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Genome Regulation and Genetic Diversity

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Editorial

It is our pleasure to introduce the current special issue on "Mass spectrometry for understanding genome regulation and diversity." We discuss mass spectrometry as it relates to genetics and epigenetics, RNA transcript analysis (rather than genome-wide transcriptomics), protein complex characterization, biomarker validation, and nutritional bioactives research. In other words, we look at many aspects of biological mass spectrometry that aren't covered in traditional proteomics disciplines including protein expression profiling and biomarker/target discovery; metabolomics; and technology development for these two applications. The human genome sequence has provided us with "the words" (although only 20,000 protein-coding genes), but we are still learning the grammar and speaking the human genomics language. The complexity of life scales obviously with non-coding RNA and proteins, not with the number of protein-coding genes. Human genomic individuality can be explained in part by genetic variation such as Single-nucleotide Polymorphisms (SNPs) and Copy Number Variants (CNVs), however these variants have only accounted for a small percentage of interindividual variability in complex phenotypes and disorders to date [1,2].

In light of all of these aspects of genomic sciences, the current issue focuses on the key regulatory and diversity levels of the genome, which are where most of the complexity of higher organisms and their inter-individual variability occur. To better grasp this complexity, we believe in and explore the combination of genetics and epigenetics with -omics. This project relies heavily on mass spectrometry, proteomics, and other related sciences. The invited papers cover a wide range of topics, from measuring genetic predisposition (in our instance, SNPs), to epigenetic regulation (histone codes and DNA methylation), to protein interactions and bioactive proteins and peptides. As a result, this issue differs significantly from others published in proteomics journals in that it does not include a technological review, does not address biomarker identification, and does not focus on a specific class of molecules, pathway, or disease/condition. Predisposition (genetics), programming (epigenetics), transcription (RNA analysis), networks (protein interactions), and diagnostics are among the topics covered in this collection. Epigenomic variation could be to blame for phenotypic variety that isn't due to changes in genomic sequence. Such processes give the organism the ability to respond to changes in the environment over its lifespan, and possibly even the lifetime of its progeny, and may thus bestow a selected evolutionary advantage.

The chemical alteration of DNA by methylation at specific nucleotide residues is a significant biochemical indication of epigenomic diversity in animals. Sheppard et al. demonstrate how mass spectrometry may be used to quantify DNA methylation patterns in human and animal populations. Following this introduction, Babu, Zhang, Sheppard, and colleagues present their research on epigenetic control of the *ABCG2* gene and its relationship to sensitivity to xenobiotic exposure in farm animals. A network of Xenobiotic Metabolising Enzymes (XME) protects cells from oxidative stress and xenobiotic exposure by converting free oxidative radicals to less harmful metabolites, while efflux pumps remove toxins and XME products from the cell. Hypoxia and multidrug resistance both have well-documented mechanisms. Another important setting is ruminant exposure to fungus toxins, which causes hepatotoxicosis and eczema. Babu et al. explored possible epigenetic controls in cellular responses to such xenobiotic exposure using sheep toxin challenge, focusing on the phase III defence efflux protein *ABCG2*. Resistance to skin eczema is favourably associated with *ABCG2* gene expression, and negatively associated with DNA methylation at CpG sites in *ABCG2*'s regulatory region, according to the Sheppard group. Individual CpG sites altering with disease development were resolved using mass spectrometric DNA methylation analysis, allowing detailed mapping of underlying transcription factor binds and identifying epigenetic mechanisms as being key to xenobiotic reactions. Histone proteins help maintain and regulate the dynamic chromatin structure, as well as gene activation, DNA repair, and a variety of other functions in the cell nucleus.

The recruitment of transcription factors to specific DNA regions, the assembly of epigenetic reader/writer/eraser complexes onto DNA, and the control of DNA–protein interactions are all mediated by site-specific reversible and irreversible post-translational modifications of histone proteins. Histones govern chromatin shape and function, pass on heredity, and provide memory functions in the cell as a result. From sample preparation to data interpretation, Sidoli discuss a variety of analytical methodologies and several mass spectrometry-based approaches for histone analysis [3-5].

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Conflict of Interest

The Author declares there is no conflict of interest associated with this manuscript.

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