WHY IS THE PREVALENCE OF KNEE OSTEOARTHRITIS BIG DATA FOR TREATMENT EFFECTIVENESS AND HOW BIG DATA AND MACHINE LEARNING COULD FROM MENDELIOME TO PERSONALISED MEDICINE IN FRIDAY, 15 JUNE 2018

Prevention of OA: yes we can!

SP0123

WHY IS THE PREVALENCE OF KNEE OSTEOARTHRITIS INCREASING?

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Invited speaker abstract submission

EULAR18-7734 WHY IS THE PREVALENCE OF KNEE OSTEOARTHRITIS INCREASING? D. Felson

I will give my lecture on: Friday, 15 June 2018

Disclaimer of Interest: None declared


SP0124

PHYSICAL ACTIVITY AND EXERCISE: OPPORTUNITIES AND CHALLENGES

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Osteoarthritis (OA) is a steadily growing public health concern in particular as there is still a lack of curative therapeutic options in a biological sense. Thus, prevention of OA becomes an increasingly important topic. Physical activity, and exercise are among the key modifiable risk factors associated with OA. Joints are built to be used, but overuse and joint injuries are also linked with incident OA. This presentation will provide some key opportunities with exercise to maintain joint health, but also the challenges when the window of opportunity is exceeded.

Disclaimer of Interest: None declared


FRIDAY, 15 JUNE 2018

Big data for musculoskeletal research

SP0125

HOW BIG DATA AND MACHINE LEARNING COULD CHANGE THE GAME

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With recent advances in the acquisition and digitisation of medical data, the use of routinely collected health data for research is on the rise. Routinely collected data comes with the promise of the 3 V’s of “big data”: volume, velocity, and variety. Recent recommendations by the UK National Institute for Health and Care Excellence and the Academy of Medical Sciences have therefore acknowledged the potential for data science methods to play an increasingly important role in healthcare research.

Against this backdrop of growing data and increasing computational resources, the use of data science methods including machine learning is becoming popular for analysing large-scale medical datasets. This talk provides a brief overview of machine learning methods for healthcare applications including an introduction to supervised and unsupervised learning, followed by real-world examples of data analysis using machine learning, such as (a) the development of prognostic models for clinical risk assessment, and (b) mining of electronic health records for detecting patterns and phenotypes within a population.

Disclaimer of Interest: None declared


FRIDAY, 15 JUNE 2018

From big data to personalised medicine in paediatric rheumatic diseases

SP0126

BIG DATA FOR TREATMENT EFFECTIVENESS AND SAFETY

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While randomised clinical trials remain the gold-standard for examining drug-effects, there are limitations to the evidence they provide. For example, studies are usually too small or too short to detect rare and long-term adverse effects. This is particularly true for kidney-related outcomes where many trials were underpowered to detect outcomes of interest such as end-stage renal disease, too historic to collect data on newly-defined entities such as acute kidney injury or simply excluded patients with chronic kidney disease. In addition, disproportionate recruitment of Caucasian men in mid- to older-life limits the evidence base for understanding risk of adverse-effects in other population groups such as women, the elderly and people of non-Caucasian ethnicity. Determining these outcomes requires long-term surveillance of population databases, usually anonymised health care records, once a drug is in routine use.

In this talk I will discuss recent work from our group where we have used routinely collected renal function measurements from primary care to precisely examine kidney-related and other adverse effects. I will discuss some of the difficulties of this approach as well as the potential it offers to better understand the balance between risks and benefits of many drugs in common use.

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FROM MENDELIOME TO PERSONALISED MEDICINE IN CHILDHOOD SLE

A. Belot1,2, on behalf of Genial/Lumugene working group. 1Pediatric Rheumatology Unit – National Referee Centre for Rheumatism and Autoimmune diseases – Raise, Chu Lyon; 2U1111, INSERM, Lyon, France

Pediatric-onset SLE is a rare condition where genetics traits are believed to play an important causal role. A few monogenic causes of SLE have been described mostly in familial forms, including complement deficiencies, so-called type I interferonopathies, and B cell-related defects. Genetic studies in mouse models and genome-wide associations studies in patients have also pointed to other genes potentially involved in juvenile SLE. However, large-scale sequencing analyses of paediatric SLE are lacking, and the overall contribution of genetic factors in disease onset is therefore unknown. Personalised medicine relies on the understanding of underlying mechanisms. Genetic discovery and functional characterization of the variants prefigure the precision medicine in complex diseases such as SLE.

We have designed a NGS panel comprising genes for which mutations are known lupus causing (KLC) (also reported as the Mendeliome) as well as prospective candidate genes, potentially lupus causing (PLC), and analysed 117 children who fulfilled ACR criteria for SLE from two large cohorts of pediatric-onset SLE in the UK and France. Genetic variants were identified and filtered to select rare (ExAC database frequency of <1% for homozygous variants and <0.01% for heterozygous variants) and predicted in silico as damaging by different algorithms. We identified mutations in KLC genes for 8 patients. Variant segregation within families and functional analyses supported the causal role of these mutations. Other patients had monoallelic variants in recessive KLC genes, which may have contributed to disease onset and other patients displayed rare and pathogenic variants in PLC genes. This enrichment was specific to the lupus cohort compared to a control cohort of healthy patients.
This large-scale analysis led to the identification of monocytic causes of lupus in about 7% of analysed patients in an unselected paediatric population of SLE. 7/8 causes are related to an innate immune disorder with effectorcytosis deficiency, emphasizing the importance of apoptotic body clearance in the pathogenesis of lupus. Other variants in KLC or PLC genes may represent novel monocytic causes of lupus or could influence disease-onset by increasing the penetrance of more severe mutations. The treatment is still poorly adapted to the underlying mechanisms but progress in immunomonitoring together with the revolution in the field of genetics prompt clinician to set up targeted therapies considering genetic background and biomarkers.

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SP0128 FINDING THE NEEDLE IN THE HAYSTACK AND USING IT: GALECTIN-9 AS A BIOMARKER IN JUVENILE DERMATOMYOSITIS

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Background: Juvenile dermatomyositis (JDM) is a rare systemic immune-mediated disease involving skin and muscle. A high disease burden exists with risk of both under- and overtreatment due to the lack of reliable biomarkers.

Methods: A multiplex immunoassay was performed in a discovery cohort for plasma levels of 45 proteins related to inflammation in 25 well-defined JDM patients, determined by clinical activity and treatment. Results were validated in two independent international external and internal validation cohorts (n=125). In a longitudinal cohort (n=30), the performance of this biomarker over time was assessed with a median 2.8 years follow-up.

Results: In the discovery cohort we found a clustering of 10 mediators of which Galectin-9 and CXCL10 distinguished best between active disease and remission. Both biomarkers had a strong correlation with clinical parameters (Spearman r with Physician’s global assessment (PGA)=0.75 for both). This was confirmed in the validation cohorts (Spearman r=0.7 with PGA, for both). In the longitudinal cohort galectin-9 and CXCL10 correlated with disease activity over time, and elevated levels could predict flares several months before clinical symptoms. Both cross-sectionally and longitudinally, galectin-9 and CXCL10 outperformed creatine kinase activity.

Conclusion: Galectin-9 and CXCL10 are robust biomarkers for disease activity in JDM. A short-term implementation into clinical practice is feasible and can facilitate individualised treatment.

Disclosure of Interest: None declared

FRIYAD, 15 JUNE 2018

Triple T: T cells, technologies and therapies

SP0129 STUDYING T CELL FUNCTION IN RA AND PSA

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Rheumatoid arthritis (RA) and spondyloarthritis (SpA) describe a group of inflammatory joint diseases affecting ~2% of the population. RA has strong genetic associations with HLA-DR, indicating a role for CD4+ T cells. CD4+ T cells are prominently present in the RA joint, where they can contribute to the inflammatory milieu. I will present recent data from our lab regarding the presence, regulation and function of different CD4+ T cell subsets that are present in the RA joint. In contrast, SpA has strong genetic associations with HLA-B/RUNX3 which imply a role for CD8+ T cells. Furthermore, genetic associations with IL23R/TRAF3IP2 and the clinical efficacy of IL-17 blockade in SpA, indicate a role for IL-17 in SpA. This provides a strong rationale to investigate the presence, phenotype and functional capacity of IL-17+CD8+ T cells in the joints of patients with SpA. I will present novel data regarding the presence, phenotype and potential function of IL-17+CD8+ T cells in the joints of patients with SpA. Collectively, our data indicate that IL-17+CD8+ T cells may be important contributors to the pathogenesis of SpA.

Disclosure of Interest: L. Taams Grant/research support from: GSK, UCB, Novo Nordisk A/S, Novartis

SP0130 TOWARDS T CELL TOLERANCE IN RHEUMATOID ARTHRITIS

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Disease modifying strategies are available for treatment of rheumatoid arthritis (RA), and good response rates are achieved. However, limitations include toxicity, a response rate ceiling, cost and rationing of biologic therapies, inability to cure or permanently reverse RA pathology, and inability to prevent disease. Immuno-therapies targeting checkpoint molecules are markedly changing the landscape of clinical oncology. In autoimmune diseases such as RA, dendritic cells represent an important target for antigen-specific immunotherapy for T cell tolerance. Antigen-specific strategies promise greater specificity and safety, without general immune suppression, and thus the potential for intervention in at-risk subjects before disease onset. In a proof-of-concept trial, delivery of autologous antigen peptide and autologous tolerogenic dendritic cells was safe and had immunomodulatory effects on T cells including reduction of effector T cells and a relative increase in regulatory T cells. We have developed and are trialling in RA patients, antigen-specific immunotherapy targeting dendritic cells in situ with liposomes encapsulating autologous antigenic peptide and calcitriol with the aim of antigen-specific T cell tolerance. I will discuss the development of antigen-specific tolerance strategies and the parallel development of immune monitoring assays to determine T cell outcomes in clinical trials in RA.

Disclosure of Interest: R. Thomas Grant/research support from: Janssen Biotech Inc, Consultant for: Janssen Biotech Inc

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Navigating the world of digital health