured Abstract *

Background:
Reactivation of Notch signaling, a pathway traditionally associated with development, is associated with obesity-related metabolic complications. We made the unexpected discovery that hepatocyte Notch activation reduced body weight when coupled with a switch from normal chow to a high-fat/high-cholesterol (HF-HC) NASH diet in mice. We repeated these experiments using another highly palatable, high-fat diet (HFD), and found again that hepatocyte Notch activation prevented HFD-induced weight gain. This prompted us to further investigate the cause of this reduced body weight by carefully phenotyping mice with liver-specific Notch hyperactivation (L-NICD).
Methods:
L-NICD mice and their littermate controls were fed HFD (60% kCal from fat) for 8 weeks, with weekly assessments of body weight and body composition by EchoMRI. Concurrently, we used a parallel cohort of L-NICD mice and littermate controls to measure energy expenditure, food intake and locomotor activity with the CLAMS/Oxymax indirect calorimetry system.
Results:
L-NICD mice gained significantly less weight than control littermates when placed on an obesogenic diet for a period of 8 weeks, with differences in body weight observed as early as one week after HFD exposure. At the termination of the experiment, L-NICD mice weighed 30.75g±0.50g (n=12) while their littermate controls weighed 37.78g±1.38g (n=11; $p \leq 0.001$). Notably, differences in body weight were fully attributable to changes in fat mass (17.89% ± 1.80% fat in L-NICD vs. 32.96% ± 2.33% fat in control; $p \leq 0.001$), without change in lean mass. Indirect calorimetry indicated that differences in fat mass were due to increased energy expenditure in L-NICD mice and heat production, as food intake or locomotor activity were unchanged.
Conclusions:
Given the striking differences in body weight and fat mass, this L-NICD mouse model affords us a unique opportunity to examine the complex interplay between liver and adipose tissue. Ongoing experiments will determine how hepatocyte Notch activity alters the liver secretome to affect energy expenditure, and adipose tissue mass.

Board 21, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	A role for DGB25 in energy expenditure and metabolic homeostasis
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Structured Abstract *

Background: Obesity, a global affliction, is most severe in the United States, with 1/3 of adults being obese and 2/3 being overweight or obese. Obesity and the metabolic syndrome cost over $250 billion per year in the United States, more than 20% of all medical spending. Weight-related illnesses such as hypercholesterolemia, hypertension, and diabetes continue to be leading risk factors for heart attack and stroke. Existing medical therapies for obesity are limited by poor efficacy or unacceptable side effects.
Human body fat is predominantly "white" adipose tissue (WAT), low in mitochondria and specialized for storing energy. Brown adipose tissue (BAT), rich in brown-staining mitochondria, dissipates energy and protects against disease. Brown fat cells (adipocytes) dissipate stored energy by thermogenesis—generation of heat from uncoupled respiration. White adipocytes can be induced in vivo by cold and adrenergic stimulation to take on thermogenic properties through "browning"/"beiging." These thermogenic beige adipocytes play a meaningful role in augmenting whole-body energy expenditure.

Methods: RNA-sequencing of subcutaneous inguinal WAT (iWAT) from mice exposed to multiple temperatures was performed to identify novel molecular candidates that may regulate metabolism and energy expenditure in beige adipocytes. RNA-seq results were validated with RT-qPCR, cell type-specific ribosomal profiling, proteomics, pharmacology, and assay for transposase-accessible chromatin (ATAC) using sequencing (ATAC-seq).

Results: We have identified DGB25, a novel molecular target in adipose with little functional characterization that is strongly induced by cold exposure, high-fat diet, and the thermogenesis-driving transcription factor PRDM16. DGB25 expression is most enriched in BAT, and ribosomal profiling demonstrated its expression to be adipocyte-specific and increased in brown and beige adipocytes after cold exposure compared to in thermoneutral conditions. Pharmacological inhibition of DGB25 protein function in mice by injection of a drug compound previously identified in a chemical screen produced significant changes in whole-body acclimation to cold exposure as well as expression of thermogenic and mitochondrial biogenic genes in adipose tissue. Further, ATAC-seq revealed significant chromatin opening around the Dgb25 locus in BAT compared to in WAT.

Conclusion: DGB25 is an adipocyte-specific candidate gene whose roles in regulating metabolism and energy expenditure have not been fully characterized. Its enrichment in brown fat and induction by known thermogenic stimuli are regulated transcriptionally and epigenetically in a tissue- and cell-type specific manner. Studies are underway to determine the mechanistic nature of DGB25's function in adipocyte thermogenesis and its relevance to whole-body energy expenditure and metabolism in animal models and humans.

Board 21, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Insights from single cell RNA sequencing analyses of human subcutaneous adipose tissues
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Structured Abstract *

Background: Human adipose tissues are located in multiple depots and are heterogeneous in terms of adipogenesis, storage capacity and metabolic features with consequences for whole body health. Overall, lower body depots, especially in premenopausal women, show increased storage capacity (bigger adipocytes) while remaining insulin sensitive. We hypothesize that heterogeneity in cellular composition can partly explain differences in adipogenesis and adipose function between depots and populations.

Objective: To obtain an unbiased view of the cellular composition of the stromavascular fraction (SVF) of human subcutaneous adipose tissues.

Methods: Adipose samples (abdominal, n=4, and paired femoral, n=2) were obtained from n=4 healthy volunteers (1M, 3F, age 28-38 y, BMI 24.5-63.0 kg/m2) via aspiration or during surgery. After collagenase digestion of 1g tissue, total SVF (≈25,000 cells) was used for single cell RNAseq analysis with the 10X Genomics Gel-in-emulsion (GEM) drop-seq platform. Raw data were demultiplexed, and quality control (QC) metrics were obtained (Cell Ranger) with downstream analyses in Seurat.

Results: SVF cells clustered into 3 major populations: adipose progenitors (APs, 42.3±10.0% of total SVF), endothelial cells/pericytes (46.4±12.3%) and inflammatory cells (11.3+5.8%). Adipose progenitors were further consistently subdivided into 3-5 subgroups, likely adipocyte precursor cells, more committed preadipocytes, fibroblasts, and subgroups co-expressing endothelial cell or pericyte markers.

Conclusions: Adipose progenitors and cells expressing endothelial and pericyte markers form the majority of SVF in human adipose tissues, followed by inflammatory cells. Adipose progenitors are a heterogeneous group. Future studies will investigate the functional characteristics of the AP subpopulations.

Board 22, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Roles of N-Acylethanolamine Acid Amide Hydrolase in Controlling Metabolism
Authors *	Chunxue Zhou, Corey Xu, Li Ling, Douglas Oberlin, Giulia Maurizi, Kenichi Sakamoto, Adrien Stanley, Christopher Benoit, Hale Egritag, Joel Dudley, Christoph Buettner.
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Structured Abstract *

Background: We recently identified N-acylethanolamine acid amidase (NAAA) as a gene whose expression is correlated with hemoglobin A1c, glucose, HDL, and triglycerides using a gene network analysis. NAAA is an enzyme that metabolizes fatty-acyl ethanolamides, such as oleoylethanolamide (OEA) and palmitoylethanolamde (PEA), endocannabinoid like substances that activate the peroxisome proliferator-activated receptor α (PPARα). PEA has been shown to reduce inflammation and pain through PPARα thereby reducing TNFα and AP2; hence NAAA has traditionally only been studied in inflammation and pain. Here we tested whether NAAA inhibition alters metabolic control in mice.
Methods: We utilized both pharmacological inhibition and genetic loss of function to define a role of NAAA in metabolic regulation. Two NAAA inhibitors (compounds 11h and 8) were administered through drinking water to male C57bl6 mice receiving either chow or high fat diet (HFD) for 28 days. NAAA knockout mice were generated with CRISPR/Cas9 and wild-type, heterozygous and homozygous knockout mice were fed chow over 12 months or HFD over 6 months. We assessed the following parameters: body weight and food intake, body composition via MRI, glucose homeostasis via glucose and insulin tolerance tests, plasma insulin, glucose, triglyceride and free fatty acids, liver triglyceride, and lipolysis and de novo lipogenesis in white adipose tissue. Results: There were no significant differences in food intake between groups fed different diets or given different NAAA treatments or between different genotypes. NAAA inhibitor compounds increased fat mass and decreased lean mass during HFD feeding compared to controls receiving water, an effect not seen in animals fed a chow diet. Male NAAA knockout mice were slightly heavier with elevated fat mass, plasma triglyceride and glucose and insulin intolerance. Importantly, NAAA knockout mice showed more liver triglyceride content after six-month HFD feeding, which is associated with adiposity, higher plasma triglyceride level, and an increase in lipolysis and de novo lipogenesis in epididymal white adipose tissue.
Conclusion: Pharmacological inhibition or genetic loss of function of NAAA worsens glucose homeostasis and increases plasma triglyceride in mice on regular chow, while NAAA deletion deteriorates high-fat diet induced hyperlipidemia and hepatic steatosis, associated with metabolic dysfunction of adipose tissue.

Board 22, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Allograft inflammatory factor-1-like (AIF1L/IBA2) acts as a genetic modifier of a mouse obesity quantitative trait locus (QTL)
Authors *	Dippal H. Parikh*, Dario F. Riascos-bernal, Smitha Jayakumar, Nicholas E. Sibinga
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Structured Abstract *

Background: We have found that inactivation of Allograft inflammatory factor-1 (AIF1) in mice prevents high fat diet (HFD)-induced weight gain and preserves insulin sensitivity. Interestingly, a paralog of AIF1 called AIF1-like (AIF1L) with amino acid sequence identity of 63% and similarity of 80%, was identified by the human genome project. Based on our findings with AIF1, the known homology of these proteins, and expression of AIF1L in adipose depots we hypothesized that AIF1L may play a functional role in diet-induced obesity (DIO).
Methods: Mating strategy employed, generated WT and AIF1L deficient mice -- with and without the presence of E2a-Cre transgene. All 4 groups of mice were subjected to HFD for 16-18 weeks, starting at 8 weeks of age.
Results: We observed that the EIIa-Cre transgene suppressed HFD-induced weight gain relative to mice lacking the transgene. Remarkably, loss of AIF1L revealed an opposite effect of the transgene, as EIIa-CreTg+; AIF1L-deficient mice (KO Tg+) weighed significantly more than EIIa-CreTg+; AIF1L-replete mice (WT Tg+). This suggests a genetic interaction between the transgene and Aif1L loci. The differences in body weight reflect an increase in adipose tissue mass in both sexes and a modest increase in lean mass in male mice. Metabolic profiles after 1 week or 18 weeks of HFD feeding showed no differences in energy expenditure (EE). In addition, measurement of food intake in socially housed mice showed no differences in feeding behavior for either sex. To determine if there is a difference in EE or energy intake, metabolic profiles after a short term HFD feeding (~6-8 wks) and single-housed, pair-feeding measurements will be performed. Preliminary results of pair-feeding suggest that KO Tg+ female mice eat more than WT Tg+ and do not gain weight when they are calorie restricted. To further understand the genetic interaction between the two loci, we localized the EIIa-Cre transgene integration site, using targeted locus amplification (TLA) technology, to a previously identified quantitative trait locus (QTL) called Obrq2, which is associated with robust metabolic phenotypes including DIO and insulin resistance.
On the other hand, WT mice and AIF1L deficient mice without the E2a-Cre transgene behaved similarly with no differences in their body weight curves, fat and lean mass, and metabolic profiles.
Conclusions: Taken together, these results show that AIF1L is not essential for the pathogenesis of obesity; however, when the Obrq2 QTL is modified by transgene integration - it confers resistance to DIO.

Board 23, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	AN ATLAS OF THERMOGENIC FAT DEVELOPMENT: CONNECTING PROGENITORS AND MATURE ADIPOCYTES
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Structured Abstract *

Brown and beige fat are specialized adipose tissues that dissipate energy for thermogenesis through UCP1 (Uncoupling Protein-1) and have potent anti-diabetic and anti-obesity effects. Despite advances in single cell genomics, application to adipose tissue has been challenging due to the large cell size and fragile nature of lipid-filled adipocytes. We have developed a robust protocol to isolate single nuclei from mature adipocytes for downstream application of RNA-sequencing. We conducted genome-wide mRNA expression analysis of 10,000 single nuclei from mouse interscapular brown adipose tissue as well as 16,100 nuclei from beige adipose tissue. Applying unsupervised clustering to the dataset enabled comprehensive determination of all cell types including mature adipocytes and stromal cells in thermogenic fat. In interscapular brown adipose tissue, we identified 5 cell types, one of which is a unique subset of UCP1+ adipocytes abundant in electron transport chain genes. In subcutaneous beige adipose tissue, we identified 9 cell types including beige and white adipocytes and two genetically distinct beige adipogenic progenitors. We have captured the state of adipocytes transitioning from white to UCP1+ beige and delineated metabolic and signaling pathways unique to the intermediate state. We used an RNA velocity algorithm to recover single-cell gene expression kinetics, allowing reconstruction of developmental trajectories from the two progenitor subsets to intermediate and terminally-differentiated beige adipocytes. We anticipate that this new adipocyte atlas will aid in the identification of novel regulators and genetic markers of adipocyte development.

Board 23, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Sox2 is a Pluripotent Stem Cell Transcriptional Regulator of Adipogenesis.
Authors *	Abhilash Gadi, Narendra Verma, Upal Basu Roy, Robert J Schneider and Alka Mansukhani.
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Structured Abstract *

Normal adipose tissue serves as an energy reserve that is highly adaptive to external physiological signals, particularly nutrients. The adipocytes of white adipose tissue (WAT) can synthesize and store lipids or release them in dynamic response to energy demands of the organism, while brown adipose tissue (BAT) is enriched in mitochondria and plays a key role in thermogenesis (heat production). Lipids are depleted under nutrient-scarce or high-energy-consuming states such as starvation or increased under nutrient-rich conditions that can lead to obesity. Thus, proper adipocyte function is essential for metabolic regulation. Adipose stem cells have been identified in fat tissues but the regulators of adipoprogenitors or their contribution to pathological conditions like obesity is not well understood. Our studies have uncovered that the essential stem cell transcription factor, Sox2, regulates bone-fat lineage fate and promotes adipogenesis in mesenchymal stem cells (MSCs). Sox2 is expressed in fat tissue and Sox2 expression increases in MSCs during adipogenesis, while its depletion reduces their levels of PPARγ, the master regulator of adipogenesis, and blocks MSC commitment to adipogenic fate. Unbiased genome-wide ChIP-SEQ, gene expression, and pathway analysis studies clearly suggest that Sox2 regulates genes involved in adipogenesis and lipid metabolism. To determine the role of Sox2 in regulating adipogenesis in vivo, we generated conditional Sox2 knockout mice by deleting Sox2 in the adipocyte lineage. We find that Sox2-Adipo CKO mice have reduced WAT. To test the role of Sox2 in adipocyte expansion and diet induced obesity (DIO), Sox2-Adipo CKO and control mice were placed on high fat diet (HFD) or control diet (LFD). Sox2 conditional knock out mice were resistant to diet-induced obesity. DEXA (dual energy X-ray absorptiometry) scan analysis revealed reduced total fat mass in the Sox2-Adipo CKO mice compared to the control mice. Sox2-Adipo CKO mice also have fewer Sox2-expressing adipose-derived progenitor/stem cells (ADSCs) and reduced macrophage infiltration. Our findings disclose a novel role for Sox2 in regulating ADSCs and fat accumulation (deletion of Sox2 reduces adipoprogenitors and increases resistance to diet induced obesity). Ongoing studies will focus on the effects of Sox2 deletion on fat metabolism, it's role in brown fat, as well as Sox2 targets in ADSCs to determine key downstream effectors that could be new therapeutic targets for diseases such as obesity and diabetes.

Board 24, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	No Association Between APOL1 Status And Metabolic Factors That Might Explain Its Link With Obesity
Authors *	Avigdor D. Arad*, Fred J. DiMenna, Hannah D. Kittrell, Kezhen Fei, Ruth J.F. Loos, Michelle A. Ramos, Jeanine B. Albu, Carol R. Horowitz
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Structured Abstract *

Background: The parent study GUARDD suggests a robust association between obesity and gene variants (i.e., apolipoprotein L1 (APOL1) G1/G2 risk alleles) found nearly exclusively in people of African ancestry. The purpose of this study was to examine metabolic factors that may be associated with pathways underlying the obesity/APOL1 relationship, such as insulin resistance, low metabolic rate, and impaired substrate selectivity at rest and during exercise.

Methods: Fifty genetically-affected (APOL1+, age 53.5 ± 10.3 yrs, BMI 33.3 ± 7.5 kg·m-2, male = 11) and 50 age-, gender-, and BMI-matched genetically-unaffected (APOL1-) patients were randomly selected from the Mount Sinai BioMe BioBank. Participants completed a 6-hr deep-phenotyping clinical-testing protocol, including body composition (BodPod) and anthropometric assessment, dietary (ASA24) and physical activity (IPAQ) analyses, blood work for biochemistry and hormonal analyses (lipids, glucose, insulin, leptin), and quantification of energy metabolism and substrate utilization (whole-body indirect calorimetry) at rest (60-min protocol) and during exercise (30-min treadmill walk at RPE 12). Patients age ≥18, yrs with self-reported African ancestry that were previously enrolled in the GUARDD study with confirmed APOL1 status were recruited. Patients were excluded if pregnant, presenting with terminal illness, unable to provide informed consent or complete the protocol, on any medication known to affect insulin resistance, lipid or glucose metabolism, and/or possessing a physical limitation that might interfere with exercise capacity.

Results: Fat-free mass, percent body fat, waist-to-hip ratio, resting V̇o2, resting rates of lipid and carbohydrate oxidation, and fasting glucose were not significantly different between groups. Surprisingly, the presence of insulin resistance was lower in APOL1+ (HOMA-IR 2.9 as cut off: 52% vs 74% for APOL1-; p=0.02). Similarly, fasting leptin was significantly lower in APOL1+ (91 ± 79 vs. 125 ± 97 ng·dL-1 for APOL1-; P<0.05). APOL1+ performed the exercise bout at a slightly lower RPE (12.3 ± 1.2 vs. 12.7 ± 0.9 for APOL1-; P<0.05); however, there were no significant differences in walking velocity, steady-state V̇o2 or rates of lipid or carbohydrate oxidation. Further analyses revealed no differences between groups in the rate of change of any of the metabolic indices per unit change in BMI or HOMA-IR.

Conclusion: Neither insulin resistance, low metabolic rate nor impaired substrate selectivity at rest or during exercise are different for individuals possessing the APOL1 variant. More research is required to determine mechanistic underpinnings of the link between APOL1 and obesity for individuals with African ancestry.

Board 24, Poster 2

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Senescence Surveillance in subcutaneous adipose tissue is key to resisting diet induced obesity
Authors *	Devi Thiagarajan, Nosirudeen Quadri*, Shabnam Jawahar, Hylde Zirpoli, Carmen Hurtado Puzo, Raquel De Lopez, Paul Gugger, Kenneth Gabbay, Annmarie Schmidt, Ravichandran Ramasamy.
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Structured Abstract *

Obesity activates infiltration of immune cells including macrophages, neutrophils, NK cells, innate lymphoid cells (ILCs), eosinophils, T cells, B1, and B2 cells, into the adipose tissue. In humans and mice, obesity driven cellular stress augments senescence in several cell types including adipocytes. We demonstrate that high fat diet (HFD) induces senescence in subcutaneous adipose tissue (scAT) and attenuates adrenergic receptor mediated lipolysis. Senescence in scAT was accompanied by increases in aldose reductase (Akr1b3) expression, and was required for attenuation of lipolysis. Mice devoid of Akr1b3-/- or mice treated with aldose reductase inhibitor were resistant to HFD induced obesity, and displayed less senescence and increased lipolysis compared to wild type mice fed HFD. We show that senescence driven Akr1b1/Akr1b3 dependent mechanism by which interferon signaling and NK cell mediate senescence surveillance to regulate lipolysis and promote diet induced obesity. These data support testing of interventions to block aldose reductase as a therapeutic strategy to combat obesity.

Board 25, Poster 1

Abstract Topic Category *	Metabolism and Integrative Physiology
Abstract Title *	Gut microbiota dysbiosis in obesity and non-alcoholic fatty liver disease
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Structured Abstract *

Background: Obesity and non-alcoholic fatty liver disease (NAFLD) are strongly associated. NAFLD is the most common chronic liver disease, with a worldwide prevalence of 25%. NAFLD includes a spectrum of diseases, from fatty liver to non-alcoholic steatohepatitis (NASH). NASH can lead to cirrhosis, liver failure, and cancer, and in patients with NASH, the presence of fibrosis is associated with increased liver-related mortality. NAFLD and obesity are associated with dysbiosis of the gut microbiota. However, it is unclear whether dysbiosis has a causal role in the development of NAFLD, and in particular, fibrosis. To study the role of the gut microbiota in the development of NAFLD, we analyzed the changes in gut microbiota in the different stages of NAFLD, and conducted fecal microbiota transplants in mice.

Methods: NASH with fibrosis was induced by feeding Ay hyperphagic mice with a western diet and adding a high-fructose corn syrup equivalent to the drinking water. Fecal microbiota transplants (FMT) were conducted by first administering antibiotics to eliminate the endogenous gut microbiota, followed by gavage with cecum content from lean mice, and housing with soiled bedding from lean mice. Control mice received fecal microbiota from mice with NASH. Obesity was evaluated by body and fat pads weight. Liver steatosis was assessed by H&E staining; liver injury was assessed by measuring ALT, inflammation was evaluated by measuring inflammatory markers, and liver fibrosis was detected and quantified using picrosirius red staining. Gut microbiota composition was determined by 16S rRNA metagenomics.

Results: NASH was associated with increased abundance of Bacteroidetes and decreased abundance of Firmicutes; these alterations were reverted by FMT with microbiota from lean mice. FMT did not prevent obesity assessed by body and fat pad weight. No changes were detected in liver steatosis (H&E), injury (ALT), or inflammatory markers. However, FMT reduced liver fibrosis assessed by picrosirius red staining.

Conclusions: In mice, NASH is associated with gut microbiota dysbiosis that reproduces the alterations described in human NASH. FMT with gut microbiota from lean mice corrects dysbiosis. FMT ameliorated fibrosis, which is the best predictor of negative outcomes in NASH.

Board 25, Poster 2

Abstract Topic Category *	Neurological
Abstract Title *	GENERATION OF HYPOTHALAMIC NEURON SUBTYPES FROM HUMAN PLURIPOTENT STEM CELLS
Authors *	Maria Caterina De Rosa1*, Vidhu V. Thaker1, George Stratigopoulos1, Daniele Neri1, Charles A. LeDuc1, Richard Rausch1, Gunnar Hargus1, James E. Goldman1, Andrew F. Teich1, Qi Su2, Yurong Xin2, Jesper Gromada2, Wendy K. Chung1, Judith Altarejos2, Rudolph L. Leibel1, Claudia A. Doege1
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Structured Abstract *

Several neuron subtypes of the paraventricular nucleus of the hypothalamus (PVH) are critical for the regulation of body weight. Of particular importance are the melanocortin-4 receptor (MC4R)-expressing neurons which are part of the leptin-melanocortin feeding circuitry. Heterozygous loss-of-function mutations in the melanocortin-4 receptor (MC4R) are the most common cause of human monogenic obesity. Rodent models and non-neuronal human cell lines have greatly contributed to our understanding of the impact of mutations in MC4R on food intake and energy expenditure. However, the molecular mechanisms underlying human MC4R deficiency are still not well understood. Therefore, we have been developing a MC4R patient-specific hypothalamic models system featuring differentiation into the MC4R neuron subtype. To generate such neuron subtype in vitro, we utilized a transcription factor approach. Specifically, 1) MC4R neuron-specific transcription factors were identified using single-cell RNA sequencing (10X Genomics) of the PVH region isolated from 5-weeks old C57BL/6Tac mice, 2) this transcription factor signature was confirmed in PVH sections from mice and human post-mortem hypothalamus using RNAscope, 3) transcription factors were tested for their capacity to induce the conversion of mouse embryonic fibroblasts into Mc4r neurons, 4) overexpression of transcription factors in human pluripotent stem cells generates functionally mature MC4R neurons. Our studies reveal that cell identity-defining transcription factors of Mc4r neurons of the PVH can drive the differentiation of human stem cells into MC4R-expressing neurons resembling those of the PVH. We will use this human neuron subtype-specific model system to investigate the pathogenetic molecular aspects of MC4R mutations in our patients as well as to perform drug testing in vitro.

Board 26, Poster 1

Abstract Topic Category *	Neurological
Abstract Title *	A Functional Near Infra-red (fNIRS) Neurocorrelate of Loss of Control Eating
Authors *	Dimitra Thomopoulos, Eram Albajri, Lisa Lanza, Hasan Ayaz, Angelo Del Parigi, Jennifer A Nasser
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Structured Abstract *

Objective: Embedded within a study examining regional prefrontal cortex activation during eating, we assessed loss of control over eating by questionnaire, and hypothesized that medial prefrontal cortex (mPFC) activity measured during eating preferred food would be greater in those self-reporting "Loss of Control" (LOC) over eating.
Methods: Seventy-seven adults (41M, 36W) completed the TFEQ, BES and two LOC questionnaire (EDE-Q and Latner LOCES), had anthropometrics measured, and consumed a self rated preferred food while wearing a fNIRS headband sensor. The ad libitum eating episode lasted between 3 and 10 minutes. Two groups were formed based on whether fNIRS data showed mPFC activation was greater or less than lPFC activation. LOC scores (EDE-Q composite score:questions 9 and 14; and LOCES) where compared between fNIRS groups.
Results: The EDE-Q composite score waslower for the mPFC > lPFC group ($p = 0.047$, controlled for sex and total eating time). There was no difference between fNIRS groups for LOCES. ($F = 1.5$, $p = 0.205$, controlled for BMI and sex). There was no significant correlation between either LOC scores and anthropometric measures orfood intake. The EDE-Q composite score correlatedsignificantly with BES scores. EDE-Q and LOCES were significantly correlated ($r = 0.71$, $p < 0.001$).
Conclusions: LOC questionnaires appear to reflect subjective feelings of loss of control, as opposed to objective consequences (BMI, waist circumference, food intake) of loss of control. fNIRS activation provides a demonstration of a potential objective measure of subjective feelings.

Funding was provided by the Clinical Translational Research Institute of Drexel University.

Board 26, Poster 2

Abstract Topic Category *	Neurological
Abstract Title *	The effect of contraceptive use on the amount of preferred food consumed and brain activation patterns during food consumption using fNIRS
Authors *	Lisa Lanza, MPH, RDN, Eram Albajri, MS, RDN, Angelo Del Parigi, MD, Hasan Ayaz, PhD, and Jennifer A. Nasser, PhD, RD
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Structured Abstract *

Background: The use of oral contraceptives containing estradiol and progesterone have been associated with changes of brain regions that are essential in socio-behavioral characteristics (Montoya & Bos, 2017). The PFC has been shown to have a high density of estrogen receptors (Petersen, Touroutoglou, Andreano, & Cahill, 2015). Estradiol correlates negatively with volume of several areas of the brain, including the prefrontal cortex (PFC) (Peper et al., 2009). Contraceptives that contain estradiol and progesterone lower the endogenous hormone levels because they bind to their respective receptors. These hormonal changes that affect brain structure may also have an effect on the PFC activation and therefore, behavior (Petersen et al.,, 2015). However, no data exists on this yet.
Methods: Thirty-six female participants attended a 2-session study. During each session, participants were asked to consume "ad libitum" food that had been previously categorized during their screening as either preferred or non-preferred. Total eating time varied between 3 minutes and 10 minutes among participants. During food consumption, PFC activation was assessed by the functional near-infrared spectroscopy (fNIRS). Participants were grouped according to relative activation of medial PFC (mPFC) vs lateral PFC (lPFC). A factorial ANOVA was conducted to evaluate the relationship between contraceptive use, consumption of a preferred or non-preferred food and PFC activation.
Results: Factorial Analysis (controlled for total eating time for both preferred and non-food preferred conditions) revealed a trend towards significance ($F(4, 35) = 2.32$, $p = 0.080$) for the corrected model of mPFC vs lPFC, hormonal contraceptive use and amount of food eaten for preferred food, and a significant difference ($F(4, 32) = 2.94$, $p = 0.039$) for the corrected model of mPFC vs lPFC, contraceptive use and amount of food eaten for non-preferred food.
Conclusions Hormonal contraceptive use may have some effect on regional PFC activation observed during ad libitum eating of preferred food. Further research seems warranted.

This research was partially funded by a grant (to JAN) from the Clinical Translational Research Institute of Drexel University College of Medicine, start-up funds from the Office of Provost for Drexel University.

Board 27, Poster 1

Abstract Topic Category *	Neurological
Abstract Title *	Neuronal nitric oxide synthase (nNOS) neurons in the ventromedial hypothalamic nucleus (VMH) express bone morphogenic protein receptor 1a
Authors *	Hamad Wajid*, Pallabi Sarkar*, Kevin B. Knapp, Vishwendra Patel and Vanessa H. Routh
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Structured Abstract *

Background: The VMH regulates 4 distinct aspects of glucose and energy homeostasis: hepatic glucose production, the counterregulatory response to hypoglycemia (CRR), brown adipose thermogenesis/white adipose browning and peripheral insulin sensitivity. The cellular fuel sensor AMP-activated protein kinase (AMPK) plays a key role in the first 3 of these processes. VMH AMPK activation increases blood glucose by increasing hepatic gluconeogenesis and stimulating the CRR. Conversely, VMH AMPK activation inhibits brown fat thermogenesis and white fat browning leading to decreased energy expenditure and weight gain. Estrogen promotes weight loss by inhibiting VMH AMPK. Bone morphogenetic protein 8B (BMP8B) mediates estrogen's thermogenic effect. VMH glucose-inhibited (GI) neurons require AMPK-induced activation of neuronal nitric oxide synthase (nNOS) for activation in low glucose. Estrogen inhibits VMH nNOS-GI neurons. These data suggest that estrogen's thermogenic effect is due, in part, to inhibition of VMH nNOS-GI neurons. We hypothesize that BMP8B mediates the inhibitory effect of estrogen on GI neurons.

Methods: We used immunohistochemistry to determine whether nNOS and the BMP8B receptor, BMPR1a, co-localize in the VMH in adult C57bl/6 mice (n= 4 males, 5 females).

Results: We observed intense immunoreactivity of nNOS in both dorsomedial (dm) and ventrolateral (vl)VMH. The vlVMH had large, clearly-defined nNOS+ cell bodies and a robust expression of BMPR1a. We observed a larger percentage of cells that were BMPR+ (50.6±4.3% in males vs. 57± 4.6% in females, of total cells) compared to nNOS+ cells (39.6±3% in males vs. 47.7±2.2% in females). Of these, BMPR1a and nNOS co-localization was observed in 12.2±1.8% of total vlVMH cells in males; whereas in the female the co-localized cells were 24.4±2.3% of total.

Conclusion: The co-localization of nNOS and BMPR1a is consistent with the hypothesis that BMP8B mediates the effect of estrogen on VMH nNOS-GI neurons. We also observe a sex difference in this pattern of co-localization.

Board 27, Poster 2

Abstract Topic Category *	Population Health and Epidemiology
Abstract Title *	The Relationship between Glycemic Measures and the Risk of Sleep Apnea in Adults with Prediabetes and Type 2 Diabetes
Authors *	Persaud, Bianca (1); Popp, Collin J., RD, PhD (2); Curran, Margaret A., MS (2); Seixas, Azizi, PhD (2); Sevick, Mary Ann, ScD (2)
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Structured Abstract *

Introduction: BMI is positively associated with greater risk of sleep apnea. Less is known regarding the relationship between glycemic variability (GV) and risk of sleep apnea. GV is characterized as daily fluctuations in blood glucose levels and measured using the mean amplitude of glycemic excursion (MAGE). The current study examines the relationship between GV and risk of sleep apnea. It was hypothesized that there would be a positive association between GV and risk of sleep apnea among adults with prediabetes and type 2 diabetes.

Methods: As part of baseline data collection, each study participant completed the Apnea Risk Evaluation System and Epworth Sleepiness Scale questionnaires. A sleep score was generated for each participant, and categorized as low risk (<4-5), high risk (6-10) or very high risk (11+) for obstructive sleep apnea. Pearson's correlations were computed to assess relationships between body mass index (BMI), glycated hemoglobin (HbA1c), MAGE and sleep score. All analyses were performed using IBM SPSS Statistics for Windows, version 25.

Results: Study participants (n = 88) were mostly female (70.5 %) with a mean (SD) age of 57.3 (11.6) years, height of 166.1 (9.5) cm, weight of 94.3 (16.9) kg, BMI of 34.1 (5.1) kg/m2 and HbA1c of 5.6 (0.4) %. Based on sleep scores, 39.8% of the participants were classified as high risk and 18.2% were classified as very high risk. There was a significant positive relationship between BMI and sleep score ($r= 0.338$, $p<0.01$). There was also a significant positive relationship between HbA1c and sleep score ($r= 0.366$, $p<0.01$), which remained significant when controlling for BMI ($r= 0.294$, $p<0.01$). There was a significant positive relationship between MAGE and sleep score for those determined to be of very high risk of sleep apnea ($r= 0.703$, $p<0.05$), which also remained significant when controlling for BMI ($r= 0.712$, $p<0.05$).

Conclusion: Among adults with prediabetes and early-stage type 2 diabetes, those with higher HbA1c and MAGE may be at higher risk for sleep apnea, regardless of BMI. This suggests that those individuals with higher GV should be assessed for risk of sleep apnea, regardless of their BMI.

Board 28, Poster 1

Abstract Topic Category *	Population Health and Epidemiology
Abstract Title *	Process Evaluation of the Long Island SNAP-Ed Healthy Corner Store Initiative: Promising Program Implementation Model Including Community Partnership Opportunities
Authors *	Alisha Gaines*, Tisa F. Hill, Zoe Wakoff, Zahrine Bajwa
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Structured Abstract *

Background: Food access remains a public health concern for low-income communities, including areas of Long Island that lack easily accessible grocery stores, leaving some residents dependent on corner stores to meet household food needs. Thus, residents have limited access to fresh, healthy, and affordable foods, increasing risk of poor diet quality and diet-related disease among vulnerable populations. The Long Island Healthy Corner Store (HCS) initiative was designed by Suffolk County Cornell Cooperative Extension SNAP-Ed staff, working in concert with community partners to increase availability of healthy foods in local corner stores. The program incorporates phased changes, beginning with nutrition education and marketing strategies and ending with sustained increases in healthy offerings. The SNAP-Ed team partnered with Cornell University in 2017-2018 to conduct a process evaluation designed to determine HCS implementation fidelity and identify facilitators and barriers to implementation.

Methods: The mixed methods evaluation design included review of HCS documentation, in-store environmental assessments, and interviews with program staff and stakeholders, including community partners and storeowners. Fidelity was assessed by comparing quantified input, activity, and output data from activity logs with the program logic model and store-specific goals. Qualitative data were analyzed thematically.

Results: Seven stores participated in HCS during the evaluation period, reaching 30-500 customers daily. Challenges and successes existed in different forms along the spectrum of work - from recruitment to program maintenance - and affected staff ability to implement program changes. Challenges included time needed to gain storeowner trust, limited store size, owners' limited purchasing power, and store staff turnover and limited buy-in. Nonetheless, SNAP-Ed staff achieved moderate-to-high fidelity to planned inputs, activities, and outputs, and stores made substantial progress toward program goals. In all stores, staff implemented early stage program goals such as labeling, promotion, and prominent display of healthy foods. Four stores implemented later-stage environmental changes, such as increasing volume and variety of healthy foods. Owners believed HCS helped improve store appearance and increase sales of healthy items like fruits, vegetables, 100% juice, and bottled water.

Conclusions: SNAP-Ed staff accomplished many program goals, and results highlighted challenges in creating sustainable changes in store environments. Implementation challenges and successes are potential influences of intervention effectiveness that informed program recommendations and an ongoing HCS outcome evaluation. Results can also inform intervention models and serve as an example of community-institutional relationships in which partners strategically allocate resources to expand program capacity and execute a shared vision of healthier communities.

Board 28, Poster 2

Abstract Topic Category *	Population Health and Epidemiology
Abstract Title *	The Use of Non-Nutritive Sweeteners, and their Associations with Sugar Intake, Glycemia and Weight Status Among Overweight Adults with Prediabetes and Type 2 Diabetes
Authors *	Paige M. Mandel*, Margaret A. Curran, David E. St-Jules, Mary Ann Sevick
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Structured Abstract *

Background: Excess sugar consumption is one of the key modifiable factors contributing to the epidemic of cardiometabolic diseases such as type 2 diabetes (T2D) in the United States. Non-nutritive sweeteners (NNS) are designed to be a physiologically-inert sugar substitute; however, there is limited information on whether they actually improve health outcomes in people with prediabetes and T2D. Therefore, we examined the associations of NNS use with sugar consumption, glycemia and weight status in overweight adults with prediabetes and T2D enrolled in a weight loss intervention.

Methods: Data used in this cross-sectional analysis were obtained during fasting baseline measurement visit. Height, weight and percent body fat (%BF) were measured using a stadiometer and bioelectrical impedance analysis scale. NNS use was assessed using an investigator-generated questionnaire. Sugar intake was estimated from 3-day food records (two weekdays, one weekend day) that were entered into the Personalized Nutrition Project mobile application. Mean amplitude of glycemic excursion (MAGE) was calculated based on three days of continuous glucose monitoring (two weekdays, one weekend day) using the Abbott Freestyle Libre Pro, and HbA1c was measured from fasting blood samples. Statistical analyses were run using Statistical Analysis Software (SAS).

Results: Almost half (38/83 46%) of the participants reported consuming NNS, with 39% of users reporting a frequency of least once per day. Although the primary stated reasons for their use were weight management (25/38, 66%) and blood sugar control (14/38, 37%), use of NNS was not associated with sugar intake, BMI, %BF, MAGE or HbA1c.

Conclusions: NNS are intended to help people reduce sugar intake, which is particularly important for overweight individuals with prediabetes and T2D. Yet, despite common use, NNS use was not associated with reported sugar intakes, glycemic control, or weight status in our sample. Given the widespread use of NNS, further investigation is necessary to verify these findings in a more representative sample.

Board 29, Poster 1

Abstract Topic Category *	Population Health and Epidemiology
Abstract Title *	Who consumes more Fruits and Vegetables: Dietitians or Pharmacists?
Authors *	Victoria Fischer PhD MS RDN CDN, Eva S. Alam, RPh., M.S., Pharm.D, Harlan E. Spotts, MBA, PhD, Shamima Khan*, MBA, PhD.
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Structured Abstract *

Background: Fruits and vegetables (F&V) consumption remains sub-optimal, despite the well-known health benefits. This study was conducted to explore F&V intake of Registered Dietitians (RDs) and Registered Pharmacists (RPhs), with respect to frequency and variety of consumption of F&V, perceived barriers to F&V consumption, and the consumption of dietary supplements (DS).

Methods: A four state (California, Illinois, New York and Texas) cross-sectional survey of RDs and RPhs was conducted between December 2015 and April 2016, by using a national Internet-based survey platform (SurveyMonkey). Relationships between variety and frequency of F&V consumption, and perceived barriers to F&V consumption were explored.

Results: RPhs reported an average consumption of 3.51 F&V per day, whereas RDs reported 2.66. Barriers to F&V consumption were explained by three factors: personal issues, time issues, and costs issues; these three factors cumulatively explained 76.5% of variance to barriers faced. The adjusted response rate was 66.7%. RPhs reported significantly higher annual household income.

Conclusions: This study found higher level of F&V consumption among RPhs as opposed to RDs, though BMI was similar. Regardless of professional expertise, respondents who faced more barriers (cost, time or personal issues) were less likely to consume a variety of F&V.

Board 29, Poster 2

Abstract Topic Category *	Population Health and Epidemiology
Abstract Title *	Temporal eating patterns among older adults with obesity
Authors *	Collin Popp*, David St-Jules, Margaret Curran, Paige Illiano, Mary Ann Sevick
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Structured Abstract *

Background: The timing and distribution of food throughout the day, also known as temporal eating patterns (TEP), are associated with obesity, dysglycemia and cardio-metabolic disease. These patterns may change with aging, as age-associated declines in hunger, sleep, and body composition (e.g., sarcopenia) have been well documented.

Objective: To describe the TEP amongst older adults with obesity

Methods: In a cross-sectional analysis, a sample (n=11) of older adults (67 [IQR 59-73] yo, BMI 31.1[IQR 30-36] kg/m2) were instructed to enter all eating occasions (EO) with caloric value (>0 kcal) into a mobile smartphone app for up to 14 days (5.4±3.5d). EO entries were confirmed by phone call or text message. EOs logged within 15 mins of each other (n=3) were combined to a single EO. The eating period was defined as the difference between the first and last EO. In a subset of participants (n=6), the GT9X Actigraph was fitted and worn for up to 8 days to measure sleep and confirm temporal eating patterns.

Results: A total of 359 EOs were recorded. The mean number of EOs was 3.6±1.7 per day, with the first EO occurring at 8:48AM±3.3hr and the final EO at 6:28PM±4.3hr. The eating period was 10.2±5.3hr, and the mean timing of daily EOs was 1:43PM±2.4hr. The average time between the first four EOs was 4.0±2.4hr. In the subset of participants, the total sleep time was 5.9±2.1hr, time out of bed was 7:06AM±1.3hr, and time in bed was 7:39PM±10.1hr. There was a delay in the first EO occurring 1.2±2.3hr after wake onset. The time from last EO to time in bed was 4.0±5.3hr.

Conclusion: Older adults appear to follow a traditional eating pattern (3 meal/day), typically eating closer to waking than bedtime, and have a smaller eating period than has been previously reported in the literature. These data provide useful information for study intervention design (i.e., time-restricted feeding).

Board 30, Poster 1

Abstract Topic Category *	Population Health and Epidemiology
Abstract Title *	Obesity Risk Comes to The Surface (Part 1 of 3): Food/Drink Advertising in Subway Stations
Authors *	Charles Pan*, BS1; Ian Dwyer, BS1; Kelsey McKenna, BA1; Andrew R. Maroko, PhD1; Clyde B. Schechter, MD, MA,3 Sean C. Lucan, MD, MPH, MS3
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Structured Abstract *

BACKGROUND: Obesity-related conditions are epidemic—and multifactorial. One important factor, unhealthful eating, may be prompted by advertisements for food/drink (especially ads for unhealthful items like fast food, candy, and soda). Such advertising may take many forms, including ads in mass-transit stations. Mass-transit ads may act as daily cues, near where food/drink can be obtained, to stimulate appetite and promote impulse consumption. Mass-transit ads specifically for alcohol were found to be targeted to vulnerable groups; such ads were recently banned. The current study aims to characterize--after an alcohol-ad ban--other food/drink ads in a large transit system and assess for targeting.

METHODS: This study is cross-sectional, involving primary data collection and secondary analyses. Investigators are assessing all advertisements, on all lines (n=7), in all stations (n=68), in the Bronx, NY, and comparing findings to characteristics of surrounding "neighborhoods" (census tracts or zip codes). Analyses will include counts and proportions of ads for food/drink, with attention to the following: (1) promotion of healthful items (fruits, vegetables, whole grains, nuts, water, milk) vs. unhealthful items ("refined sweets" like candy, cookies; "salty/fatty fare" like processed meats, fried foods; sugar-sweetened beverages), (2) directed at youth vs. not, (3) featuring racial/ethnic minorities vs. not, (4) in English vs. other languages. Correlations will be to neighborhoods characteristics--demographics (from U.S. Census) and diet and disease rates (from City health department).

PRELIMINARY AND ANTICIPATED RESULTS: So far, 21 of 68 stations have been assessed. Counting duplicate ads (0-7 per station), there have been 191 ads; 24 (12.6%) have been for food/drink. Healthful items (e.g., cherries) only tended to appear in ads explicitly for unhealthful items (e.g., cherry ice cream). 80% of ads have been for unhealthful items; there is already suggestion such ads are directed at youth (p=0.11). It is anticipated that unhealthful ads (particularly directed at youth, in Spanish, and/or featuring racial/ethnic minorities), will be directly correlated with the following neighborhood characteristics: higher poverty; less schooling; more foreign-born residents; higher percent children; lower fruit-and-vegetable intake; higher sugary-drink consumption; and higher rates of obesity, diabetes, and hypertension.

CONCLUSIONS: Even minus alcohol ads, ads for unhealthful food/drink may target vulnerable groups in neighborhoods with greater demographic, diet, and diet-related-health challenges. Findings could support further policies to restrict unhealthful advertising (or support initiatives to promote healthful ads) to reduce community disparities related to obesity.

Board 30, Poster 2

Abstract Topic Category *	Population Health and Epidemiology
Abstract Title *	Obesity Risk Comes to The Surface (Part 2 of 3): Food/Drink Availability in a Subway System
Authors *	Kelsey McKenna*, BA1; Ian Dwyer, BS1; Charles Pan, BS1; Andrew R. Maroko, PhD2; Clyde B. Schechter, MD, MA3 Sean C. Lucan, MD, MPH, MS3
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Structured Abstract *

BACKGROUND: Sources of food/drink in communities may cue both appetites and impulse consumption. Community sources of food/drink include those in the spaces where daily commutes occur--e.g., in mass-transit stations. The extent and character of food/drink sources in mass-transit stations has not been previously reported. If distributions are similar to those of food/drink sources elsewhere, unhealthful items may be disproportionately present in vulnerable neighborhoods. The aim of the current study is to assess sources of food/drink in a large transit system and determine associations with surrounding-neighborhood characteristics.

METHODS: Investigators are conducting primary data collection and will be performing secondary data analyses. Primary data collection includes assessment of all food/drink sources, on all lines (n=7), in all stations (n=68), in the Bronx, NY. Analyses will include counts and proportions of food/drink sources offering healthful items (fruits, vegetables, whole grains, nuts, water, milk) vs. unhealthful items ("refined sweets" like candy, cookies; "salty/fatty fare" like processed meats, fried foods; sugary drinks). Secondary analyses will be correlations with characteristics of surrounding "neighborhoods"--census-tract demographics (from U.S. Census data) and zip-code-level data on diet and disease rates (from the City health department).

PRELIMINARY AND ANTICIPATED RESULTS: So far, 21 of 68 stations have been assessed. Two stations each have had a single food/drink seller (a concession stand and a convenience kiosk). Both sellers offered unhealthful items (candy, chips, soda); both also offered healthful items (unsweetened nuts, water) and items categorized as neither healthful nor unhealthful (100% juice, diet drinks). The convenience kiosk sold fresh produce (e.g., apples, tomatoes); the concession stand sold a whole-grain product (granola bars). Neither sold milk. It is anticipated that additional sources of food/drink will include newsstands, fast-food kiosks, and street vendors; these sources will be present more often in stations in lower-income neighborhoods (yet to be assessed), home to mostly black and Hispanic residents having poor diet (e.g., high sugary-drink consumption) and high rates of diet-related disease (e.g., obesity)

CONCLUSIONS: Sources of food/drink include those in spaces where individuals go about daily activities, potentially supporting impulse purchases and consumption. Greater availability of unhealthful items in stations in certain communities are of particular concern. Findings will suggest opportunities for transit-level policy changes to reduce community disparities related to obesity.

Board 31, Poster 1

Abstract Topic Category *	Population Health and Epidemiology
Abstract Title *	Obesity Risk Comes to The Surface (Part 3 of 3): Food/Drink Availability on Streets Immediately Around Subway Stations
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Structured Abstract *

BACKGROUND: Food-environment research most often considers availability of food/drink around people's homes. However, other locations in people's lived activity spaces may be relevant for food/drink exposures. Among such locations are those along daily commutes--e.g., around entrances/exits to mass transit stations. Food/drink sources around mass-transit stations may offer both temptation and opportunity to consume (both upon entering and upon exiting the transit system). Nonetheless, the sources of food/drink around mass-transit stations have not previously been described. This study aimed to assess the sources of food/drink around all entrances/exits of a large transit system.

METHODS: Investigators are using Google Street View to make observations along streets adjacent to subway stations in the Bronx, NY. Of interest are all businesses, within 300 feet of any subway-station entrance/exits. Relevant measures are counts and proportions of businesses that are food/drink sellers (food stores, restaurants, or other businesses with exterior signage indicating food/drink selling). Analyses are being conducted at the level of the subway station (n=68), subway line (n=7), and subway system. Consideration will be given to business category (e.g., food store, restaurant, other storefront business, street vendor) and whether businesses appear closed (boarded up, "under renovation", "coming soon", etc.).

PRELIMINARY AND ANTICIPATED RESULTS: For businesses not appearing closed, there were 2,602 (range 1-133) within 300 ft of stations, of which 1,058 (range 1-48) were food/drink sellers. There were 896 businesses (range 0-51) within 100 ft of stations; there were 1,706 (range 0-85) within 100-300 ft. The number of businesses that sold food/drink was 443 (range 0-22) within 100 ft, 615 (range 0-26) within 100-300 ft. The overall proportions offering food/drink were thus 0.49 within 100 ft, and 0.36 within 100-300 ft. By subway station, the proportions ranged 0.00-1.00 and 0.00-0.69, respectively. By subway line, the proportions ranged 0.41-0.85 and 0.23-0.47, respectively. Analyses by business category, including closed businesses, are pending.

CONCLUSIONS: Opportunities to obtain food/drink cluster around subway entrances/exits. While absolute counts and proportions are sizeable, they undoubtedly underestimate total food/drink selling; various other storefront businesses (e.g., those having vending machines or checkout snacks not obvious form exteriors) would be missed. Findings will be relevant to city planners and policy makers, and for initiatives to address community risks for obesity.

Board 31, Poster 2

Abstract Topic Category *	Population Health and Epidemiology
Abstract Title *	Measures of poor sleep quality are associated with higher energy intake and poor diet quality in a diverse sample of women from the Go Red for Women Strategically Focused Research Network
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Structured Abstract *

Background: Insufficient sleep leads to higher risk for the development of obesity, and diet likely plays a role in this relationship. While emerging studies have linked sleep duration to diet quality, there is limited epidemiological data on the association of measures of sleep quality with habitual dietary patterns, despite the documented roles of these factors in cardiovascular health.
Objective: This study aimed to examine the association of subclinical and clinical measures of sleep quality with dietary intakes in a diverse sample of women.
Methods: Baseline data from 506 participants in the AHA Go Red for Women prospective cohort study (age: 19-76 y; 61% racial/ethnic minority) were examined. Sleep quality and sleep onset latency were measured using the Pittsburgh Sleep Quality Index (PSQI) and insomnia using the Insomnia Severity Index. The validated Block Brief Food Frequency Questionnaire was used to assess diet quantity and quality, including the total food weight and energy consumed as well as intakes of nutrients and foods linked to obesity and cardiovascular disease risk. Linear regression models adjusted for age, BMI, race/ethnicity, education, and health insurance were used to examine associations between sleep quality and dietary intake.
Results: Higher PSQI scores, indicative of poorer sleep quality, were associated with lower unsaturated fat (B=-0.14, P=0.048) and dairy intakes (B=-0.014, P=0.030) as well as higher weight of food (B=14.9, P=0.024) and added sugar consumed (B=0.44, P=0.037). Longer sleep onset latency was related to greater intake of food by weight (B=47.5, P=0.049) and energy (B=93, P=0.020), and lower intakes of dairy (B=-0.06, P=0.013) and whole grains (B=-0.09, P=0.046). Greater insomnia severity was associated with higher food weight (B=9.4, P=0.018) and energy (B=17, P=0.012) consumed and lower total (B=-0.15, P=0.011) and unsaturated fat intakes (B=-0.11, P=0.007).
Conclusion: Poor sleep quality was associated with a lower-quality diet and greater food intake in a diverse sample of women. These findings provide insight into a potential mechanism underlying the sleep-obesity relation. Given that poor diet and overeating contribute to obesity, future studies should test whether experimental promotion of sleep quality would augment lifestyle efforts to improve cardiometabolic health in women or whether dietary patterns could be modified to influence sleep quality and insomnia symptoms.

Board 32, Poster 1

Abstract Topic Category *	Population Health and Epidemiology
Abstract Title *	Adiposity is related to cerebrovascular and brain volumetry outcomes in the RUN DMC Study
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Structured Abstract *

Objective. Adiposity predictors, body mass index (BMI), waist circumference (WC), and blood leptin and total adiponectin levels were associated with components of cerebral small vessel disease (CSVD) and brain volumetry in 503 adults with CSVD who were ≥50 years of age and enrolled in the Radboud University Nijmegen Diffusion Tensor and Magnetic Resonance Imaging Cohort (RUN DMC).

Methods. RUN DMC participants were followed up for 9 years (2006–2015). BMI, WC, brain imaging, and dementia diagnoses were evaluated at baseline and follow-up. Adipokines were measured at baseline. Brain imaging outcomes included CSVD components, white matter hyperintensities, lacunes, microbleeds, gray and white matter, hippocampal, total brain, and intracranial volumes.

Results. Cross-sectionally among men at baseline, higher BMI, WC, and leptin were associated with lower gray matter and total brain volumes, and higher BMI and WC were associated with lower hippocampal volume. At follow-up 9 years later, higher BMI was cross-sectionally associated with lower gray matter volume, and an obeseWC(>102 cm) was protective for ≥1 lacune or ≥1 microbleed in men. In women, increasing BMI and overweight or obesity (BMI ≥25 kg/m2 or WC>88 cm) were associated with ≥1 lacune. Longitudinally, over 9 years, a baseline obeseWC was associated with decreasing hippocampal volume, particularly in men, and increasing white matter hyperintensity volume in women and men.

Conclusions. Anthropometric and metabolic adiposity predictors were differentially associated with CSVD component and brain volumetry outcomes by sex. Higher adiposity is associated with a vascular–neurodegenerative spectrum among adults at risk for vascular forms of cognitive impairment and dementias.