WEIGHT MANAGEMENT GENETIC PANEL
Healthcare Professional Information

Obesity – having an excess of body fat – has become a worldwide epidemic; rates having doubled since 1980. In 2008, according to the World Health Organization, over 1.4 billion adults ages 20 and older were overweight; of these individuals about 500 million were obese. Furthermore, obesity is rising among children, with 40 million young people under age five being overweight in 2011.[1]

While many people know the risks of obesity, this has not impacted their ability to successfully lose weight. When it comes to losing weight and keeping it off for a healthy lifestyle, every person is different. The Kashi Health Weight Management Panel allows the patient to receive a personalized weight loss program including preferred food ratios, exercise, and lifestyle recommendations tailored to their own genetic makeup.

Clinical Utility:

Diet and exercise programs are critical to weight management success. However, with an abundance of plans to choose from the trial and error period can lead to frustration. For many, a personalized weight management program tailored to their own genetic code can make a significant impact.

In-depth research efforts have discovered that each person's genetic background may also influence which type of weight management program is the most likely to be effective for them. The Weight Management Panel uses the latest findings in scientific research to inform patients about how their specific genes influence their body weight and, perhaps more importantly, which types of weight management strategies are the most likely to be effective considering their specific genetic background.

What is Included in the Panel?

The genes chosen for the panel are based on identification of SNPs (single nucleotide polymorphisms) that have been shown to correlate with weight gain and obesity, including:

- **FTO mutation –** A variant of the human fat mass and obesity associated (FTO) gene, which was first discovered in 2007, is one of the strongest genetic risk factors for obesity.[2, 3] The pivotal Frayling et al. 2007 study found an additive association between BMI and the FTO risk allele in 38,759 participants. It was determined that adults who were homozygous for the risk allele weighed an average of 3 kilograms more and had a 1.7-fold increased risk of developing obesity when compared with those not carrying a risk allele.[2] The association between the FTO risk allele and obesity has also been confirmed in multiple populations of differing ethnicities.[3-4]

IDEAL CANDIDATES ARE PATIENTS WITH THE FOLLOWING SYMPTOMS AND COMPLAINTS:

- Poor Results from Previous Dietary Changes
- Frequent Cravings and Overeating
- Sedentary Lifestyle
- Persistent Weight Gain
- High BMI (>25)
- Weight Gain in the Stomach, Hips and Thighs

HOW ARE TEST CATEGORIES SELECTED?

Kashi Clinical Lab is extremely selective when creating its unique weight management genetic panel. Doctoral-lev- el scientists carefully research each genetic marker to ensure that only the most informative genetic markers with a well-established impact on health are included. Selection of each marker is based on the following criteria:

1. A reported connection with body mass index in a nationally-recognized peer-reviewed journal;
2. An established connection with metabolism, fat storage, nutrient absorption, or other physiologically important affiliation with weight management;
3. The variant allele of each marker is present in at least 10 percent of the population or is associated with a medical implication that has been well-established by the scientific community;
4. Evidence of the marker being associated with a health outcome in multiple publications and in individuals of varying ethnicities.

- **MC4R mutation –** The Melanocortin 4 receptor (MC4R) is a g protein-coupled receptor that is highly expressed in the hypothalamus. Upon stimulation by melanocortin hormones, MC4R acts on hypothalamic effector nuclei to trigger neural pathways that ultimately lead to the suppression of nutrient intake and the enhancement of me- tabolism.[5] Carriers of this variant allele are more likely to have difficulty suppressing their appetite and limiting excessive snacking behavior. The body of literature regard- ing this gene variant leaves little room for doubt that carriers of the MC4R variant allele are more likely to develop obesity.

- **FABP2 mutation –** Fatty Acid Binding Protein 2 (FABP2) is an intracellular protein found within cells of the small intestine, which aids in fat trafficking and absorption.[6] The risk allele causes its binding affinity for both long-chain saturated and unsaturated fatty acids to increase by two-fold.[7] Clinical studies examining the effects of this SNP in subjects consuming a diet high in saturated fat found that carriers of the risk allele had increased fasting plasma glucose and lipid concentrations when compared to non-carriers.[8] This hyperlipidemia could consequently impair the rate of insulin-stimulated glucose uptake by cells, thereby increasing fasting insulin concentrations and the likelihood of developing insulin resistance. Increased absorption of dietary fatty acids due to this variation is a potential contributor to the development of obesity and obesity-related ailments such as cardiovascular disease and diabetes.[8, 9]

- **ADRB2 mutation –** Beta adrenergic receptors are trans-membrane proteins that are activated by catecholamine hormones to direct the physiological response to stress. A growing body of research suggests that mutations in the genes that code for these receptors may be important risk factors for the development of obesity, and may affect how an individual's weight changes in response to exercise[10] or a carbohydrate rich diet.[11]

- **SH2B1 mutation –** The SH2B adapter protein 1 (SH2B1) has been identified as a positive regulator of insulin, IGF–1 and leptin action.[12] It is well known that insulin's primary role is to regulate glucose and lipid metabolism. SH2B1 deletion results in marked insulin and leptin resistance, obesity, and type 2 diabetes in mice as well as humans, indicating that SH2B1is required for the maintenance of normal body weight, insulin sensitivity, and glucose metabolism.[13] In addition, it has been consistently demonstrated that SNPs in the SH2B1 gene are associated with obesity and/or BMI. The association of increased BMI with SH2B1 risk alleles has been robustly replicated in several large studies of individuals of various ethnicities.[14]

Method:

Kashi Clinical Laboratories utilizes a variety of molecular biology techniques including Luminex, Real-Time PCR, Sanger Sequencing, and Next Generation Sequencing.

Tying it all Together

The Weight Management Genetic Panel includes current health statistics matched with personalized goals, a weight management genetic profile, as well as dietary and exercise recommendations tailored to the patient. Your patient's individ- ualized weight management plan is guaranteed to be delivered within five business days of specimen receipt.

References:

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