RP and for prevention of DUs onset and treatment of PAH, both intravenous prostanoid iloprost (ILO), and the dual endothelin-1 receptor antagonist (ERA) BOSE are used, respectively [10]. Bosentan seems to block pathogenic activities of Endothelin-1, the endothelial derived mediator determining both vasoconstriction and also the fibrosis genes induction [11–14].
Previous long-term follow up studies, showed that treatment with BOSE in combination with ILO interferes with progression of nailfold microvascular damage, evaluated through both capillary number semi-quantitative scoring at NVC and fingertip blood perfusion (FBP) at LDF [15,16].
In particular, an open label, prospective study of 4 follow up years showed that long-term treatment with BOSE added to ILO infusions administered quarterly in SSc patients, exerts a remodelling effect on structural and functional microvascular alterations and on stabilization of lung function, compared to ILO mono-therapy [17].

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SP0177 NEW APPROACHES BY TARGETING SOLUBLE MEDIATORS

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Although the aetiopathogenesis of systemic sclerosis (SSc) remains incompletely understood there is now sufficient knowledge about the pathobiology of the disease and mechanisms underlying development of fibrosis, autoimmunity and vasculopathy to permit informed selection of candidate soluble mediators that may be important drivers of the disease. This has permitted testing of potential targeting approaches in preclinical models and in vitro tissue culture systems. The data from these studies has informed understanding of the disease and has started to be translated into clinical trials that test hypotheses in vivo in patients. This approach has in turn fueled the concepts of reverse translation that are being applied to further understand SSc mechanisms in model systems and observational cohort studies. Soluble mediators that have emerged as strong targets for therapeutic intervention include TGFbeta superfamily members, connective tissue growth factor, IL13, IL4 and IL6. Studies of agents that target these proteins have been proposed or undertaken. Targeting TGF-beta appears to have benefit for skin thickening and attenuate some of the characteristic TGF-beta regulated genes and proteins in skin. However, the most encouraging data have emerged from targeting the IL6 axis using anti-IL6R neutralizing antibodies. This approach was promising in a Phase II study and further trials are ongoing. Interestingly this approach appears to attenuate macrophage gene expression signatures in the skin, may prevent worsening of lung fibrosis and showed significant benefit in the skin by biomarker analysis and a strong trend of benefit over 48 weeks for skin sclerosis score. Other small clinical trials testing TNF-alpha blockade have been more disappointing. Finally, it is possible that soluble mediators may be identified that directly attenuate the fibroproliferative mechanism of SSc. Experimental studies have suggested that increasing alpha-MSH may have benefit for skin fibrosis in a small controlled clinical trial. Clinical trial design is critical to the success and interpretation of studies targeting soluble mediators to define target engagement, mechanism of action, and possible clinical benefit. Advances in trial design are facilitating progress and it seems likely that, as in other rheumatic diseases, targeting key soluble mediators will become a therapeutic reality of the next few years. Defining the place of such approaches compared to other emerging treatment strategies will remain challenging.

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SATURDAY, 17 JUNE 2017

How diet influences musculoskeletal diseases

SP0178 GUT DYSBIOSIS AND OTHER CHALLENGES PRECIPITATE ARTHRITIS

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Environmental factors contribute to development of autoimmune diseases. For instance, human autoimmune arthritis can associate with intestinal inflammation, cigarette smoking, periodontal disease, and various infections. The cellular and molecular pathways whereby such remote challenges might precipitate arthritis or flares remain unclear. We have defined many of the pathways in the gut that contribute to homeostasis, particularly GPCRs such as GPR43 and their ligands the short chain fatty acids. Such receptors and their ligands are anti-inflammatory. To probe peripheral inflammation connections to arthritis, we used a transfer model of self-reactive arthritis-inducing CD4 cells from KRNtg mice that, upon transfer, induce a very mild form of auto-inflammatory arthritis in recipient animals. This model enabled us to identify external factors that greatly aggravated disease, such as microbiota effects or disruption of gut homeostasis. We show that several distinct challenges precipitated full-blown arthritis, including intestinal inflammation through DSS-induced colitis, and bronchial stress through Influenza infection. Both triggers induced strong IL-17 expression primarily in self-reactive CD4 cells in lymph nodes draining the site of inflammation. Moreover, treatment of mice with IL-1b greatly exacerbated arthritis, while transfer of KRNtg CD4 cells lacking IL-1R significantly reduced disease and IL-17 expression. Thus, IL-1b enhances the autoaggressive potential of self-reactive CD4 cells, through increased Th17 differentiation, and this influences inflammatory events in the joints. We propose that diverse challenges that cause remote inflammation (lung infection, colitis, gut dysbiosis) result in IL-1b -driven Th17 differentiation, and this precipitates arthritis in genetically susceptible individuals. Thus the etiology of autoimmune inflammatory arthritis likely relates to diverse triggers that converge to a common pathway involving IL-1b production and Th17 cell distribution.

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Can targeting disease activity in hand osteoarthritis improve our treatment in the 21st century

SP0179 WHAT IS DISEASE ACTIVITY IN FINGER OA?

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Osteoarthritis of the interphalangeal finger joints constitutes one of the most prevalent musculoskeletal diseases with variable clinical impact ranging from nearly asymptomatic to severe inflammatory pain in and around affected joints, presence of soft tissue and bony swelling, stiffness and gradual loss of function. Current therapeutic options are limited to analgesic treatment but research on targeted therapies is increasing.
In order to improve the current treatments, a critical appraisal of the needs for improvement in finger OA is needed and how disease activity is best defined.
Assessing disease activity or joint activity in finger OA is challenging: disease activity can comprise pain, inflammatory activity and structural damage.
In clinical practice, a combination of patient-reported (e.g. visual analogue scale or Likert scale pain), more objective and performance-based measures (e.g. grip strength) are used to assess and follow disease activity. In clinical research, pharmacological trials and epidemiological studies, a standardized approach to assess the disease activity is necessary to estimate the burden of disease and to evaluate the efficacy of potential new treatments. The instruments being used, depend mostly on the aim of the study or research question. In case structural disease progression is being studied, imaging-based outcome measures are mostly used. Structural changes can be assessed on joint level or on patient level, both by conventional radiographs, ultrasound and magnetic resonance imaging. Several imaging based outcome measures and scoring systems are being suggested but true consensus about the instruments of preference is still lacking. Therefore, further validation of these instruments is warranted.
This lecture will give an overview of the current instruments to measure activity in finger OA in several domains and discuss its strengths and limitations.

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SP0180 BIOLOGICS AND OTHER INFLAMMATORY THERAPIES IN FINGER OA. WHAT HAVE WE LEARNED?

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Hand osteoarthritis (HOA) is the most frequent form of osteoarthritis. A subset of digital hand OA is marked by an “inflammatory” like presentation with painful interphalangeal joints, refractory to NSAIDS and analgesics.