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Advancement of
Science, Inc.

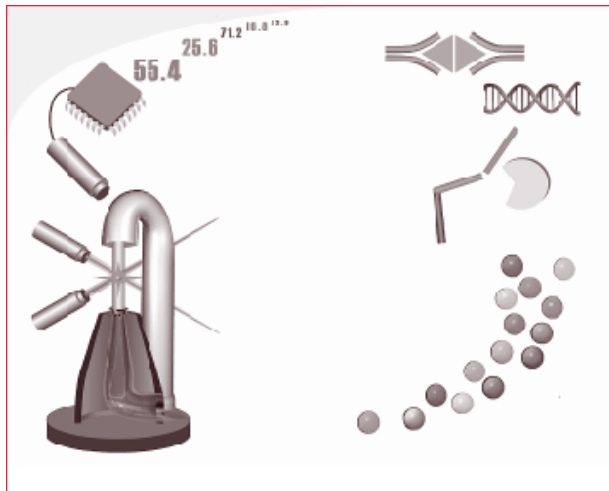
VitalLongevity™

Logo: Life's blood flows through the hourglass; the stopcock represents the alteration of aging and disease as biomedical research progresses.

September 2004

MAPPING THE FUTURE

The discovery in the late 1800s that microbes cause many deadly illnesses sparked a revolution in medical care, ushering in the age of sterile surgical procedures, vaccinations, and antibiotics. Today, a fallout from remarkable new technologies places medicine on the verge of another revolution—comprehensive biomarker testing. Biomarkers, typically blood proteins or lipids, can signal or even predict diseases and are not new; many laboratories joined the quest to find specific disease biomarkers years ago. What is new and exciting is the ability to simultaneously measure hundreds, some day thousands, of biomarkers in a single drop of blood and to do so both quickly and economically. If biomarker testing could reliably predict the diseases in your future, wouldn't you want such testing—especially if early intervention or lifestyle changes could alter the image in the medical crystal ball?



Rules-Based Medicine's MAP technology employs bioassays, dyed microspheres, high speed fluidics, and digital signal processing. Reprinted by permission.

MAP™ (MULTI-ANALYTE-PROFILE)

Driven by the needs of the pharmaceutical industry to improve detection of drug safety problems early in clinical trials and to lower costs, one company, Rules-Based Medicine, Inc., devised a sophisticated assay employing technology from both biology and physics. Using antibodies, dyes, lasers, and computers to detect the presence and concentration of proteins in the blood, the MAP assay measures hundreds of individual biomarkers of, for example, autoimmunity, cancer, infectious diseases, cardiovascular risk, and inflammation. This fall, the company will make its test of 230 biomarkers available to consumers and their physicians, delivering the most comprehensive evaluation of health available. If performed annually, the MAP can not only detect changes indicative of a broad range of diseases but can also chart the 'velocity' of the change, which is often predictive of the severity of a disease. Another company, ProteinLogic, Ltd.,

calls its system a "universal disease diagnostic system"; its first planned use is rapid diagnosis of appendicitis.

Both systems are poised to fundamentally change how diseases are diagnosed and treatments monitored; the pattern or "fingerprint" of the proteins in your blood could alert your physician to problems before they become clinically evident. Much research remains to be done before achieving that level of prognostication; and, of course, preventing illness before it happens (or at least before it progresses) runs counter to the way medicine and health insurance currently work. But now that it is possible to have hundreds of laboratory tests done on one tiny blood specimen, will medical care improve? Two examples might make the case.

DIABETES AND THYROID DISEASE

The future is now for both diabetes and thyroid disease, diseases that remain remarkably underdiagnosed and undertreated but for which biomarkers exist. An estimated 5 million Americans unknowingly suffer from diabetes and many millions more from the predisposing Metabolic Syndrome. The subsequent

complications—including kidney failure, blindness, and heart disease—and their associated costs are astronomical. An insurance company, however, is unlikely to pay for testing unless your doctor detects clinical symptoms.

Preclinical thyroid disease, with its mild and non-specific symptoms, can trigger other medical problems such as elevated cholesterol, fluid retention, and weight gain, and it is particularly dangerous during pregnancy. Some argue against screening non-symptomatic persons, and yet a statewide health fair in Colorado, which tested blood levels of thyroid-stimulating hormone in 26,000 visitors, found that nearly 10% had a previously undetected abnormality. Perhaps you feel confident that your physician would order tests for these conditions if warranted. But could your physician today predict your risk of autoimmune disease or tell you that you have an early, otherwise undetectable, still highly curable tumor? How about an infection that causes no symptoms but that puts you at risk for stomach cancer?

INFECTIOUS DISEASE DETECTION

The discoveries of microbial causes of some cancers, e.g., *Helicobacter pylori*/stomach cancer and Herpes virus human h.8/Kaposi's Sarcoma, and possibly other disorders, e.g., atherosclerosis, prostatitis, and a variety of autoimmune diseases, continue to amaze us. Although most infectious organisms make themselves known in obvious ways, others remain dormant but ready to attack when the immune system falters. The value of MAP for ferreting out latent, symptomless infections as well as the assay's potential utility for rapid diagnosis of life-threatening diseases with non-specific symptoms is incalculable. Future uses of MAP will likely include controlling disease spread in developing countries, ensuring safety of blood transfusions, testing of livestock for mad cow disease, and identifying new, emerging infectious diseases.

AUTOIMMUNE DISEASE PREDICTION

Autoantibodies circulate in the blood and can target your body's own protein; specific autoantibodies characterize each autoimmune disease such as rheumatoid arthritis, lupus, Addison's disease, and Type 1 diabetes. Notoriously difficult to diagnose, especially in the early stages, autoimmune diseases can cause irreversible damage to joints, organs, and other tissues. Some studies suggest that early intervention with immunosuppressive therapy can delay onset, slow the course of, or even prevent full-blown disease. So, should we be looking for biomarkers of these common diseases in presently healthy individuals? Some reports suggest yes. Particularly useful in this regard are studies involving pregnant women; autoantibodies associated with rheumatoid arthritis, postpartum autoimmune thyroid diseases, lupus, and Sjögren's syndrome that show up during pregnancy are highly predictive of subsequent occurrence of these illnesses in the mothers. Also, a study using the US Armed Services Serum Repository showed that autoantibodies specific for lupus can predate

diagnosis by 10 years. Predictive autoantibodies also exist for an autoimmune form of liver cirrhosis, Type 1 diabetes, and Addison's disease, which affects the adrenal glands. Many more prospective studies of large numbers of healthy individuals monitored for development of autoimmune diseases are needed; with MAP technology, hundreds of autoantibodies can be screened simultaneously to establish their predictive values.

CANCER PROFILING

Perhaps the greatest potential for averting misery through biomarker testing lies in the early detection of malignancy. Currently under FDA review, *OvaCheck™*, a diagnostic test for early ovarian cancer, looks for a characteristic pattern of assorted but unidentified proteins that occurs in ovarian cancer patients but not in healthy persons. Theoretically, such profiling could be done for all types of malignancy. In the meantime, the inventory of more specific biomarkers for various cancers will grow, adding to the current list, e.g., prostate specific antigen (PSA) and carcinoembryonic antigen (CEA). Further, levels of cytokines and immune-system biomarkers that help to predict relapse after cancer surgery could prove useful for screening healthy populations; also, levels of growth factors and inhibitors of blood vessel formation could signal an individual's risk of cancer. The war on cancer will more likely be won through early detection than by specific, slow-to-be-discovered cures.

OFAS is currently evaluating comprehensive biomarker testing; future plans include applying biomarker testing in studies of alopecia areata and prostate cancer.

POTENTIAL USES FOR MAP

- Universal disease diagnosis
 - Identification of emerging diseases, e.g., SARS, West Nile Virus
 - Detection of diseases with long preclinical phases
 - Rapid diagnosis of diseases with non-specific symptoms
- Treatment monitoring
- Disease progression monitoring
- Drug safety and efficacy evaluation
- Blood testing before organ transplantation
- Disease prediction and prevention
- Assessment of environmental toxin exposure

The next issue of VitaLongevity will discuss MAPPING THE PRESENT, that is, how to make the most of the laboratory tests available today.

The OFAS VitaLongevity newsletters are designed to alert you to those strategies that are valid, those that are not valid, and new suggestions for making your life as long and healthy as possible.

INFORMATION FOR DONORS

The Orentreich Foundation for the Advancement of Science, Inc., was founded in 1961. OFAS is a non-profit institution dedicated to biomedical research to prevent, halt, or reverse those disorders that decrease the quality or length of life. It is duly registered with the US Internal Revenue Service as an Operating Private Foundation under Section 4942(j)(3).

No accomplishment of OFAS is possible without your encouragement and generous support. Your tax-deductible contribution should be mailed to:
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