

The Onco-Genomic Alterations Existing in Cancer Genotypes

Qiang Nai*

Department of Anatomy and Neurobiology, University of Tennessee, USA

Abstract

Furthermore, Immunohistochemistry is often being used to validate findings from alternative proteomic studies. For example the validation of prognostic and predictive protein biomarker candidates derived from cell line experiments is commonly performed in clinical tumour samples.

Keywords: Standardization; Immunohistochemistry; Signalling proteins; Antibody-microarray; Expression patterns; Microscopic quantities

Introduction

The validation of proteomic-based discovery using clinical specimen is reviewed by Hewitt. Although, antibody signals can be directly assigned to cellular localizations and thus laser micro-dissection is not required, Immunohistochemistry results are nonetheless influenced by pre-analytic tissue processing and antigen retrieval. Inconsistent quality of Immunohistochemistry reagents and antibodies is also discussed to influence robustness of Immunohistochemistry results [1]. Despite automation and knowledge, Immunohistochemistry, still lacks uniformity of technique, appropriate controls, and standardization of antibodies and grading techniques, making it difficult to compare results across institutions, laboratories and experiments [2]. The statistical analysis of Immunohistochemistry-based multiple markers may be complicated by the nonlinear nature of Immunohistochemistry staining, the impact of different slide scoring thresholds for different immune-stains and different subcellular localization of markers. Limitations of Immunohistochemistry have been addressed by other techniques, including isotopic labelling and in situ hybridization, which allow for more quantitative analysis of variations in protein expression. Protein microarrays, one emerging class of proteomic technologies, have broad applications for discovery and quantitative analysis of protein expression patterns. This technology is uniquely suited to generate an overview map of known cellular signalling proteins and their activation status, reflecting the state of information flow through cellular networks in individual specimens. In the simplest sense, protein microarrays are immobilized protein spots. Thus, proteins can be arrayed on solid surfaces, capillary systems or immobilized on beads [3]. The spots may be homogeneous or heterogeneous and may consist of a bait molecule, such as an antibody, a cell or phage lysate, a nucleic acid, drug or a recombinant protein or peptide.

Methodology

In the array, detection is achieved by probing with a tagged antibody, ligand or serum/cell lysate. The most advanced format of this technique is the antibody-microarray, in which the targeted proteins are detected by specific antibodies, which were coated on solid surfaces [4]. The reverse-phase protein microarrays for example, immobilize one sample per array spot, enabling an array to comprise hundreds of different cellular lysates or patient samples. The detection of proteins is conducted using phosphor-specific and total protein antibodies to determine the activation status of key signalling molecules. This technology has been widely been used to analyse distinct cellular signalling pathways or to screen cell line panels as well as collections

of clinical specimens for disease-related protein expression patterns as shown in (Figure 1).

For example, Jones comprehensively analysed the protein interaction network for the ErbB receptor family, which may have implications in epidermal growth factor receptor targeted anticancer therapy [5].

Results

Chan first showed the application of multiplexed reverse-phase protein microarrays to the study of signalling kinetics and pathway delineation in a leukemic T lymphocytes cell line after activation of certain receptors. An example of for the use of RPPA to screen protein expression patterns in cell line panels is a study of Nishizuka, screening the NCI60 cell line panel using a reverse-phase protein lysate microarray. A finding from this study was that the patterns of protein expression compared with those obtained for the same genes at the mRNA level showed a striking regularity [6]. Cell-structure-related proteins almost invariably showed a high correlation between mRNA and protein levels



Figure 1: Genotyping.

*Corresponding author: Qiang Nai, Department of Anatomy and Neurobiology, University of Tennessee, USA, E-mail: qiangnai@yahoo.com

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across the NCI60 cell lines, whereas non-cell-structure-related proteins showed poor correlations. They also proposed that, this technology can be expected to contribute significantly to the identification of molecular markers and targets for individualized anticancer therapy. On this basis, Ma determined whether proteomic signatures of untreated cancer cells were sufficient for the prediction of drug response using the NCI60 panel. In this study, a machine learning model system was developed to classify cell line chemo-sensitivity exclusively based on RPPA proteomic profiling [7]. The accuracy of chemo-sensitivity prediction of all the evaluated 118 anticancer agents was significantly higher than that of random prediction. This study provided a basis for the prediction of drug response based on protein markers in the untreated tumour.

Discussion

Cell line panels find broad application in the proteomic analysis of individual chemo-sensitivity and drug discovery. Protein microarray platforms that can provide a quantitative, multiplexed read-out for cellular signalling and that can utilize microscopic quantities of tissue specimens for upfront analysis are needed for the implementation of this technology in the clinical situation. Therefore, the RPPA format has been improved to be able to measure the abundance of many specific proteins in complex solutions and has been adapted to use of very small amounts of protein [8]. Thus, this technology is well suited for signal transduction profiling of clinical samples, e.g. biopsy specimens. The identification of critical nodes or interactions within these networks is essential to drug development and the design of individualized anticancer therapy, especially with targeted drugs. Using breast cancer as an example, Wulfhuhle stated that, phosphor-protein-driven cellular signalling events represent most of the new molecular targets for anticancer therapy [9]. Therefore, the application of reverse-phase protein microarray technology for the study of on-going signalling activity within breast tumour specimens holds great potential for elucidating and profiling signalling activity in real-time for patient-tailored therapy. Moreover, their data demonstrate the requirement of laser capture micro-dissection (LCM) for analysis and reveal the metastasis-specific changes that occur within a new microenvironment [10]. Micro-dissection should be a necessary component of molecular analysis since dramatic changes within specific protein phosphorylation levels were noted between a majority of the un-dissected and micro-dissected samples. Laser capture micro-dissection technology permits a selection of a homogenous tumour population from a field of normal-appearing cells and vice versa, to improve the accuracy of comparative proteomics studies. Furthermore, Haab noted that, the sensitivity of individual antibody-antigen interactions for any given detection system are highly dependent on the relative abundance of the antigen-antibody species and the binding affinities between the probe antibodies and the immobilized antigens [11]. Liotta reported on the analytical challenges faced by protein arrays and proposed a practical guide for optimizing construction and study design. Additionally, a difficulty is associated with preserving proteins in their biologically active conformation before analysis. This will further limit the application of this technology as a routine proteomic strategy, unless clinical samples are routinely taken by the use of highly specified procedures [12]. The broad application of protein arrays in personalized medicine is also impaired by the costs of producing antibodies and the limited availability of antibodies with high specificity and high affinity for the target. Nevertheless, protein microarrays in combination with technologies such as LCM and high standardization will greatly contribute to the improved description of the multi-factorial network, underlying individual response to anticancer therapy and will allow the design of personalized medicine [13]. For most of the history of medicine, doctors relied on their senses

mainly vision, hearing, and touch to diagnose illness and monitor a patient's condition. Since then, biomedical research has made huge progress in diagnosis and treatment strategies. The traditional trial-and-error practice of medicine is progressively eroding in favour of more precise marker-assisted diagnosis and safer and more effective molecularly guided treatment of disease. The aim of personalized medicine is to tailor disease detection, diagnosis and therapy to each individual's profile, using molecular profiles to predict disease development, progression, clinical outcome and response to anticancer therapy as shown in (Figure 2).

Recent advances in high-throughput technologies have raised new opportunities in the fields of personalized- and predictive medicine. Thus, enabling researchers to screen the whole genome, proteome, transcriptome, and metabolome for biomarkers, in tumour tissues and body fluids [14]. In addition, new cellular models such as 3D organoid cultures or spheroid systems opened new opportunities in drug discovery and translational research. These models reflect the *in vivo* situation much better than common 2D models which are however, well suitable for high-throughput screenings. The introduction of modern technologies such as mass spectrometry and protein and DNA arrays, combined with the understanding of the human genome, has enabled simultaneous examination of thousands of proteins and genes in single experiments. These technologies are capable of performing parallel analysis, in contrast to serial analysis conducted with older methods. Due to the variety of data points, they provide opportunities to identify distinguishing patterns for cancer diagnosis and classification as well as for prediction of response to anticancer therapies. Furthermore, these technologies provide the means by which new tumour markers could be discovered. At the current stage, the molecular prediction of response to anticancer therapy is more exploratory, aiming at advancing scientific knowledge within clinical investigations rather than routine in clinical practice. Although numerous biomarkers have been discovered, only a handful of them, such as HER2 amplification, BCR-ABL translocation, KRAS, BRAF and EGFR mutations have been validated for the use in the clinical reality [15]. Molecular research in human tumors is currently predominantly performed retrospectively, using residual tissue specimens obtained from surgical resection procedures. Those tissues are used for generating hypotheses regarding the clinical relevance of the observed markers in the studied patient populations, target validation, and assay optimization. Often these tissue samples are obtained by core needle biopsies, e.g. fine needle aspiration, resulting in small sample amounts, which are often insufficient for comprehensive molecular analysis with currently available technologies. Therefore, the miniaturization of new emerging technologies is urgently needed. Furthermore, several studies have shown that tissue samples change their molecular profiles and start degrading immediately after resection from the patient's blood supply. Several exogenous factors such as ischemia time, drugs administered during surgery and processing



Figure 2: Genotype-guided cancer therapy.

protocols have been identified, which affect the molecular and genetic profiles of human tissue samples before, during and after the surgical resection. We propose that tissue samples that reflect molecular reality are a requirement to enable efficient cancer drug profiling and biomarker discovery. Besides technology-based challenges, regulatory issues are also limiting factors in the development of personalized medicine and predictive biomarkers. The clinical validation of putative functional regulators of drug response will run the risk of failure similar to other biomarker development efforts unless strict reporting guidelines are adhered to. Finally, the NCI-EORTC recommends that predictive biomarker studies require even stricter considerations, requiring validation in large randomized trials with sufficient power to detect drug-specific differences in tumour response.

Conclusion

Using, combining and further improving state of the art technologies and establishing stringent guidelines, the individualization of anticancer therapy especially in second-line treatment, will become accomplishable.

Acknowledgement

None

Conflict of Interest

None

References

1. Connor BO (2000) Conceptions of the body in complementary and alternative medicine. Routledge UK 1-279.
2. Lynch K (2019) The Man within the Breast and the Kingdom of Apollo. Society56: 550-554.
3. Saarinen R (2006) Weakness of will in the Renaissance and the Reformation. *OSO UK* : 29-257
4. Rovner MH (2005) Likely consequences of increased patient choice. *Health Expect US* 8: 1-3.
5. Marc EL, Chris B, Arul C, David F, Adrian H, et al. (2005) Consensus statement: Expedition Inspiration 2004 Breast Cancer Symposium : Breast Cancer – the Development and Validation of New Therapeutics. *Breast Cancer Res Treat EU* 90: 1-3.
6. Casamayou MH (2001) The politics of breast cancer. *GUP US*: 1-208.
7. Baralt L, Weitz TA (2012) The Komen–planned parenthood controversy: Bringing the politics of breast cancer advocacy to the forefront. *WHI EU* 22: 509-512.
8. Kline KN (1999) Reading and Reforming Breast Self-Examination Discourse: Claiming Missed Opportunities for Empowerment, *J Health Commun UK*: 119-141.
9. Keller C (1994) The Breast, the Apocalypse, and the Colonial Journey. *J Fem Stud Relig USA* 10: 53-72.
10. Berwick DM (1998) Developing and Testing Changes in Delivery of Care. *Ann Intern Med US* 128: 651-656.
11. Rovner MH (2005) Likely consequences of increased patient choice. *Health Expect US* 8: 1-3.
12. Marc EL, Chris B, Arul C, David F, Adrian H, et al (2005) Consensus statement: Expedition Inspiration 2004 Breast Cancer Symposium : Breast Cancer – the Development and Validation of New Therapeutics. *Breast Cancer Res Treat EU* 90: 1-3.
13. Casamayou MH (2001) The politics of breast cancer. *GUP US*: 1-208.
14. Baralt L, Weitz TA (2012) The Komen–planned parenthood controversy: Bringing the politics of breast cancer advocacy to the forefront. *WHI EU* 22: 509-512.
15. Kline KN (1999) Reading and Reforming Breast Self-Examination Discourse: Claiming Missed Opportunities for Empowerment, *J Health Commun UK*: 119-141.