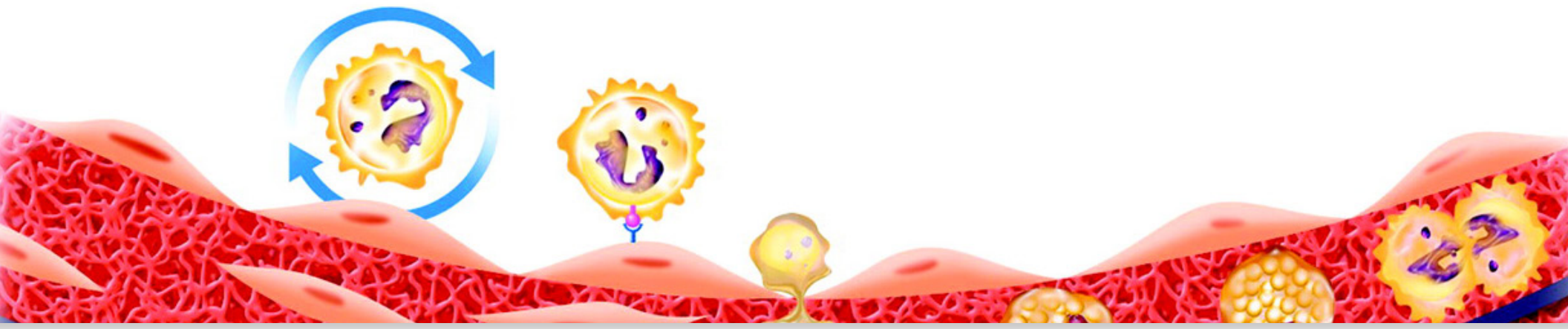


The Pathways Within and the Quest for Answers

From physics to philosophy to fiction, we continue to search for all-encompassing solutions to life's mysteries. Although not designed to address all of medicine's myriad questions, Cytovas's Vascular Health Profile promises sweeping ramifications for the assessment of one's risk of heart attack and stroke.

THE MATTER AT HAND

Cardiovascular disease (CVD) is the leading cause of death in the United States with one person succumbing every 40 seconds. Despite treatment advances and numerous drugs developed to prevent and treat heart attack and stroke, CVD-related deaths are expected to increase during the coming decades, as sufferers of such conditions as obesity, high-blood pressure and diabetes increase. Unfortunately, many people most at risk for heart attack and stroke don't show signs they're ill until it's too late. There is an urgent need for effective cardiovascular diagnostics that can identify asymptomatic people at risk for cardiovascular events, stratify symptomatic patients' risk, evaluate efficacy of preventive therapies, and evaluate potential cardiovascular side effects earlier during drug development.

THE ORIGIN OF VASCULAR HEALTH AND DISEASE

Just as bumps and potholes in the road create hazards for motorists, atherosclerosis, the source of cardiovascular events like heart attack and stroke, creates bumps and potholes in the lining of blood vessels. Sometimes called "hardening" of the arteries, atherosclerosis is the buildup of cholesterol, fatty, and inflammatory deposits, known as plaque, beneath the lining (endothelium) of artery walls. These plaques restrict blood flow and sometimes even rupture, leading to a clotting cascade that can completely block the artery, compromising the cardiovascular system's ability to convey oxygen and nutrients to the entire body.

CURRENT DIAGNOSTICS FALL SHORT

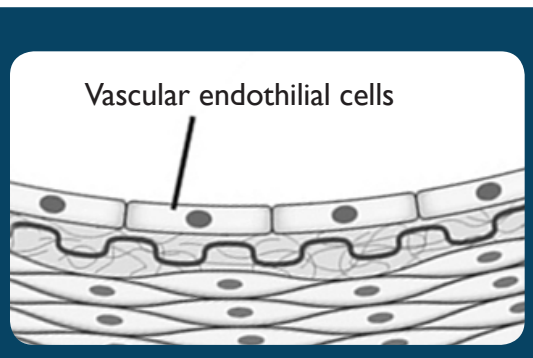
For people with a low or intermediate risk of CVD, available imaging tests, such as chest X-ray, ultrasound, CT angiography, MR angiography, and arteriography involve exposure to radiation or are too expensive to use as routine monitoring tools. Also, they don't identify unstable arterial plaque or determine who is most at risk for a cardiovascular event. As a result, about two-thirds of women and 25 percent of men with substantial atherosclerosis are missed. That is because 20 percent of all vascular events occur in the absence of such conventional risk factors as high blood pressure, smoking, diabetes and high cholesterol. Indeed, 50 percent of such events occur in the absence of significant lipid abnormalities such as high LDL (bad) cholesterol or high triglycerides (fats).

Today, the only way to determine that a patient with no observable symptoms is at risk from CVD is after the fact, when they suffer a heart attack or stroke, even while undergoing such preventive measures as monitored diet and exercise programs, not to mention actual blood pressure or cholesterol drugs. To prevent death and morbidity from CVD, we have to be able to identify asymptomatic patients who could be candidates for intensive, evidence-based interventions that reduce CVD risk, and to monitor effectiveness of preventive treatments chosen for them.

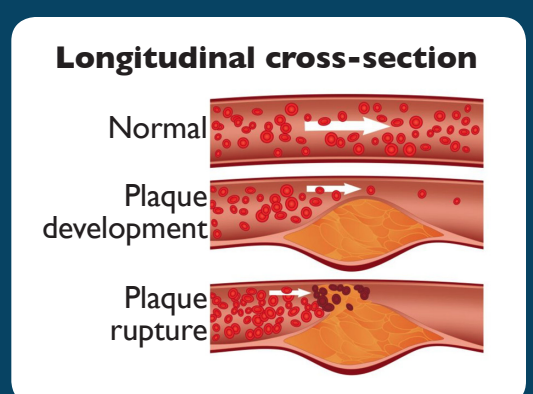
ENTER THE CYTOVAS SOLUTION

Two cellular "markers" may have the potential to assess the health of the endothelial cells lining blood vessels–circulating **endothelial progenitor cells** (EPCs), the reparative vascular stem cells from the bone marrow, and circulating **microparticles** (MPs) from the breakdown of the endothelial vascular lining cells, inflammatory white blood cells, and platelets (a circulating blood component that initates clotting). Studies show that high circulating levels of EPCs have a direct correlation with decreased vascular complications. High circulating levels of MPs, on the other hand, suggest significant numbers of damaged endothelial cells that contribute to inflammation and intravascular blood-clot formation.

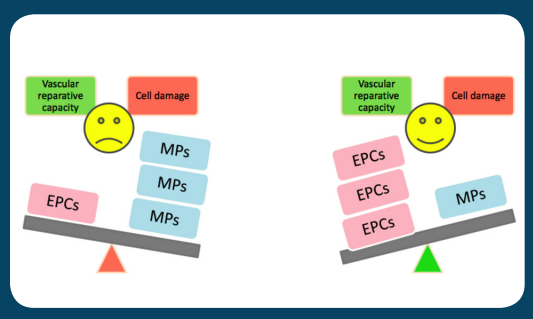
High-throughput flow cytometry is a lab technique that identifies and counts the numbers of different cell and particle types in the blood at the rate of hundreds of thousands of cells and particles per second, as they stream through multiple beams of laser light. CytoVas's technology processes the many megabytes of high-throughput flow cytometry data, collected from a tube of blood, in real time, using advanced computer algorithms, identifying multiple ratios of EPCs to MPs, and creating a cytometric fingerprint, called the VASCULAR HEALTH PROFILE (VHP). The VHP can provide accurate assessment of the integrity of the vascular endothelium. Because the vascular endothelial cell lining is, in essence, "where the rubber meets the road" in atherosclerosis, the VHP,



Vascular endothelial cells form the smooth pavement of blood vessels, and are the ones affected by atherosclerosis (hardening of the arteries).

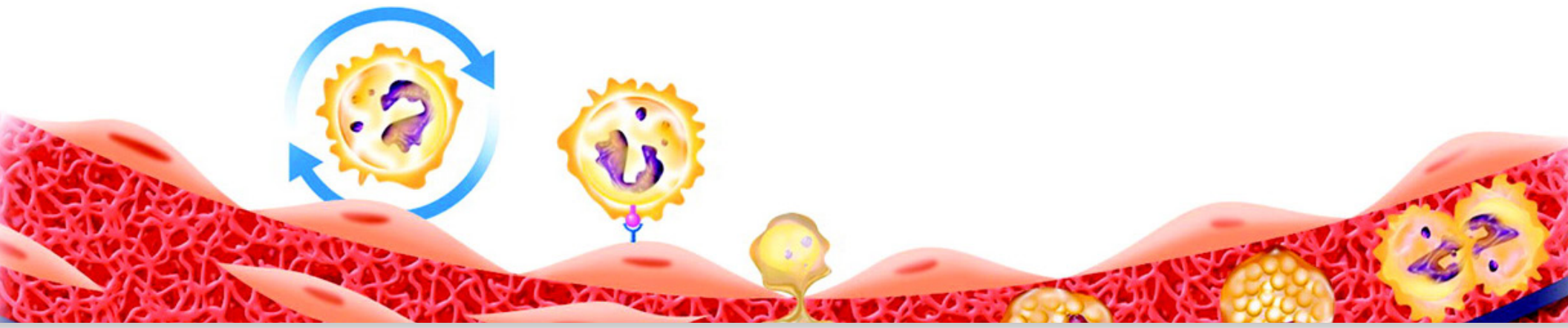


Current diagnostics cannot always reliably detect atherosclerosis until endothelial plaque rupture causes heart attack or stroke.



Cytovas's VASCULAR HEALTH PROFILE is a fingerprint of vascular health based on ratios between bone marrow stem cells (EPCs) and endothelial breakdown debris (MPs).

CytoVas is able to identify cell-surface markers to create a *cytometric fingerprint,* forming an accurate measurement of a person's vascular health.



therefore, is a perfect snapshot of the precise state of an individual's vascular health at any point in time. The VHP product consists of a sample preparation reagent kit, a custom laser/detector instrument, and a proprietary computational software algorithm. Unlike most cytometric analyses, the VHP is highly reproducible, because it involves no human component in the result.

THE GAME CHANGER

Not only does the VHP offer the potential to identify nonsmoking marathon runners with normal blood pressure, cholesterol, and blood sugar, who are still at risk of keeling over dead during their next race—the "Holy Grail" of cardiology—it could also assess the success or failure of preventive therapy chosen to prevent such an event. Right now doctors can only find out preventive therapy failed when a treated patient still suffers a catastrophic heart attack or stroke. But this is only part of the implications of the game-changing impact VHP technology offers.

Most cardiovascular clinical trials are outcomes trials, where thousands of participants must be followed for long periods of time, to determine the actual outcome resulting from a new drug or device. CytoVas's Vascular Health Profile could, in the future, become a "surrogate endpoint" for predicting outcomes, thereby vastly shortening the process of developing drugs for cardiovascular applications. For example, while testing a new cholesterol-lowering drug, rather than having to wait for such long-term results as incidence of heart attacks or strokes over several years across the study population, Cytovas's Vascular Health Profile could be used to gauge the drug's effect on individual study patients at any point in time, as well as how long the drug takes to work.

But that's not all … The technology platform on which the VHP is based could also be adapted for other uses, for example, detection of cancer and the efficacy of treatment chosen early on.

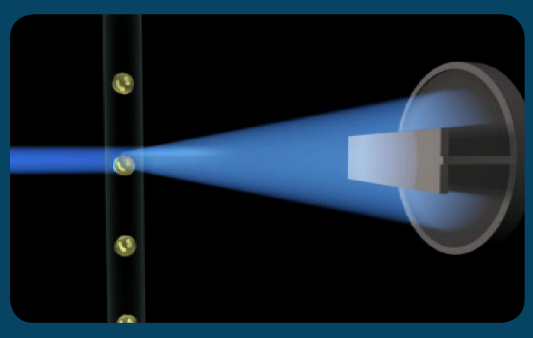
ACCELERATING THE JOURNEY FROM BENCH TO BEDSIDE

CytoVas recently completed a pilot study successfully demonstrating its VHP could be useful in identifying asymptomatic diabetic patients with no symptoms, but at high risk for vascular events.

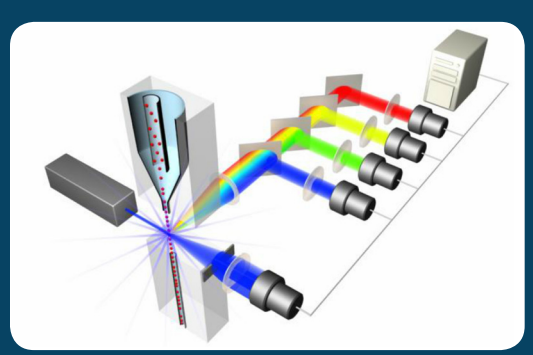
American Heart Association's Science & Technology Accelerator's investment is funding a clinical trial to demonstrate the VHP can not only identify asymptomatic people at high cardiovascular risk, it can also determine the effectiveness of preventive therapy. From there, Cytovas should easily be able to attract private equity and/or industry investment to conduct the trials necessary for the VHP to become as standard a part of everyone's yearly lab profile as measurement of blood pressure, fasting glucose, and cholesterol.

IN SUMMARY

Using a single vial of blood, the Vascular Health Profile can accurately determine a person's vascular health. It would be a challenge to overstate the enormous value of the information provided by Cytovas's blood test.



During flow cytometry, a laser strikes MPs and EPCs, sending scattered light data to a detector.



CytoVas's unique and patented technology then uses software analysis to process the data and create the Vascular Health Profile.

THE CYTOVAS TEAM

Emile R. Mohler III, MD, FACC/Co-Founder

Professor of Medicine; Director, Division of Vascular Medicine and Biology, Perelman School of Medicine at the University of Pennsylvania

Dr. Mohler also holds appointments at the Perelman School of Medicine's Cardiovascular Institute, its Institute for Translational Medicine and Therapeutics and its Institute for Diabetes, Obesity and Metabolism. He is certified by the American Board of Internal Medicine, the American Board of Cardiovascular Disease and the American Board of Vascular Medicine, and has been primary or coauthor of several hundred publications, as well as author of five books on vascular medicine. Dr. Mohler holds a patent in Optical Measurement of Tissue Blood Flow Hemodynamics Oxygenation.

Jonni S. Moore, PhD/Co-Founder

Professor of Pathology and Laboratory Medicine; Director, Clinical & Research Flow Cytometry; and Director, Abramson Cancer Center Flow Cytometry and Cell Sorting Resource Laboratory, Perelman School of Medicine at the University of Pennsylvania

Dr. Moore has more than 25 years of experience in clinical laboratory pathology and immunology. One of the world's leading experts in cytometry, she holds several patents in the field. Dr. Moore's work as a scientist and mentor has been distinguished by numerous awards, most recently the Peter C. Nowell teaching award, the FOCUS award for the advancement of women in medicine and the David B.P. Goodman award in pathology and laboratory medicine. She developed many of the flow cytometry applications used in her research.

Wade Rogers, PhD/Co-Founder

Director, Computational Biology and Research Informatics at Path BioResource; Adjunct Associate Professor of Pathology and Laboratory Medicine at the Perelman School of Medicine at the University of Pennsylvania

Dr. Rogers holds a Master's degree in engineering, and a PhD in physics. After beginning his career at the National Bureau of Standards, he held positions at DuPont Pharmaceuticals, Bristol-Myers Squibb and Cira Discovery Sciences. Dr. Rogers combines pharmaceutical industry and academic research experience and is an internationally recognized expert in the relatively new field of computational biology, with many peer-reviewed publications and five patents to his name.

Todd Johnson, MBA, MD/President

Dr. Johnson has nearly 20 years of experience in the life sciences industry, and also serves as a Venture Partner at Ampersand Ventures, a leading Boston-area life science investor. Most recently, he was VP, Global Marketing for Abbott Labs' Pharmaceutical Pipeline products. Prior to that, he led Early Stage Development for MDS Pharma Services, which he sold to Bain Capital and SV Life Sciences. Before MDS, Dr. Johnson spent five years as a consultant with McKinsey & Company. He previously served as CEO of Tangerine Technologies, a provider of drug discovery software and as a basic science researcher at the Dana-Farber Cancer Institute.