Continuous Health Monitoring and Early Disease Detection

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Summary: Overview: It is clear that the current practice of using increasingly sophisticated and expensive methods to treat patients that present with serious illness cannot be sustained. Moving from a reactive to proactive healthcare system is critically dependent on the ability to diagnose and treat disease early in its progression – to maintain health through continuous measurement and relatively minor adjustments rather than attempting to fix a system that is on the verge of failure. The diagnostic community has paid lipservice to the concept of early diagnosis for the last 20 years with little to show for it. This is because the mindset has been to search for the presence of primary biomarkers of disease – the molecules directly and uniquely produced by the disease itself – but these are present in such small quantities that current detection techniques are far too insensitive, and too nonspecific, to accomplish the task. For early diagnosis this has been a fundamentally flawed approach. Nature solved this problem by developing the immune system: a highly amplified system that continuously looks for changes in the molecular and cellular make-up of the body. Interestingly, the immune system detects far more things than it can actually correct. If we could read this information, we would be able to intervene in those cases where the body's defenses prove inadequate.

Immunosignatures: Stephen Albert Johnston, co-director of the Center for Innovations in Medicine (CIM) in the Biodesign Institute at Arizona State University invented a clever, simple and inexpensive method for reading the antibody profile of a person. He and his colleagues in CIM and has shown that this profile, named *immunosignature,* can serve as a highly sensitive and specific indicator of health status. The B-cells that produce the antibodies are constantly patrolling the body. When they encounter an aberrant protein, cell or foreign pathogen they are activated and amplify their response 10^{11} fold in one week. Using this natural difference amplification system is probably the most practical method to accomplish early disease detection. Like many truly new approaches, the immunosignaturing concept initially met with considerable skepticism. There were seemingly legitimate concerns that such an approach would only pick up general responses, such as inflammation, and would provide little, if any, specific information useful in diagnosis and treatment. However, for reasons that are themselves of fundamental interest to our understanding of immunology, these fears were unfounded, and specific immunosignatures have been identified for over 20 specific diseases including valley fever, brain cancer, breast cancer and Alzheimer's.

The elegance of immunosignaturing is its simplicity. The antibody profile of a person can be displayed on an array of random peptides. In other words, a single device – a single diagnostic test – has the potential to be a comprehensive diagnostic system. Because this approach is aimed at profiling the entire distribution of antibodies, rather than specifically detecting a particular biomarker, the same, simple, inexpensive array can be used for diagnosing essentially any disease. Further, it naturally takes into account the heterogeneity of the human population because it uses pattern recognition coupled to

time-dependent changes in an individual, rather than binary signal levels in a one-time measurement, to detect and identify disease.

The ultimate vision for this technology is to allow the continuous monitoring of everyone's health. To accomplish this vision we recognized that it would ultimately be necessary to perform millions if not billions of diagnostic assays per year. CIM therefore worked with experts in the peptide synthesis and the electronics fabrication industry, to merge these two technologies, recently demonstrating the ability to produce immunosignature peptide arrays at densities that dramatically reduce cost and increase production scale and will ultimately allow the direct integration of this powerful molecular diagnostic technology with sophisticated electronic circuitry, further empowering the approach. Finally, CIM has shown that the method requires only microliters of blood with no sample preparation other than dilution, and that small blood samples can be accurately analyzed even if they are dried onto filter paper and sent to a central lab through the mail. To ensure rapid translation of this technology into useful practice, Johnston and Professor Neal Woodbury founded a company, HealthTell, which has set up to produce these peptide-chips and develop their application.

Value proposition:

CIM scientists and collaborators have invested 7 years of time and funds to bring this concept to reality. It is a robust platform that can be applied in any number of clinical opportunities. Strong ties to the DoD for use in infectious disease have been established and a company, HealthTell, formed.

Collaboration objectives:

For further development of the technology itself, collaborators in chemistry, engineering, informatics, signal processing and immunology are important. Collaborators with particular disease expertise and experience in clinical trials are of interest.

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