Editorial: mass spectrometry for adductomic analysis

Health & Medicine

Editorial on the Research Topic

Mass Spectrometry for Adductomic Analysis

Individuals are continually exposed to physicochemical agents from the internal and external environments. The majority of these exposures act, at least in part, via the modification of DNA, or proteins, generating a wide range of adducts. DNA (Cooke et al., 2003), and some forms of protein (Barrera et al., 2015), damage impact cellular function, and play a critical role in the pathogenesis of, arguably, all major human diseases. Therefore, the assessment of DNA and protein damage is central to a wide variety of biomedical, and related fields. However, the majority of the literature describes the use of targeted analyses of damage, measuring only single, or a few, adducts, and while of value, this approach fails to reflect the totality of adducts, and therefore exposures.

Adductomics refers to the totality of cellular adducts associated with, to date, proteins (Rappaport et al., 2012), or DNA (Kanaly et al., 2006), and both are considered in the present collection. These untargeted approaches provide a most comprehensive profile of the damage derived from combinations of known and/or unknown exposures and, to some extent, the biological response(s) to such exposures (Chang et al., 2018).

In their mini review, Chen and Li focus on catechol quinone (CQ)-derived protein adducts. The presence of the CQ motif in many biologically relevant molecules (including products of endogenous metabolism, certain foods, drugs, and environmental pollutants), and the fact that CQ-adducted proteins may exhibit cytotoxicity or biological functions different from their

unmodified forms, make this class of adducts highly worthy of study, but this is technically challenging. Chen and Li advocate the protein adductomics approach for studying CQ-adducted proteins; for both their characterization, and quantification in blood, as biomarkers of exposure. The authors also provide valuable insight into some of the technical challenges that these analyses present.

In an exciting potential medical application of protein adductomics, Geib et al. characterize the specific adducts formed when the products of acetaminophen (APAP; paracetamol) interact with key cellular defenses against toxicity (the glutathione *S* -transferases). APAP-induced hepatotoxicity is the most common cause of acute liver failure in the Western world, making it a major public health problem. Metabolism of APAP generates a reactive intermediate which can react with glutathione and protein thiols. LC-MS/MS analysis revealed seven modified cysteine sites, including two unique sites, demonstrating the power of both untargeted and targeted approaches.

The identification of both DNA and protein adducts, discovered during adductomics analysis, is challenging due to the large size of the datasets generated, and the lack of data processing approaches. Whereas, proteomics analysis has benefited from technological advances in mass spectrometry, and bioinformatics, this has yet to fully translate to protein (and DNA) adductomics. Nunes et al. , inspired by the workflows used in metabolomics, developed a novel analysis approach for the identification of covalently-modified peptides. The strategy was tested by the analysis of

histone-derive adducts from HepG2 and THLE2 cells treated with glycidamide, and the results compared against standard methodology. Crucially, the new strategy identified adducts not seen with the conventional approach, and appears likely to advance the protein adductomics field further.

Although cellular DNA adductomics is less well-established than protein, the field is gaining momentum. In this collection, two reports illustrate the strengths of DNA adductomics, the potential for it to significantly advance our understanding of the links between environmental exposures and disease, and the scope for further methodological and application advances.

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