MOLECULAR ANALYSIS, PREDICTIVE GENOMICS & DNA PROFILING

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ABSTRACT

Molecular Analyses provides Predictive Genomics and DNA Profiling services [human and non-human] as well as research & development in Genomics & Genetics. Employed platforms include MLPA DNA-microchip, DNA-MAP Microsphere, Real-Time PCR and Fluorescence Capillary DNA Electrophoresis for high throughput DNA sequencing and genotyping. Molecular Analyses is pursuing highest quality standards as certified by international ISO 18125 accreditation.

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PREDICTIVE GENOMICS

DNA holds information about the biological past, present, and future. DNA variations that predict one's predisposition towards many serious - and often preventable - common diseases and allow doctors to modify gene expression through precise, targeted, individualized interventions. Molecular Analyses provides Predictive Genomic services to consumers, health care professionals, physicians, medical professionals, hospitals and clinics. The personalized & individualized genetic information is essential knowledge for individuals to take responsibility for their own health and well-being.

By harnessing the ingenuity of new breakthroughs in genomic science with the power of preventive biomedicine, Predictive Genomics offers an innovative, advanced health care model for more effectively preventing and treating chronic disease.

Predictive genomic profiles assess genetic variations in each person that, when combined with modifiable factors in the environment, may increase disease risk. This empowers physicians and patients to realize:

- Earlier, more effective preventive interventions-years before disease develops
- Precise, customized therapies that truly address each individual's needs
- Improved clinical insight into patients with treatment-resistant "chronic" conditions

Predictive Genomics provide a previously unseen glimpse into each person's potential health future, assessing their genetic susceptibility to conditions such as heart disease, osteoporosis, chemical sensitivity, adverse drug reactions, allergies, and immune disorders. Evaluation of selected sections of the patient's genetic "blueprint," a carefully targeted, customized health care plan to help reduce disease risk even before pre-disease imbalances become apparent.

PREDICTIVE GENOMICS – HEALTH. HEART & CARDIOVASCULAR DISEASE - SALT SENSITIVE HYPERTENSION

Genetic screen for variants in genes that determine genetic predisposition to heart disease as compared to that of the general population. These genes are involved in biological processes that among others relate to:

- Metabolism of Folic Acid, Vitamin B Complex, Homocysteine, Lipids and Cholesterol
- Blood Pressure regulation
- Salt Sensitive Hypertension

Osteoporosis

The genetic screening evaluates genetic variations, that influence how bone tissue is formed and broken down in the body. These genetic variations influence how an individual utilizes key nutrients such as calcium or vitamin D in the bone-building process. The genetic screen indicate if an individual will respond better to Vitamin D or calcitonin or Fosomax to improve bone mass.

Genetic screen for variants in genes associated with the body's ability to maintain strong, healthy bones as we age as compared to that of the general population. It identifies individuals who need more than the standard guidelines to prevent osteoporosis and it is especially important for women. These genes are involved in biological processes that among others relate to:

- Bone formation (collagen synthesis)
- Bone breakdown (resorption)
- Bone recycling

- Calcium & Vitamin D3 metabolism
- Inflammation

Insulin Resistance – Diabetes Mellitus

Insulin resistance is the condition in which normal amounts of insulin are inadequate to produce a normal insulin response from fat, muscle and liver cells which is essential to lower blood glucose [blood sugar]. Insulin resistance in fat cells results in break down of stored triglycerides, which elevates free fatty acids in the blood plasma. Insulin resistance in muscle reduces the uptake of glucose whereas insulin resistance in liver reduces glucose storage; both elevate blood glucose. High plasma levels of insulin and glucose due to insulin resistance lead to the metabolic syndrome and Diabetes Mellitus Type 2

Genetic screen for variants in genes to determine genetic predisposition to Insulin Resistance as compared to that of the general population. These genes are involved in biological processes that among others relate to:

- Fat metabolism
- Blood pressure regulation
- Inflammation

Antioxidation & Detoxification – Inflammation

Anti-Oxidation relates to the body's defense mechanism to prevent formation of free radical molecules and their elimination when formed. Free radical molecules cause tissue and cellular damage as well as cellular aging and death under many circumstances, including radiation, damage from environment chemicals and the aging process. Detoxification relates to the body's mechanism to eliminate harmful chemicals we come in contact with in our daily life such as Xenobiotics, Carcinogens, Mutagens, Synthetic Allomethanes, Hydrophobic and Electrophilic elements as well as Industrial Chemicals.

Genetic screen for variants in genes to determine the body's Anti-Oxidation and Detoxification abilities. These genes are involved in biological processes that among others relate to:

- Anti-Oxidation
- Free radical defense
- DNA Damage & Repair
- Detoxification
- Reaction to environmental insults such as Xenobiotics, Carcinogens, Mutagens, Allomethanes & Industrial Chemicals

CoQ10 is a powerful antioxidant known to be very important to cardiovascular health, neuronal health, skin health as well as functioning in the protection against environmental toxins. CoQ10 changes are increasingly associated with "metabolic syndrome," an important clustering of conditions that are powerful determinants of cardiovascular disease and diabetes.

The CoQ10 Efficiency Assessment is designed to determine which form of CoQ10 an individual is able to efficiently use. The fully oxidized form of COQ10 called (ubiquinone) or the active form of CoQ10 called (ubiquinol). Many people (approximately 30% of the population) may not be able to efficiently use the more popular form of CoQ10 (Ubiqionone) and would likely benefit from utilizing the Ubiquinol, the active form of the antioxidant.

Thrombosis, Embolism & Hemochromatosis

Thrombosis is the formation of a blood clot (thrombus) inside a blood vessel, obstructing the flow of blood through the circulatory system. Thromboembolism is a general term describing both thrombosis and its main complication which is embolization. Embolism occurs when a blood clot cause blockage of a blood vessel with very serious consequences when they occur in the so-called "end-circulation": areas of the body that have no redundant blood supply, such as the brain, heart, and lungs. The specific genes investigated are associated with increased predisposition to form blood clots and decreased ability to dissolve them when they are formed.

Genetic screen for variants in genes to determine the body's genetic predisposition to Thromboembolism & Hemochromatosis as compared to that of the general population. These genes are involved in biological processes that among others relate to:

- Blood clot formation
- Ability to resolve blood clots when formed
- Iron storage

Hemochromatosis is an inherited iron overload disease that causes the body to absorb and store excessive amounts of iron. Iron is stored as ferritin that breaks down to Hemosiderin, which is toxic to tissues. The excess

iron builds up in organs and damages them, especially the liver, heart and pancreas. Without treatment the disease can cause organ failure. Individuals with mutations in the HFE-HHC gene can not reduce iron absorption in response to increased iron levels in the body which results in an increased iron load.

Breast, Prostate & Colon cancer

Breast cancer: is cancer that forms in tissues of the breast, usually the ducts (tubes that carry milk to the nipple) and lobules (glands that make milk). It occurs in both men and women, although breast cancer in males is not as frequent as in females. Genetic screen for variants in genes to determine the body's genetic predisposition to breast cancer as compared to the general population. These genes are involved in biological processes that among others relate to:

- Programmed cell death
- Regulation of the cell cycle
- Tumor suppression

Prostate cancer develops most frequently in men over fifty years of age. It is a cancer that forms in tissues of the prostate gland, which is in the male reproductive system found below the bladder and in front of the rectum. This cancer can occur only in men, as the prostate is exclusively of the male reproductive tract. Rates of prostate cancer vary widely across the world. According to the American Cancer Society, prostate cancer is least common among Asian men and most common among black men with figures for European men in-between. Many factors, including genetics and diet, have been implicated in the development of prostate cancer.

Genetic screen for variants in genes to determine the body's genetic predisposition to prostate cancer as compared to the general population. These genes are involved in biological processes that among others relate to:

- Steroidogenic pathways
- Activation of gene transcription
- Growth and development pathways

Colorectal cancer, also called colon cancer or bowel cancer, includes cancerous growths in the colon, rectum and appendix. It is the third most common form of cancer and the second leading cause of death from cancer in the Western world. Genetic screen for variants in genes to determine the body's genetic predisposition to colon cancer as compared to the general population. These genes are involved in biological processes that among others relate to:

- Programmed cell death
- Regulation of the cell cycle
- Glutathione reduction

Alzheimer's disease

Alzheimer's disease is the most common cause of dementia among the aging population. It affects parts of the brain that control thought, memory, and language. Alzheimer's damages a person's ability to reason, remember, speak, perform simple calculations, and carry out routine tasks. Over time, patients also may become anxious or aggressive or wander away from home. In the later stages, they may forget how to do basic tasks, like brushing their teeth or dressing themselves. Eventually, patients need total care. Genetic screen for variants in genes to determine the body's genetic predisposition to Alzheimer's disease, as compared to the general population. These genes are involved in biological processes that among others relate to:

- Transmission of signals throughout the central nervous system
- Regulation of gluconeogenesis
- Intracellular signaling

PREDICTIVE GENOMICS – WELL BEING

DermaGenomics – Skin Health

Variations in key skin aging genes that are extremely important to the skin's overall health and appearance. Specifically the genetic propensity for Collagen breakdown; Photo aging; Skin wrinkling; Skin slacking; Mild irritation; and skin's ability to tolerate Environmental pollutants.

The presence of one or more gene variations (SNPs) causes the gene product –the protein- related to that skin health area is functioning less than optimally. Using this genetic information the skin care products can be custom formulated with genetically selected active ingredients (SNPActives) chosen through clinical studies for their ability to help compensate for any disadvantaged genes. The skin care products one would need to utilize should be customized, individualized and personalized to meet the individual genetically determined skin health needs. Alternatively, the information can be utilized to guide for the selection of a suitable commercially availablebeauty product based on the specific individual needs.

Caffeine – Wine Metabolomics

Caffeine is a widely consumed compound that acts as a central nervous system (CNS) stimulant temporarily reducing fatigue, restoring alertness, increasing focus, and elevating mood. Long-term effects of caffeine can include fatigue, anxiety, increased blood pressure, tachycardia, and disrupted sleep pattern. The genetic based Caffeine Test will determine if an individual has the "fast" or "slow" caffeine metabolizing gene. It is important to know how the individual's body processes caffeine as a "slow" metabolizer of caffeine is at a higher risk of a nonfatal heart attack compared to a person who metabolizes caffeine rapidly. Caffeine has also been linked to increased risk of miscarriages and decreased fertility in women who are "slow" metabolizers of caffeine. Knowledge of the genetic make-up, one can adjust the daily caffeine intake [coffee, tea, chocolate, cold medicine] accordingly and manage the over-all well-being.

Wine is a widely consumed product that has been found to aggravate certain physical conditions and illnesses as well as provide certain beneficial effects such as the lowering of cholesterol levels. The problem lies in knowing just how much alcohol (wine) consumption is enough? The answer lies in the DNA. Based on gene variations, drinking moderately can lower cholesterol levels and risk of heart attacks.

Reward Deficiency Syndrome [Feedback/Response Mechanisms]

A number of hormones, secreted by adipocytes, play a pivotal role in the control of body weight. Thus, certain mutations in these hormones were found to contribute to human obesity. The answer to why you may be gaining weight do lie in the DNA. Based on genes variations, the feedback/response mechanism gene determinesthe genetic predisposition to weight gain as compared to that of the general population

Obesity

Over 300 million people from all over the world are considered to be obese, while four to ten individuals exceed their normal weight by 14 kilos. Worldwide almost 50% of the adults (especially women) in developed countries are overweight. High Body Mass Index (BMI), is considered to be a major risk factor for many chronic diseases such as cardiovascular diseases, diabetes mellitus type 2, muscoskeletal disorders (especially osteoarthritis), sleep apnea and certain types of cancers (endometrial, breast and colon). One's genetic profile modulates weight at approximately 40-70%. Genes affect the amount of fat the body stores, where it is distributed as well as how easy the human body converts fat to energy, by burning calories. The Obesity Predisposition Gene Test investigates the genetic predisposition to obesity as compared to the general population.

Athletic Performance [Strength, Duration, Elitism]

Athletic performance is influenced by a number of factors including genetics, environment, psychology, training, coaching and nutrition. The Athletic Performance Gene screen offers information about an individual's genetic contribution to the athletic performance. Some gene variants result in a predisposition to excel at endurance sports (medium/long distance running), while other gene variants predispose to an individual to excel at sprinting or power activities (weight lifting).

The Athletic Performance Gene Test investigates the genetic predisposition to specific athletic achievements. Thus, knowing which gene variants one carries will help determine which type of sport and event one may be most likely to succeed, develop a training program best suited for the specific needs and achieve the full athletic potential. It also examines genes variants that are only found in elite athletes that can indicate an individuals potential to become an elite athlete.

PHARMACOGENOMICS

Inherited variations in genes that dictate drug response and explores the ways these variations can be used to predict whether a patient will have a good, a bad or no response at all to a drug. When it comes to medicines, one size rarely fits all. Many variables influence how efficient a medication can be, including the genes. Genes screened metabolize more than half of all prescribed drugs — including some antidepressants, beta blockers, anti-diabetics, anti-ulcer/reflux medications and pain relievers. Other genes included in the screening influence efficiency of medications utilized in treatment of Hypertension, Tuberculosis and Cancer Management.

In the US , about 15% of Caucasian and 20% of African-American asthma sufferers receive no benefit from using their daily inhaler containing albuterol, salbutamol or salmeterol. These individuals have a unique genetic variation in their ADRB2 gene. Several studies have found that individuals with the Arg/Arg genetic variable in their ADRB2 gene actually improved their asthma symptoms when they stopped using inhalers containing the above medications.

Knowing the genotype at the ADRB2 gene will help the physician personalize asthma treatment to make it more effective and less costly than trying several medications that may not be efficient.

DNA PROFILING

Human

· **Fetal Sex Determination**

From Maternal blood from the 7th week of pregnancy onwards. From the earliest stages of a normal pregnancy, small amounts of DNA from an unborn fetus are able to find their way into the mothers bloodstream. It is possible to determine whether any of the fetal DNA is derived from the Y chromosome - a DNA region that is only present in males. If this DNA can be detected in the mothers blood, then she must be carrying a male child. If there is no male DNA present, the child must be female. The techniques used are extremely accurate, with large-scale scientific studies which followed thousands of pregnant women finding that it had a 95% accuracy rate.

· **DNA Fingerprinting**

o Database Creation

§ Criminal, Military, Commercial

o Paternity, Relationship determination, Inheritance management

o Forensics

Non-Human [among others]

· **Genetically Modified Food Determination**

Determination of presence of foreign genes in fruit and vegetables

· **Animal Feed Fingerprinting**

Presence of vertebrate & non-vertebrate animal species in animal feed

· **Fishery Management**

Point of Origin – Traceability – Genetic Heterogeneity

· **Beef Tracing through DNA fingerprinting**

Quality control – quality assurance.

· **Bird Sexing, Canine Fingerprinting, Horse Fingerprinting**

· **Plant fingerprinting**

o **Olive Cultivars**

control oil mixing fraud from foreign oils or cultivars not declared

authenticate olive oil to support Labels of Origin & Preserved Origin

o **Grape Vine**

authenticate wine to support Labels of Origin & Preserved Origin

classify grape vine varieties and relate them to other world varieties

Research & Development

Development of in-house methodologies that will reduce the costs and turnaround times of the services offered while at the same time will increase its quality.

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