mediated by CB₂, more often expressed in immune cells, than by CB₁, and more often implicated in neurotransmission. Several studies have already investigated the role of the eCB system in different immune-mediated diseases, such as multiple sclerosis, Type 1 diabetes, and rheumatoid arthritis. In this summary, the data available in the literature were summarised and discussed. In addition, the role of eCB signalling in 10 female patients with systemic lupus erythematosus (SLE) and ten age and sex-matched healthy subjects has been presented. In these subjects, AEA, 2-AG, and N-palmitoylethanolamine plasma levels were quantified using liquid chromatography-tandem mass spectrometry, overall demonstrating an unprecedented alteration of eCB system in SLE patients. The audience to this presentation at EULAR appeared really interested in the topic, and appreciated the value of eCBs as novel molecular signatures of SLE with potential as disease biomarkers.

INFLAMMATORY MEDIATORS IN INFLAMMATORY MYOPATHIES

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Idiopathic inflammatory myopathies (IIM) constitute a heterogeneous group of chronic disorders which include the four main subtypes recognised today: dermatomyositis (DM), polymyositis (PM), sporadic inclusion body myositis (IBM), and necrotising autoimmune myopathy (NAM). These diseases represent distinct pathological entities but share an autoimmune origin and often display chronic inflammation that damages the skeletal muscle tissue. In DM, membrane attack complexes form on blood vessel endothelia, causing capillary loss and muscle ischaemia. In PM/IBM, non-necrotic muscle fibres are invaded by autoaggressive CD8+ T cells. The perforins and granzymes they release result in cytotoxic necrosis of the fibres. In IBM, the inflammatory process is accompanied by degenerative phenomena and the accumulation of abnormal protein aggregates inside the muscle fibres. In NAM, the most prominent myopathological feature is muscle fibre necrosis, and generally less severe intramuscular inflammation can be observed.

The early immunopathogenic processes that cause the IIM remain poorly understood, however the detrimental role played by various mediators in sustaining inflammation becomes more and more clear. Induction of major histocompatibility complexes on the muscle fibre membranes makes IIM muscle fibres participate by becoming antigen presenters. B cells become activated and new types of autoantibodies are continuously being recognised in patient sera. Tissue sites and specific tissue constituents are marked for destruction, by upregulation of adhesion, co-stimulatory molecules, and complement deposition. Thus, both humoral and cell-mediated immune processes are involved in perpetuating the build-up of inflammation and the muscle tissue itself plays an active role by nurturing a pro-inflammatory tissue environment.

In the talk, the focus was placed upon cytokines as they are the master regulators of immune cell activation and migration. These small cell signalling proteins are known to be crucial factors in IIM, regulating inflammation from initiation toward progression. Cytokines can display both local muscle tissue activities as well as systemic effects through secretion into the blood stream. Ten essential cytokine sets were singled out based upon current knowledge of cytokine expression patterns in healthy individuals, versus IIM skeletal muscle tissues and patient serology. The list contained interferon (IFN)-α and β, tumour necrosis factor (TNF) family members.
(TNF-α, BAFF), interleukins ([IL]-1, 2, 6, 12, 17, 23), and chemokines (CXCL9, 10, 11, CCL2). All of these factors are prominently expressed in patients, and many have been found to be associated with disease activity.

The potential of targeting these factors for selective immunosuppressive therapy was thoroughly discussed. For TNF-α, IFN-α, IL-1, and IL-6, clinical tests evaluating biologicals that block their activities have already become available and more are on the way. Results for infliximab and etanercept (both are therapeutic anti-TNF-α antibodies) and anakinra (a recombinant soluble IL-1 receptor agent) were varied, with responses ranging from clinical improvement to patients getting worse. A Phase I study evaluating sifalimumab (an anti-IFN-α therapeutic antibody) improved muscle strength in patients with DM/PM. Individual patients treated with the IL-6 receptor antibody tocilizumab reacted well to treatment. Interpretation of therapeutic responses reported in the available studies is however difficult due to small study size, different treatment regimen, and high drop-out due to disease deterioration.

It can be concluded that indeed the complex inflammatory network in IIM pinpoints targets for neutralisation. Selective immunosuppression is a valuable therapeutic approach and presents a necessary alternative for patients that do not respond to conventional treatments. Results so far are promising but have also shown the necessity for further subtyping of patients in order to develop future precision therapies and predict treatment outcome. It was suggested that for clinical evaluation, one should strive to isolate more homogeneous populations by prognostic subtyping of patients. This could be accomplished through in depth characterisation of myopathological patterns and profiling of autoantibodies and cytokines.

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**SYSTEMATIC REVIEWS AND META-ANALYSES FOR DUMMIES: A TUTORIAL ON HOW, WHEN, AND WHY TO GET STARTED**

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Prior to the 1990s, the task of combining data from multiple studies had been primarily based on narrative reviews; the problem with this was that a narrative review suffered from being subjective by nature, unlike a ‘systematic review’, which includes the application of scientific strategies that limit bias to the systematic assessment and critical appraisal of all relevant studies on a specific topic. The term ‘meta-analysis’ covers a series of statistical methods combining the results (with informative measures of heterogeneity) of several studies; not necessarily systematic, these can include ‘simple’ estimations across. However, a good meta-analysis can only be based on a thorough systematic review.

Systematic reviews and meta-analyses are valuable and play an essential role when guideline panels need evidence synthesis in order to explicitly communicate benefits and harms, following a systematic review of all the available evidence. Also evidence-based research suggests no new studies should be planned without a prior systematic review of the existing evidence. Before initiating any searches or meta-analyses, it is important that there is a pre-specified protocol, the goal is to design your evidence synthesis as a ‘prospective project’ (i.e. trying to counteract its retrospective nature). The protocol should be available via PROSPERO. As part of good planning, key emphasis should be placed on defining the clinical question which can be clearly formulated using the PICOS framework; i.e. a clinically-relevant or policy-relevant question that takes into account...