Editorial

ProteinChips: the essential tools for proteomic biomarker discovery and future clinical diagnostics

The field of clinical proteomics is growing rapidly and increasingly demonstrates promise to identify new targets for treatment and therapeutic intervention, as well as biomarkers for diagnosis, prognosis, and therapeutic efficacy through comparison of proteome profiles between differing physiologic and disease states (1, 2). The proteome is defined as a dynamic collection of proteins that demonstrate variation between individuals, between cell types, and between entities of the same type but under different pathological or physiological conditions (3). The states of proteins within a patient also change over time and in response to multiple external stimuli. Technical advances and new discoveries in protein purification and identification have driven proteomics research to a different approach where comprehensive protein databases for individual conditions can be used to characterize individual patients and disease states (4) by studying systems biology.

In this issue of CCLM there are several studies and reviews highlighting different protein chip technologies. Depuy et al. (5) offer a comprehensive review of different protein biochips for use in clinical investigation. There is also thorough discussion of Randox Evidence biochips by Molloy et al. (6). Harwanegg et al. (7) discuss the use of protein microarrays profiling antibodies in allergic diseases. In addition, the approach using SELDI-based protein profiling by Bons et al. (8) reviews the use of these chips for clinical chemistry, while Clarke et al. (9) discuss the use of this technology to investigate the proteomics of breast cancer. While protein chips and other proteomics technologies serve as useful tools for clinical investigation, proper study design is the key to deliver any successful outcomes.

The traditional notion of one gene-one protein has gone by the wayside in light of discoveries demonstrating that one gene can produce a heterogeneous protein population that has multiple related structures with similar physiochemical properties due to post-translational modification (phosphorylation, glycosylation, ubiquitination) at multiple sites within a protein or conformational changes from genetic polymorphisms (10, 11). It is also important to note that the quantity of protein produced can vary greatly based on the individual in question or the patient/system environment. These factors lead to the conclusion that comprehensive proteomics is potentially much more challenging than genomic analysis (12).

Investigators should be aware that systemic errors can be introduced in a study that will artificially discriminate disease from non-disease, such as differences in sample collection (e.g,. arterial vs. venous blood, plasma vs. serum) or using non-matched patient groups (e.g., everyone in the disease group is over 60 years and everyone in the control group is under 40 years). In addition, possible diurnal variation of protein expression must be accounted for, so the time of sample collection should be controlled as closely as possible. In a recent study by Karsan et al., (13) their group was unable to find a protein expression profile that differentiates patients with breast cancer from those with benign lesions. However, they were able to identify proteomics patterns that were able to classify samples based on the collection site where the specimens were obtained, and also by the date on which the specimens were processed. A further consideration is that patients with benign conditions, or with disease not related to the clinical condition of interest, should be included in the control group so that the study is in fact examining differences between persons with a specific disease condition and those without, rather than measuring differences between generally sick and generally healthy patients. These study details can be difficult to manage, especially in a retrospective study, but paying attention to these details in study design will give a greater chance of success in protein profiling studies.

We believe that the future laboratory diagnostics will come from the discovery of proteomic biomarkers. Examples of protein chips described in articles from this issue will facilitate the effort of biomarker discovery. Extensive clinical validation is needed and will move these potential biomarkers closer to reality. Protein chips have the advantage of testing multiple biomarkers simultaneously, which has the potential to accelerate the validation process. Multiplex measurement of biomarkers coupled with advanced bioinformatics applications will enhance the clinical utility and lead to new targeted diagnostics for personalized medicine.

References

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