

The following potential conflict of interest relationships are germane to my presentation.

Equipment: none

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Status of off-label use of devices, drugs or other materials that constitute the subject of this presentation NA/Non-Clinical

Genetics' Impact on Wellness & Weight Loss Resistance

JJ Virgin, CNS, CHFS

Nutrition & Fitness Expert

What is Weight Loss Resistance

- Failure to lose 1-3# of fat consistently each week with > 25 BMI despite following a sound diet & exercise program based on genotype

Bank Account



What is Weight Loss Resistance

- The body is not a bank account, it's a chemistry lab and a history book influenced by a multitude of factors including:
 - Stress & sleep
 - Digestion & gut bacterial overgrowth
 - Toxic burden & food sensitivities
 - Hormone imbalances & deficiencies (thyroid, insulin, sex hormones)
 - Genetics
 - Social relationships

What is Weight Loss Resistance

- Keith SW, et al. Putative contributors to the secular increase in obesity: exploring the roads less traveled. *Int'l Journal of Obesity* 2006 ;30:1585–1594.
- Taubes, Gary. *Why We Get Fat and What To Do About It*. Alfred A. Knopf, New York, 2011.

Human Obesity: A Heritable Neurobehavioral Disorder That Is Highly Sensitive to Environmental Conditions

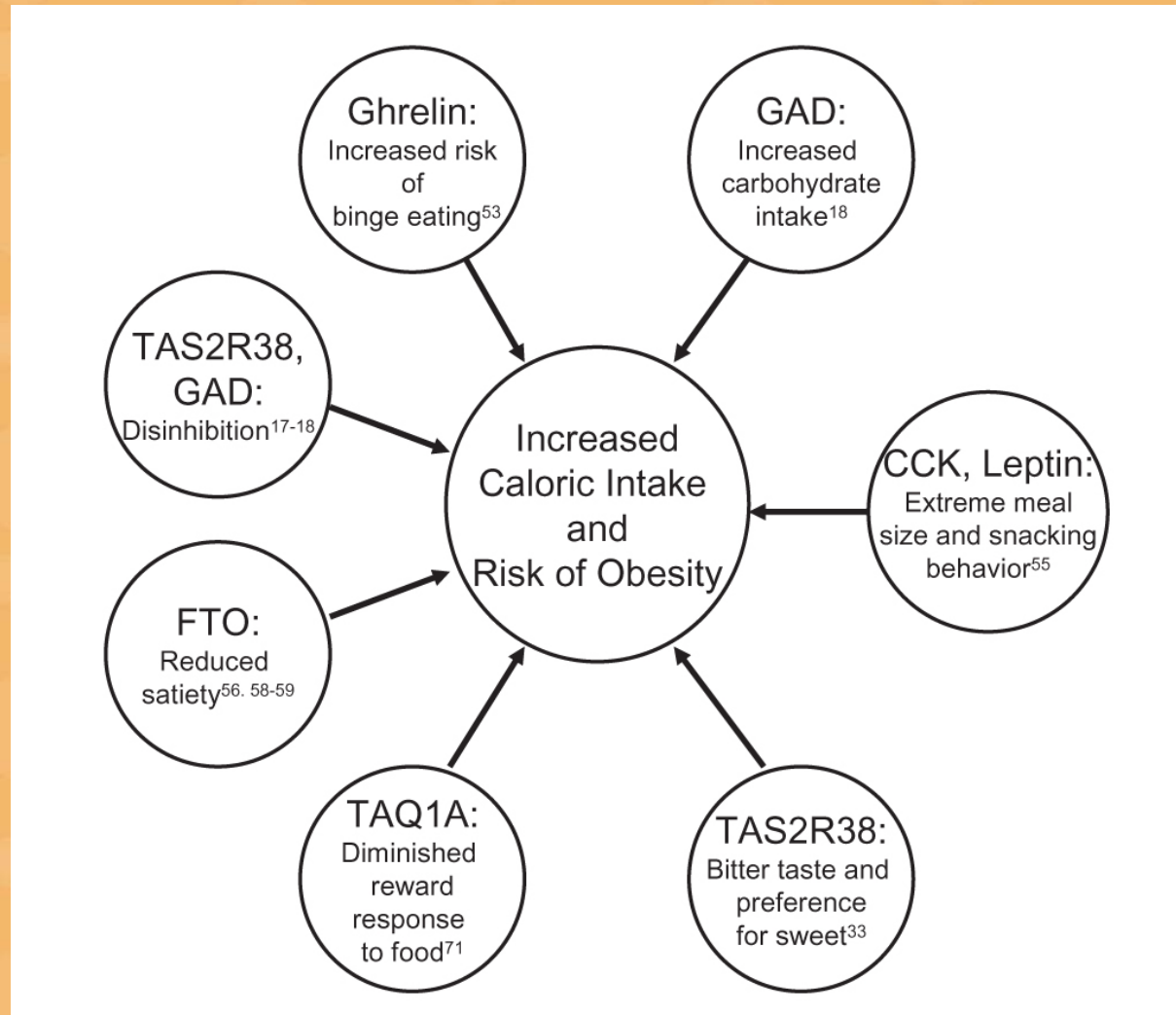
- Notably, a number of single gene disorders resulting in human obesity have been uncovered and, strikingly, all of these defects impair the central control of food intake.
- While the rising prevalence of obesity is related to increasing ease of access to high-energy palatable food combined with diminishing requirement for physical activity, differences in inter-individual susceptibility to obesity are likely to be related to inherited variation in the efficiency of central control mechanisms influencing eating behavior.

Stephen o'Rahilly and I. Sadaf Farooqi

Diabetes: November 2008 vol. 57 no. 11 2905-2910

Impacts cognitive behavior

Impacts food selection



Genes identified with common variants influencing eating behavior with potential impact on obesity

A Twin Study of Human Obesity

- Height, weight, and body mass index (BMI) were assessed in a sample of 1974 monozygotic and 2097 dizygotic male twin pairs. Concordance rates for different degrees of overweight were twice as high for monozygotic twins as for dizygotic twins. Classic twin methods estimated a high heritability for height, weight, and BMI, both at age 20 years (.80,.78, and .77, respectively) and at a 25-year follow-up (.80,.81, and .84, respectively).

A Twin Study of Human Obesity

- Height, weight, and BMI were highly correlated across time, and a path analysis suggested that the major part of that covariation was genetic. These results are similar to those of other twin studies of these measures and suggest that human fatness is under substantial genetic control

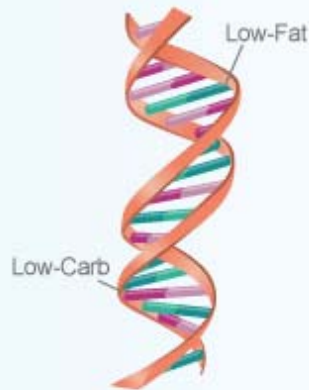
*Stunkard MD, Albert, Foch PhD, Terryl, Hurbec, ScD, Zdenek;
JAMA. 1986;256(1):51-54.*

Stanford Study on Customized Genetics Diet

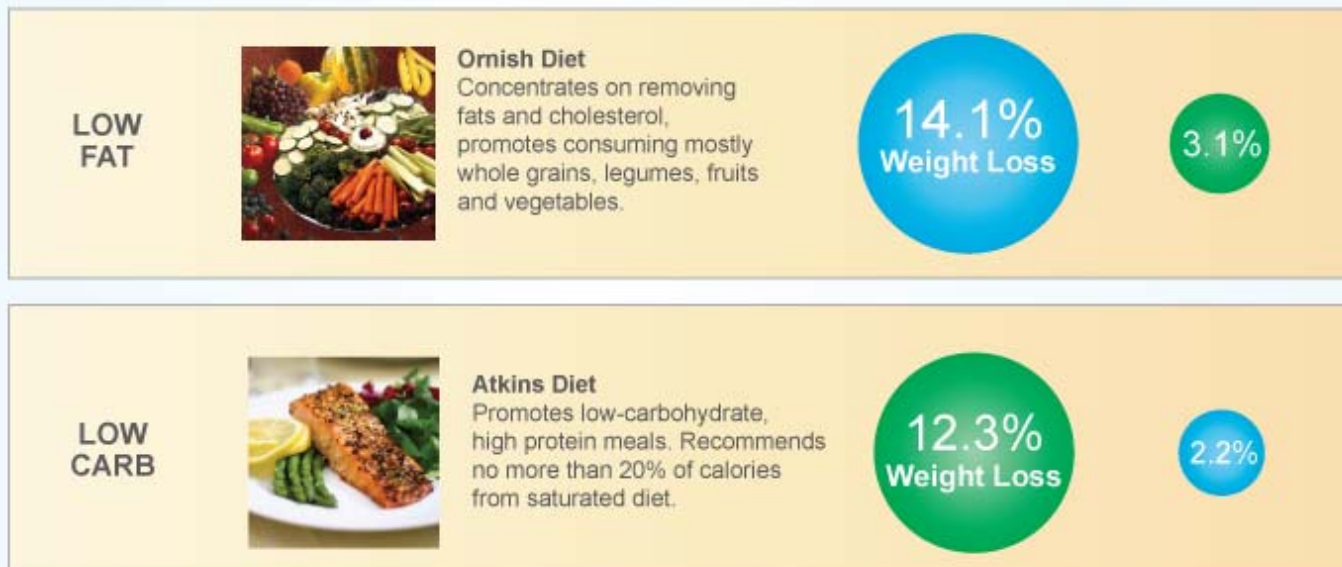
- Individuals on a diet identified as appropriate to their genotype by the Weight Management Genetic Test lost an average of over **2.5 times more weight** than individuals on diets that were not appropriate.

– Stanford University, March 2010

STANFORD UNIVERSITY STUDY (MARCH 2010)



Stanford University Study shows that women on genetically appropriate diets lose significantly more weight



Source: Wall Street Journal, March 2010 (Interleukin Genetics)



Why Fad Diets Work Well For Some & Not For Others

- Fruit fly research suggests that genetic interaction with diet primarily determines variations in metabolic traits such as body weight, as opposed to diet alone.
- This helps explain why some diets work better for some people than others, and suggests that future diets should be tailored to an individual's genes.

Why Fad Diets Work Well For Some & Not For Others

- Genetics, Vol. 185, 1009-1019, July 2010, doi:10.1534/genetics.109.113571
- Genotype-by-Diet Interactions Drive Metabolic Phenotype Variation in *Drosophila melanogaster*
- Laura K. Reed^{*,1}, Stephanie Williams^{*}, Mastafa Springston^{*}, Julie Brown^{*}, Kenda Freeman^{*}, Christie E. DesRoches, Marla B. Sokolowski and Greg Gibson



WILLPOWER

Genetics of eating behavior: established and emerging concepts

- Understanding why we eat and the motivational factors driving food choices is important for addressing the epidemics of obesity, diabetes, and cardiovascular disease. Eating behavior is a complex interplay of physiological, psychological, social, and genetic factors that influence meal timing, quantity of food intake, and food preference.

Genetics of eating behavior: established and emerging concepts

- Reviewed here is the current and emerging knowledge of the genetic influences on eating behavior and how these relate to obesity; particular emphasis is placed on the genetics of taste, meal size, and selection, and the emerging use of functional magnetic resonance imaging to study neural reactions in response to food stimuli in normal, overweight, and obese individuals.

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Eating Behavior Traits

- Indeed, we have known for 40 years or more that quantitative measures of such appetite-related variables are clearly linked to obesity¹ and that measurable and stable measures of eating behavior are heritable².

1. Schachter S: *Obesity and eating: internal and external cues differentially affect the eating behavior of obese and normal subjects. Science* 161 :751-756, 1968

2. Rankinen T, Bouchard C: *Genetics of food intake and eating behavior phenotypes in humans. Annu Rev Nutr* 26 :413 –434, 2006

The notion that genes can affect our apparently voluntary behavior is understandably uncomfortable to many.

Eating Behavior Traits: Hunger & Satiety

- **Hunger**-above average feeling of hunger, variation in NMB gene (NMB-rs1051168)
- **Satiety**-reduced postprandial feeling of fullness, FTO gene variation (FTO-rs9939609)
- Strategies:
 - Dietary fat, protein and fiber
 - Water in between meals
 - Neurotransmitter balance
 - High Response Costs foods – soups, non starchy veggies, salads
 - Slow down, chew more, put fork down

Eating Behavior Traits: Hunger & Satiety

- Bouchard, L. et al. Neuromedin beta: a strong candidate gene linking eating behaviors and susceptibility to obesity. *Am J Clin Nutr* 80, 1478-86 (2004).
- Wardle, J. et al. Obesity associated genetic variation in FTO is associated with diminished satiety. *J Clin Endocrinol Metab* 93, 3640-3 (2008).

Eating Behavior Traits: Snacking

- Increased **snacking** behavior
- Variants in the leptin receptor LEPR rs2025804
- Divide daily caloric and macronutrient needs between mini-meals and eat every 2-3 hours
- Carry “emergency food” with you
- Plan healthy snacks and meals
- Use smaller plates and serving containers

Eating Behavior Traits: Snacking

- de Krom, M. et al. Common genetic variations in CCK, leptin, and leptin receptor genes are associated with specific human eating patterns. *Diabetes* 56, 276-80 (2007).

Eating Behavior Traits: Eating Disinhibition & Food Desire

- **Eating Disinhibition**-eat more than normal in response to a stimulus
 - Gene variant in TAS2R38-rs176866
- **Food Desire**-willingness to make an extra effort to get their favorite foods
 - Gene Tested: ANKK1/DRD2-rs1800497

Eating Behavior Traits: Eating Disinhibition & Food Desire

Strategies:

- Remove food triggers and avoid challenging situations(e.g. “all you can eat buffets”)
- Don’t make seconds easily available
- Go out for limited amount of “treat/trigger food” with accountability partner
- Brush teeth/mint directly afterward eating
- Manage stress
- Replace eating with other pleasurable activities

Eating Behavior Traits: Eating Disinhibition & Food Desire

- Dotson, C.D., Shaw, H.L., Mitchell, B.D., Munger, S.D. & Steinle, N.I. Variation in the gene TAS2R38 is associated with the eating behavior disinhibition in Old Order Amish women. *Appetite* 54, 93-9 (2010).
- Epstein, L.H. et al. Food reinforcement, the dopamine D2 receptor genotype, and energy intake in obese and nonobese humans. *Behav Neurosci* 121, 877-86 (2007).

Eating Behavior Traits: Sweet Tooth

- **Sweet Tooth** - craving sweet foods
 - Gene Variant in SLC2A2-rs5400
- **Strategies:**
 - Retrain taste buds; exposure increases preference
 - Maintain good serotonin levels
 - Ensure optimal protein intake and digestion
 - Keep blood sugar balanced, consider supplementation
 - Eat low glycemic index, slow release carbs
 - Xylitol, stevia, cinnamon and vanilla

Eating Behavior Traits: Sweet Tooth

- Eny, K.M., Wolever, T.M., Fontaine-Bisson, B. & El-Sohemy, A. Genetic variant in the glucose transporter type 2 is associated with higher intakes of sugars in two distinct populations. *Physiol Genomics* 33, 355-60 (2008).

Food Reactions: Sweet Taste

- Gene variant in TAS1R3-rs35744813
- Receptors on tongue programmed by your genes determine how you taste sweetness
- “Decreased” sensitivity **sweet tasters** prefer sweeter foods as they are less likely to taste sweetness

Food Reactions: Sweet Taste

- Fushan, A.A., Simons, C.T., Slack, J.P., Manichaikul, A. & Drayna, D. Allelic polymorphism within the TAS1R3 promoter is associated with human taste sensitivity to sucrose. *Curr Biol* 19, 1288-93 (2009).

Food Reactions: Bitter Taster

- Genes variants in TAS2R38-rs713598, TAS2R38-rs1726866
- **Taster**, Non-taster or inconclusive in response to chemical PTC
- Taster may also have preference towards salty foods
- Tasters often sensitive to bitter flavors (coffee, grapefruit, dark chocolate, cruciferous vegetables)

Food Reactions: Bitter Taster

- Hayes, J.E., Sullivan, B.S. & Duffy, V.B. Explaining variability in sodium intake through oral sensory phenotype, salt sensation and liking. *Physiol Behav* 100, 369-80 (2010).

Case Studies

- **Amber** – bitter taste gene variant, eating behaviors ‘trifecta’ – variants for eating disinhibition, food desire, hunger



Move More



NAME: ...
SEX: FEMALE
LAB ID #:
DATE:



EXERCISE



PAGE 27

▶ YOUR RESULTS ◀

	ENDURANCE TRAINING	<i>page: 28</i>	ENHANCED BENEFIT
	STRENGTH TRAINING	<i>page: 29</i>	BENEFICIAL
	MUSCLE POWER	<i>page: 29</i>	LESS MUSCLE POWER
	ACHILLES TENDINOPATHY	<i>page: 30</i>	TYPICAL
	WEIGHT LOSS RESPONSE TO EXERCISE	<i>page: 30</i>	EXERCISE STRONGLY RECOMMENDED
	BLOOD PRESSURE RESPONSE TO EXERCISE	<i>page: 31</i>	EXERCISE RECOMMENDED
	HDL (GOOD) CHOLESTEROL RESPONSE TO EXERCISE	<i>page: 31</i>	ENHANCED BENEFIT
	LOSS OF BODY FAT RESPONSE TO EXERCISE	<i>page: 32</i>	NORMAL BENEFIT
	INSULIN SENSITIVITY RESPONSE TO EXERCISE	<i>page: 32</i>	ENHANCED BENEFIT

The Sad Facts



NAME:
SEX: FEMALE
LAB ID #:
DATE:



YOUR BODY AND WEIGHT

PAGE 33



▶ YOUR RESULTS ◀



OBESITY INDEX

page: 35

BELOW AVERAGE



WEIGHT LOSS-REGAIN

page: 36

MORE LIKELY TO
GAIN WEIGHT BACK



METABOLISM

page: 36

NORMAL



ADIPONECTIN LEVELS

page: 37

POSSIBLY LOW



Hope for the Genetically Disadvantaged

- **Victor** – bitter taster, elevated blood sugar, increased hunger, decreased satiety, increased food desire, lactose intolerant, more likely to gain weight back, high risk for obesity, low fat diet recommendation, increased need for exercise for weight loss, blood pressure response



Doctors Can Influence Patients to Lose Weight: Studies

- If patients are told by their doctors that they are overweight or obese, they are more likely to see themselves that way and are more likely to want to lose weight and to try to lose weight.

The influence of physician acknowledgment of patients' weight status on patient perceptions of overweight and obesity in the United States

Arch Intern Med. 2011 Feb 28;171(4):316-21.

Post RE, Mainous AG 3rd, Gregorie SH, Knoll ME, Diaz VA, Saxena SK

Genetic Testing Can Help Change Behavior

- People who find out they have high genetic risk for cardiovascular disease are more likely to change their diet and exercise patterns than are those who learn they have a high risk from family history, according to preliminary research.
- Findings from a personalized medicine study at the Coriell Institute for Medical Research, a non-profit research institute based in Camden, NJ

Genetic Customization:

The Future of Fat Loss & Weight Management

- Of 452 randomly selected adults in Germany, 45% of respondents claimed they would participate in genetic risk profiling in order to receive personalized nutrition advice and functional food products adapted to their individual nutrigenetic profile.

Test, Don't Guess