editorial

Affinity Proteomics in the mountains: Alpbach 2015

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The 2015 Alpbach Workshop on Affinity Proteomics, organised by the EU AFFINOMICS consortium, was the 7th workshop in this series. As in previous years, the focus of the event was the current state of affinity methods for proteome analysis, including complementarity with mass spectrometry, progress in recombinant binder production methods, alternatives to classical antibodies as affinity reagents, analysis of proteome targets, industry focus on biomarkers, and diagnostic and clinical applications. The combination of excellent science with Austrian mountain scenery and winter sports engender an atmosphere that makes this series of workshops exceptional. The articles in this Special Issue represent a cross-section of the presentations at the 2015 meeting.

The affinity based approach to proteome analysis involves the generation and use of specific binding molecules (a.k.a. 'binders') as protein detection reagents, of which antibodies, their fragments and engineered constructs are the most familiar, though by no means the only ones in production. Their applications address many of the key issues in proteomics, including protein expression, modification and distribution in health and disease. The Alpbach workshops on Affinity Proteomics bring these applications together with progress in methods for generation, validation and quality control of antibodies and other binding reagents. The 7th workshop was held from March 9th to 11th 2015, with 120 academic and industrial participants from Europe and the USA. The focus areas included: the complementarity of affinity methods and mass spectrometry (MS); recent developments in methods of recombinant binder production; molecular alternatives to immunoglobulins; analysis of proteome targets; the interests of industry in discovery of biomarkers; and diagnostic and clinical applications.

The workshop was linked to and supported by the EU AFFINOMICS consortium (http://www.affinomics.org), which has continued the aims of the two previous EU funded projects, ProteomeBinders (2006–2010) and AffinityProteome (2009–2012), of generating a proteome-wide resource of well characterised, high quality protein-binding molecules for analysis of human proteins (http://www.proteinbinders.org). The particular targets for AFFINOMICS are in signal transduction and cancer. The importance of such comprehensive resources has not been limited to Europe and a parallel programme in the USA funded by the NIH, under The Common Fund's Protein Capture Reagents Program, has pursued similar objectives, focusing on human transcription factors [1]. These research and infrastructure initiatives have reflected a common concern for the importance of binder resources for biomedical research, while recognising and attempting to rectify the deficiencies which are frequently apparent in the quality and availability of commercial antibodies. Both the EU and NIH programmes have now reached the end of their funding and it remains to be seen if similar projects can be supported to continue these objectives.

The articles in this Special Issue of New Biotechnology represent a cross-section of the presentations at the 2015 meeting. In his accompanying Editorial, Ulf Landegren (Uppsala) gives his overview of the contribution made by AFFINOMICS to the design of binder-based assays for protein detection, focusing on the key linked issues of ensuring, as nearly as possible, target specificity, where antibodies inevitably cross-react to some degree, and enabling multiplexing.

Morteza Razavi and colleagues (Washington, USA and Victoria, Canada) describe a detailed protocol for SISCAPA (Stable Isotope Standards and Capture by Anti-Peptide Antibodies), an important example of the interface between MS and affinity methods for multiplexed protein biomarker quantification and clinical application. Another such interface, the GPS

http://dx.doi.org/10.1016/j.nbt.2016.04.003
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(Global Proteome Survey) described by Christer Wingren and colleagues (Lund), combines single chain antibody fragments (scFv) against short peptide motifs with MS analysis; in the GPS design a small number of scFv against widely shared peptides are used to target a large number of proteins and the paper describes the critical step of optimising the coupling the scFv to magnetic beads. The application of the recent technology of mass cytometry to muscle progenitor cell populations using a panel of eight antibodies is described by Gianni Cesareni and coworkers (Rome).

In regard to protein modifications, the intricate regulatory mechanisms involved in the action of the SHP-2 phosphatase in the RAS pathway and identification by MS of phosphotyrosine residues in 53 different affected proteins are described by Salvatore Corallino and colleagues (Rome and London). For the detection of phosphothreonine (pThr)-containing peptides, Brian Kay's group (Chicago) describe using the Forkhead Associated (FHA) domain as a scaffold for selection of pThr-specific binders by phage display; the selected FHA variants bound pThr peptides in various transcription factors and kinases with exquisite specificity.

In the article by Sarah Schumacher and Harald Seitz (Potsdam and Berlin), the factors to be considered in the important issue of antibody specificity validation are discussed, focusing on detection of drugs of abuse as targets. In respect of the generation and application of 'classical' monoclonal antibodies (mAbs), James Trimmer and colleagues (UC Davis) review the work of the NeuroMab facility in developing and validating mouse mAbs against mammalian brain targets and the issues involved in antibody-based neuroscience research. For recombinant antibody selections, where phage display remains a pre-eminent and highly popular technology, the article from the group of Michael Weiner (Axiomx, Branford, CT) discusses library design using pre-defined CDRs.

Microarray technologies figure in two articles as part of the binder selection and analysis processes. Jörg Hoheisel and colleagues (Heidelberg, Munich, Braunschweig, Kassel, Copenhagen) describe screening of candidate binders on antibody arrays to accelerate the process of selection, focusing on scFv against pancreatic and bladder cancers; only antibodies passing the initial selection were then further characterised by protein microarrays and surface plasmon resonance. In another application of microarrays, Peter Nilsson and colleagues (Stockholm) have used up to 21,120 arrayed protein fragments to analyse the specificities of polyclonal antibodies generated against them in the Human Protein Atlas project; the arrays were also used to investigate autoantibodies in the plasma of multiple sclerosis patients.

The Alpbach workshops take place in a 'gemütliche' alpine ambiance where the combination of excellent science with wonderful scenery and winter sports, not forgetting the Austrian cuisine, engender an atmosphere that makes this meeting stand out from the crowd, as evidenced by the large number of returnees. We look forward to welcoming participants again to the next workshop, scheduled for 2017.

Acknowledgements

The meeting was an activity supported by EU contract 241481, 'Protein Binders for Characterisation of Human Proteome Function: Generation, Validation, Application' (AFFINOMICS). The organisers thank Dr Oda Stoevesandt and Dr Alison Smith for their excellent assistance in the arrangements for and during the meeting.

Reference

[1] Stoevesandt O, Taussig MJ. European and international collaboration in affinity proteomics. N Biotechnol 2012;29:511–4.

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