Journal of Chromatography B, 877 (2009) 1221

Contents lists available at ScienceDirect

Journal of Chromatography B

journal homepage: www.elsevier.com/locate/chromb

Preface

Quantitative analysis of biomarkers by LC–MS/MS

The past decade has witnessed an explosion in our understanding of the molecular basis of human illness, and with it an understandable increase in expectation that cures will be found against the major killer diseases, such as cancer. Unfortunately, with this phenomenal growth in knowledge has also brought an exponential increase in the cost and complexity of developing medicines, resulting in stagnation in the regulatory approval of new chemical entities [1]. In this milieu, the US National Institute of Health's "Road Map" and US Food and Drug Administration's "Critical Path Initiative" have both identified the '**biomarker**' as one of the potential saviours of the current crisis.

A biomarker is a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacologic responses to a therapeutic agent [2]. Thus, biomarkers may enable more reliable and earlier detection of illness, enhance the selection of patients most likely to respond to targeted therapeutics and allow real time monitoring or even prediction of efficacy to treatment. Throughout the long and costly cycle of drug development, biomarkers are seen as facilitating go/no go decision making by either accelerating the promotion of active compounds into man or rejecting early those compounds destined to fail [3]. In the future, biomarkers may pave the way for optimal therapeutic intervention on a case-by-case basis (personalized medicine), or identify those at risk of disease enabling early or preventative intervention.

At least 5 different categories of biomarker assays have been recognized based on the level of quantitation inherent in the methodology ranging from: nominal (yes/no); ordinal (discrete, non-quantitative, arbitrary scores); quasi-quantitation; relative quantitation to absolute quantitation [4]. Thus, biomarker assays span across a wide diversity of technology platforms.

Chromatographic techniques, such as LC, coupled to mass spectrometry (MS), or MS on its own, represents one of only a limited number of analytical platforms which can claim to offer absolute quantitation and is being increasingly utilised in the quantitative analysis of biomarkers. However, the technological challenges that LC–MS/MS faces in this arena remain formidable. Serum concentrations of potential biomarkers, such as proteins, can vary by a factor of 10^8–10^{10} between high abundance species such as albumin and classic biomarkers such as prostate specific antigen (PSA). It is conceded by many that immunoassays still offer far greater sensitivity, reproducibility and dynamic range than LC–MS/MS [5]. In Europe when biomarker measurements are performed on samples collected from subjects entered into clinical trials, laboratories conducting these analyses are subject to the Clinical Trials Regulations, requiring the implementation of a full quality assurance (QA) system. In order to comply with the regulations, the biomarker assay also has to undergo extensive method validation, a whole science in itself [6].

Therefore, it was considered timely that Journal of Chromatography B should devote a special issue (SI) to the subject of quantitative analysis of biomarkers. Although focused on LC–MS/MS, the SI does include papers on closely related chromatographic methodologies, for example GC. We have attempted to span the analytical spectrum from technology developments through biomarker discovery and development of validation methodologies to informatics. At the same time we have tried to incorporate a range of applications in both *in vitro* and *in vivo* settings. Due to the nature of the subject material, method validation and clinical applications are intentionally prominently featured.

To conclude, we would like to thank all the authors and reviewers for their support and sterling contributions. We would also like to extend our gratitude to Dimitros Tsikas for all his advice and encouragement throughout the editorial phase of this special issue and especially for having the vision to champion its production in the first place.

References

[1] I. Kola, J. Landis, Nat. Rev. Drug Discov. 3 (2004) 711.
[2] NIH, Clin. Pharmacol. Ther. 69 (2001) 89.
[3] D. Sarker, P. Workman, Adv. Cancer Res. 96 (2007) 213.
[4] J.W. Lee, V. Devanarayan, Y.C. Barrett, R. Weiner, J. Allinson, S. Fountain, S. Keller, I. Weinryb, M. Green, L. Duan, J.A. Rogers, R. Millham, P.J. O'Brien, J. Sailstad, M. Khan, C. Ray, J.A. Wagner, Pharm. Res. 23 (2006) 312.
[5] D.E. van der Merwe, K. Oikonomopoulou, J. Marshall, E.P. Diamandis, Adv. Cancer Res. 96 (2007) 23.
[6] J.W. Lee, R.S. Weiner, J.M. Sailstad, R.R. Bowsher, D.W. Knuth, P.J. O'Brien, J.L. Fourcroy, R. Dixit, L. Pandite, R.G. Pietrusko, H.D. Soares, V. Quarmby, O.L. Vesterqvist, D.M. Potter, J.L. Witliff, H.A. Fritche, T. O'Leary, L. Perlee, S. Kadam, J.A. Wagner, Pharm. Res. 22 (2005) 499.

Guest Editors
Jeffrey Cummings [a,*]
Richard Unwin [a]
Timothy D. Veenstra [b]
[a] *University of Manchester, Manchester, UK*
[b] *SAIC-Frederick, Inc., Frederick, USA*

* Corresponding author.
E-mail address: jcummings@picr.man.ac.uk
(J. Cummings)

Available online 6 March 2009

doi:10.1016/j.jchromb.2009.03.001