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Solvent interaction analysis: A new approach to structure-focused clinical proteomics

T is well known that a disease process is commonly associated with changes in protein structure or protein-protein interaction. These changes are under-utilized in clinical practice. In complex diseases such as cancer, structural changes in proteins within the tumor cells are vast, ranging from alternative splicing to post-translational modifications and can be used as highly efficacious markers for clinical diagnostics. The lack of robust low-cost technologies to evaluate structural changes in proteins, however, precludes the use of these changes in clinical diagnostics. Hence protein biomarkers are defined solely based on changes in their relative expression. We present a new hypothesis-free technology based on the firm physicochemical principles enabling one to discover, develop and apply new structural protein biomarkers directly in circulating biofluids. These biomarkers are defined via changes in protein structure instead of variations in protein amounts. Solvent Interaction Analysis (SIA) is a novel technology that could be combined with many downstream conventional proteomics and clinicallevel instruments. The method is based on analytical application of protein partitioning in aqueous two-phase systems which is highly sensitive to changes in protein structure and protein-partner interactions. The technique is simple, low-cost and can be conducted manually or with conventional lab automation. The technology can be used for discovery of single protein markers using ELISA or for finding multiplexed biomarkers by interfacing with downstream multiplexed bead-based assays or for label-free discovery of structure-based biomarkers using mass spectrometry. We demonstrate the utility of the SIA technology as basic tool for clinical diagnostics and discuss a recently introduced assay that monitors changes in the structure of Prostate-Specific Antigen (PSA) for prostate cancer diagnosis instead of evaluating the PSA amounts in serum. We illustrate the assay development, clinical performance results vs. gold-standard assays and commercial implementation. Finally, we discuss the future of structure-based approaches to protein biomarkers as a basis for high performance clinical-grade protein biomarkers.

Biography

Boris Zaslavsky graduated in Analytical Chemistry from the Moscow State University. He holds a PhD and a DSc (USSR Academy of Sciences), was a scientist at USSR Academy of Sciences (1971-1991), Visiting Fellow at Cornell University Medical School (NYC, 1991-1992), and KV Pharmaceuticals (1993-1994), Argonne National Laboratory (1994-1995). He is the founder of Analiza, Inc. (1996-present) and Cleveland Diagnostics (2014-present), where serves as a Chief Scientific Officer. He published 1 monograph, over 120 scientific papers and 7 patents. His research interests are development of analytical applications of aqueous two-phase partitioning, new clinical tests for early cancer detection and other applications, role of water in biology and protein-water interactions.

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