Editorial

Musculoskeletal Diseases

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Musculoskeletal diseases represent a major challenge to patient, clinical and scientific communities. Chronic joint pain, inflammation, stiffness and joint damage characteristic features of this group of diseases. The term arthritis refers to inflammation within a joint. In addition to impacting day-to day activities, arthritis can result in disability through irreversible joint damage and co-morbidities such as cardiovascular disease, hypertension and depression.

For the clinician, suppression of inflammation is paramount to prevent some of the long term associated morbidity and mortality. Current 'treat-to-target' regimens are aimed at establishing disease remission as early as possible after diagnosis. However, beyond conventional measures of inflammation, a key feature of many musculoskeletal conditions, few specific biological markers exist to assist in the management of these complex conditions. C-reactive protein is frequently used either in isolation or in combination with disease activity scoring systems to assess treatment efficacy. Its use however belies the multifactorial nature of many of these conditions. Put simply, the current tests do not accurately reflect the complexity of the disorders we are attempting to treat.

The synovial membrane is the primary site of pathology in inflammatory arthritis. In arthritis this normally nourishing tissue becomes hyperplastic; activated cells producing a wide variety of cytokines and proteolytic enzymes as well as chemokines that attract immune cells and thus perpetuate the inflammatory process. Thus analysis of joint fluid and tissue as well as blood are ideal sources for novel protein identification in arthritis.

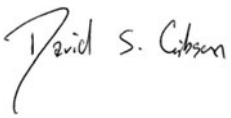
This focus issue on 'Musculoskeletal diseases' highlights research and reviews which cut across a range of diagnoses. There are five research articles and two reviews included: First, Collins et al. describe a translational research study using synovial membrane biopsies to identify putative biomarkers of anti—TNF treatment response in psoriatic arthritis patients. Biologic therapies are often designed to target inflammatory cytokines, and can be extremely effective in up to 70% of psoriatic arthritis patients. For those who do not respond however the disease remains active and risk of long-term damage remains. Furthermore the ability to allocate expensive drugs to the most responsive patients could bring benefit to healthcare providers also. The authors move from gel based candidate marker discovery to development of targeted MRM assays. Dwivedi et al. capably illustrate the process and some of the pitfalls involved in developing targeted mass spectrometry based assays, in the context of rheumatoid arthritis. Results demonstrate changes in signal to noise ratio dependent on removal of high abundance proteins such as albumin and immunoglobulin.

The effects of smoking and specifically nicotine on articular chondrocytes, the cells within joint cartilage, is investigated in the context of osteoarthritis by Lourido et al. The study combines a metabolic labelling strategy with LC-MALDI-TOF analysis, showing increased secretion of several molecules including degradative enzymes. Qundos et al. have used antibody bead arrays to profile 92 proteins within plasma samples from osteoporosis patients. Autocrine motility factor receptor (AMFR) emerges as a candidate marker; reduced in osteoporosis. The authors postulate that the drop in AMFR may be due to reduced physical activity in the patients.

A broad range of proteomic discovery methods are used by McArdle et al. to differentiate psoriatic and rheumatoid arthritis. Label-free LC-MS, antibody bead arrays and aptamer array platforms identified a combined 172 lead proteins that distinguish psoriatic arthritis patients from those with rheumatoid arthritis. The first of the reviews by Eakin et al. focuses on the importance of Siglec receptors and ligands regulating tolerance and immune cell activity in the context of autoimmune disorders, in particular rheumatoid arthritis. Is hypothesized that glyco-immunological pathways could be used as surrogate measures or disease activity or targets for novel treatments. Finally, Hinchliffe et al. overviews the current knowledge on the

use of array platforms to detect novel autoantigens and autoantibodies for better management of Lupus.

In recent years proteomics research has offered the opportunity to study musculoskeletal disorders in a more holistic fashion. Many studies have collectively given fresh insight into disease mechanisms, identified potential biomarkers to manage treatment, monitor disease activity and generated new hypotheses to test. Translating these findings into the clinic to improve the lives of patients remains a major hurdle. As proteomic technologies improve in terms of sensitivity, precision and robustness we can start to envision a future where multiplex platforms, whether array or mass spectrometry based, will be absorbed into clinical laboratories. There are promising initiatives from proteomics organisations such as HUPO, EUPA, CPTAC and MSACL which indicate interest in coordinating and accelerating research efforts. We hope you find the articles in this special issue of interest and wish to thank all the authors for their valuable contributions.



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