IAS Institute of Advanced Studies

UNIVERSITY OF SURREY

Musculoskeletal Health in the 21st Century

An International Workshop

30 June – 1 July 2015

Oak Suite 1 and 2, University of Surrey

Faculty of Health and Medical Sciences

Programme and Abstracts

SPONSORS

The Institute of Advanced Studies (IAS) at the University of Surrey hosts small-scale scientific and scholarly meetings of leading academics from all over the world. The workshops are multidisciplinary events at the 'cutting edge' of science, engineering, social science intended to bring together international scholars and Surrey researchers to share perspectives on common problems.

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School of Veterinary Medicine (FHMS); School of Biosciences and Medicine (FHMS)

Novel Diagnostics and Biomarkers for Early Identification of Chronic Inflammatory Joint Diseases

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O**steoarthritis** (OA) is one of the most prevalent chronic health problems affecting hundreds of millions of people worldwide. The aim of the D-BOARD consortium is to bring together leading academic institutions and European Small and Medium Enterprises (SMEs) to focus on the identification, validation and qualification of new combination biomarkers and the development of diagnostic tests capable of subclinical disease diagnosis. **D-BOARD is funded by the European Commission's Seventh Framework Programme (FP7/2007-2013) under grant agreement no. 305815.**

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SPONSORS

Arthritis Research UK | centre for sport, exercise & osteoarthritis

The aim of the Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis is to improve the understanding of the effects of sport and exercise on joint injury and osteoarthritis. The Centre's research will lead to plans for prevention, assessment and treatment of injury, aimed at reducing the risk of later osteoarthritis. The centre's aims are to provide people with evidence-based advice and information about taking part in sports and exercise so they can reduce their risk of injury and development of osteoarthritis, to identify and train researchers in the field of sport and osteoarthritis research, to understand why some injuries can lead to osteoarthritis; to predict who will develop symptomatic osteoarthritis post-injury and to engage with key sporting bodies, patients and the public.

Centre for Musculoskeletal Ageing Research

MRC Arthritis Research UK Centre for Musculoskeletal Ageing Research

The MRC-Arthritis Research UK Centre for Musculoskeletal Ageing Research aims to understand how ageing results in loss of musculoskeletal function and to use this knowledge to intervene and minimise age-related musculoskeletal decline and disease. The major focus is on exercise and diet, incorporating motivational psychology research to underpin improved uptake and adherence to lifestyle changes. The Centre will also train the next generation of researchers, building capacity in this vital area to ensure that older adults are able to enjoy rather than endure old age.

MUSCULOSKELETAL HEALTH IN THE 21ST CENTURY

Introduction

We live in a world with an ever-increasing ageing population. Studying healthy ageing is a key research priority, along with a better mechanistic understanding of the pathophysiology of ageing that occurs in a number of age related musculoskeletal disorders. Arthritis and musculoskeletal problems represent a major cause of disability and morbidity globally and result in enormous costs for our health and social care systems. By gaining a better understanding of healthy musculoskeletal ageing we can provide better care and new therapies for common musculoskeletal disorders.

"Musculoskeletal Health in the 21st Century" is a multidisciplinary workshop that will bring together the major stakeholders including clinicians, basic scientists and funding bodies to focus on musculoskeletal health and the concept of intervention and disease prevention. We will discuss and debate the effects of physical activity, body condition, diet, vitamins and supplements on the musculoskeletal system, focusing specifically on the synovial joint. The workshop will include sessions on joint health, arthritis prevention through physical activity (including biomechanics of musculoskeletal tissues), effects of diet and nutrition, understanding the underlying physiology and pathophysiology of cartilage and bone, prognostic biomarkers and new insights from genetic diseases of the musculoskeletal system.

The workshop is unique because it will focus on musculoskeletal health and arthritis prevention by taking a unique "One Health" approach, including presentations by medical professionals, veterinarians and scientists. After each session there will be ample time for discussion, and participants will have the opportunity to debate unresolved issues with experts in the field. Postgraduate students and early career researchers are especially welcome to attend and there will be dedicated session for young investigators.

We look forward to your participation and contribution to the workshop, and to welcoming you to the University of Surrey and the historic and beautiful County Town of Guildford.

Professor Ali Mobasheri, School of Veterinary Medicine

Dr. Constanza Gómez Álvarez, School of Veterinary Medicine

Dr. Rebecca Lewis, School of Veterinary Medicine

Professor Susan Lanham-New, School of Biosciences and Medicine

Professor Margaret Rayman, School of Biosciences and Medicine

Professor Mike Hughes, Biomedical Engineering, invited chair

Mirela Dumic, Institute of Advanced Studies

Aimee Jones, Faculty Events Coordinator

PROGRAMME

30 June 2015

08.30 - 09.15: **Registration, tea & coffee**

09.15 - 09.30 Welcome & Introduction – Chris Proudman Head of School of Veterinary Medicine (Surrey, UK)

Morning Session Chairs: Ali Mobasheri and Constanza Gómez Álvarez

09.30 - 10.00 An overview of a common MSK problem in dogs elbows: "Pathomechanics of developmental canine elbow disease: the implications of supraphysiological overload" – Noel Fitzpatrick (Surrey, UK)

10.00 - 10.30 Mechanisms of FAI Cartilage Damage: Experimental & Simulation Studies. Richie Gill (Bath, UK)

10.30 - 11.00 Coffee Break

11.00 - 11.30: Musculoskeletal health from the "One Health" perspective – what can we learn from large and small animal models? René van Weeren (Utrecht, the Netherlands)

11.30 - 12.00 Diabetes-induced osteoarthritis: role hyperglycaemia in joint destruction. Alexandrina Ferreira Mendes (Coimbra, Portugal)

12.00 - 13.30: Lunch and poster viewing

Afternoon Session Chairs: Mike Hughes and Becky Lewis

13.30 - 14.00 Physical Therapy and Exercise in Osteoarthritis Prevention. Janet Lord (Birmingham, UK)

14.00 - 14.30 The role of physical therapy and exercise on OA prevention. Maria Stokes (Southampton, UK)

14:30 - 15:00 MSK health and OA in the UK army – the ADVANCE study (Armed Services Trauma Rehabilitation Outcome study). Alex Bennett (Epsom, Surrey, UK)

15.00 - 15.30 Surgeon General's Bone Health Project: Translation of Research to Mitigate Injury Risk in Royal Marines Recruits. Joanne Fallowfiled (Alverstoke, UK)

15.30 - 16.00: The importance of translating MSK research. James Bilzon (Bath, UK)

16.00 - 16.20: Coffee Break

16.20 - 16.50 Development of mesenchymal stem cell-based therapies for intervertebral disc regeneration: towards a novel therapy for back pain. Stephen M. Richardson (Manchester, UK)

16.50 - 17.20 Canine chondrodystrophic intervertebral disc disease (Hansen type I disc disease). Clare Rusbridge (Surrey, UK)

17.20 - 17.35 Session Close. Ali Mobasheri (Surrey, UK)

19.00 **Dinner at Kinghams, Shere**

PROGRAMME

1 July 2015

08.30 - 09.00	**Registration, tea & coffee**
Morning Session Chairs: Margaret Rayman and Rebecca Lewis	
9.00 - 9.30	Animal models and systems biology approaches for the functional validation of genetic determinants of skeletal diseases. Peter Bell (Newcastle, UK)
9.30 -10.00	What can we learn from rare and orphan diseases? Jim Gallagher (Liverpool, UK)
10.00 -10.20	Latest approaches on the management of OA in humans. Nidhi Sofat (London, UK)
10.20 - 10.45	**Coffee Break**
10.45 -11.15	Diet, Nutrition and OA. Margaret Rayman (Surrey, UK)
11.15 -11.45	Vitamin D and bone health. Susan Lanham-New (Surrey, UK)
11.45 -12.15	Biomarkers of prognosis and efficacy of treatment in OA. Yves Henrotin (Liège, Belgium)
12.15 -12.45	Non-Invasive techniques for studying macrophages in joint inflammation. Harrie Wienans (Utrecht, Netherlands)
12.45 -14.05	**Lunch and poster viewing**
Afternoon Session Chairs: Sue Lanham-New and Ali Mobasheri	
14.05 -14.25	Living Well with Arthritis. Judi Rhys (London, UK)
14.25 -14.45	Time to move. Ainslie Cahill (Australia)
14.45 -15.05	Osteoarthritis of the Knee. Jean McQuade (Australia)
15.05 -15.25	Collaboration and Partnership in Orthopaedics and Musculoskeletal Research: Academia, Industry, Health Services, and Patients. Arash Angadji (London, UK)
15.25 -15.45	Machine Learning for Knowledge discovery from omics/clinical OA data. Jaume Bacardit (Newcastle, UK)
15.45 -16.15	**Coffee Break**
16.15 -17.00	Plenary Lecture: Global burden of osteoarthritis and MSK diseases. Anthony Woolf (Truro, UK)
17.00 -17.35	Discussion and closing remarks. Ali Mobasheri (Surrey, UK)

PLENARY LECTURE

Professor Anthony D Woolf

Global burden of Osteoarthritis and Musculoskeletal Diseases

Professor Anthony D Woolf, University of Exeter Medical School

Over the past century, global health priorities in health over the past century were largely focused on the communicable diseases. With the world's population growth, increased average age and decreased death rates, people are now living longer and becoming increasingly susceptible to the non-communicable diseases, including musculoskeletal (MSK) disorders. The recent Global Burden of Disease (GBD) Study estimated the burden disability in 187 countries and 21 regions of the world for the years 1990, 2010 and 2013 of all MSK disorders - osteoarthritis (OA), rheumatoid arthritis (RA), gout, low back pain (LBP), neck pain (NP) and all other musculoskeletal disorders. Throughout the world, the prevalence and burden from MSK conditions were exceptionally high. All MSK disorders combined caused 21.3% of the total years lived with disability (YLDs) globally - second to mental and behavioural problems (23.2%). When taking into account both death and disability, all MSK disorders combined accounted for 6.7% of the total global disability-adjusted life years (DALYs), which was the fourth greatest burden on the health of the world's population (third in the developed countries). Out of the 291 conditions studied, LBP ranked first (highest) for the disability (YLDs), and sixth for the overall burden (DALYs). For NP, the condition ranked fourth highest for YLDs, and 21st for DALYs. 'Other MSK disorders' ranked sixth highest for YLDs and 23rd for DALYs. Osteoarthritis, RA and gout were also significant contributors to the global disability burden. In addition to this burden of disability as estimated by these summary measures of health, there is the impact on the individual's quality of life and economic independence as well as the costs to society due to health and social care and due to work loss. Despite this enormous and growing burden there is a lack of priority and of policies focusing on musculoskeletal health. This needs to change if we are to meet the demands of an ageing population that needs to be able to remain economically independent.

Biography

Professor Anthony D Woolf

Professor Anthony Woolf is Honorary Professor of Rheumatology, University of Exeter Medical School, and Plymouth Peninsula Medical and Dental College; and Clinical Director of the NHS National Institute of Health Research Clinical Research Network Southwest Peninsula. He is Chair of the International Coordinating Council of the Global Alliance for Musculoskeletal Health of the Bone and Joint Decade, and Chair of the UK Arthritis and Musculoskeletal Alliance (ARMA).

He is involved in various initiatives to raise awareness of the impact of musculoskeletal conditions and priority for education, prevention, treatment and research at a national, European and global level. He leads the Bone and Joint Monitor Project, a global health needs assessment that provides the evidence base for the Decade; edited the WHO Report on the Burden of Musculoskeletal conditions at the Start of the New Millennium; and coordinated the European Bone and Joint Health Strategies project. He is co-lead of the Musculoskeletal Expert Group of the Global Burden of Disease Study and co-chair of the WHO Musculoskeletal Topic Advisory Group that is revising ICD 10. He has lead the European Musculoskeletal Surveillance and Information Network – an initiative supported by the European Community to promote a comprehensive strategy to minimise the impact of musculoskeletal conditions across Europe. He is Editor-in-Chief of Best Practice and Research Clinical Rheumatology which provides an evidence-based update on the management of musculoskeletal conditions. As Clinical Director of the NHS National Institute of Health Research Clinical Research Network Southwest Peninsula he is promoting a culture of research and innovation to improve the overall quality of care.

SPEAKERS

Arash Angadji ..... London, UK

Jaume Bacardit ..... Newcastle, UK

Peter Bell ..... Newcastle, UK

Alex Bennett ..... Epsom, Surrey, UK

James Bilzon ..... Bath, UK

Ainslie Cahill ..... Australia

Joanne Fallowfield ..... Alverstoke, UK

Alexandrina Ferreira Mendes ..... Coimbra, Portugal

Noel Fitzpatrick ..... Surrey, UK

Jim Gallagher ..... Liverpool, UK

Richie Gill ..... Bath, UK

Yves Henrotin ..... Liege, Belgium

Susan Lanham-New ..... Surrey, UK

Janet Lord ..... Birmingham, UK

Jean McQuade ..... Australia

Margaret Rayman ..... Surrey, UK

Judi Rhys ..... London, UK

Stephen Richardson ..... Manchester, UK

Clare Rusbridge ..... Surrey, UK

Nidhi Sofat ..... London, UK

Maria Stokes ..... Southampton, UK

Rene van Weeren ..... Utrecht, the Netherlands

Harrie Weinans ..... Utrecht, the Netherlands

Anthony Woolf ..... Truro, UK

Arash Angadji. London, UK

Collaboration and Partnership in Orthopaedics and Musculoskeletal Research: Academia, Industry, Health Services, and Patients

Keywords: Innovation, Research, Medical Charity, Orthopaedics, Collaboration, Industry

Arash Angadji, Senior Project Manager, Orthopaedic Research UK

The main activity of Orthopaedic Research UK (ORUK) is to provide funding to centres of excellence to conduct research in the field of orthopaedics, in order to benefit patients suffering from bone and joint disorders. However, the majority of the grants awarded will not make it to the market as products, surgical techniques or novel rehabilitation approaches. Therefore, in general, grants are made with no expectation of a financial return and very often with no measureable patient benefit. But in the event when the researchers manage to generate intellectual property (IP) and a commercial opportunity, it is expected that the funder should also share the financial benefits in order to reinvest the money back into its pursuit of its mission.

Since 2004, ORUK has invested over £8.2m on 120 projects in 37 institutions, which has thus far generated nil return on investment. Even though so far ORUK has managed to file three patents – in 2009, 2013 and 2014 - the organisation has yet to see the long-term benefits for the stakeholders.

ORUK is addressing a perceived lack of efficiency to show impact on patients by implementing a new approach through a specific translation research funding (TRF) programme within its strategy. ORUK is aiming to promote the innovation process to ensure that the money invested in research is given the best opportunity to translate into meaningful outcomes.

Biography

Dr Arash Angadji is currently the Senior Project Manager at Orthopaedic Research UK (ORUK). He obtained his PhD from Queen Mary University of London in 2008, where he was studying the tribological performance of artificial metal-on-metal hip replacements, under the supervision of Professor Julia Shelton. He joined the Furlong Research Charitable Foundation as a Research Assistant whilst he was writing up his PhD thesis. In 2010 he was sponsored by his employer to undertake a degree programme in MBA, in an effort to help the organisation to modernise itself and demonstrate a greater impact as a funding body in the field of orthopaedics and musculoskeletal research. This led to the rebranding of the organisation in September 2011, and development of a new strategic focus on translational research towards the end of 2013. He has been regularly teaching at the MSc in Biomaterials and Tissue Engineering course at UCL since 2008. His ultimate goal is to achieve the vision of the charity: to eliminate bone and joint disease.

Peter Bell. Newcastle, UK

Animal models and systems biology approaches for the functional validation of genetic determinants of skeletal diseases

Peter A. Bell1, EU-FP7 SYBIL, Michael D. Briggs1

1 Institute of Genetic Medicine, Newcastle University, UK

Rare skeletal diseases are a diverse group of diseases that primarily affect development of the skeleton. There are more than 450 unique phenotypes that, although individually rare, have an overall prevalence of at least 1 per 4,000 children. Pseudoachondroplasia (PSACH) and multiple epiphyseal dysplasia (MED) are skeletal diseases caused by missense mutations/deletions in the genes encoding important cartilage extracellular matrix proteins (ECM), and are characterized by disproportionate short stature, joint pain and early-onset osteoarthritis.

In-depth characterization of MED and PSACH mouse models has revealed that endoplasmic reticulum (ER) stress, reduced cell proliferation and abnormal ECM assembly are important pathological consequences of mutant protein expression. Ongoing work aims to consolidate data from other models of skeletal disorders using a systems biology approach as part of the EU FP7 SYBIL (Systems biology for the functional validation of genetic determinants of skeletal diseases) project, in order to gain a mechanistic understanding of disease processes and to deliver new and validated therapeutic targets.

Key to delivery of new targets and therapies is the identification of relevant disease biomarkers, which will allow the monitoring of responses to therapeutic interventions. This is particularly critical for skeletal diseases, for which biopsy material is not readily accessible. We have identified differences in the extractability of a number of ECM components from the cartilage of MED and PSACH mouse models, relative to controls. The differences in extractability of these proteins (which include FACIT collagens (types XII and XIV), tenascins (C and X), and fetuin A) may represent differences in the stability of these proteins within the cartilage ECM, which might potentially be exploited for use as biomarkers of disease progression. We are currently using biochemical and mass spectrometry analysis of easily obtained biological samples such as blood, urine and cell culture medium in order to identify and validate novel biomarkers for skeletal diseases.

Biography

Current Research: Research Associate – Institute of Genetic Medicine, Newcastle University, UK. Laboratory of Prof. Mike Briggs. Ongoing research is divided into the following primary themes: 1) Investigation of the role of MANF in cartilage/bone health and disease; 2) Characterisation of chondrodysplasia disease mechanisms resulting from extracellular matrix protein aggregate formation; 3) Identification of novel biomarkers for the monitoring of cell stress in multiple epiphyseal dysplasia.

PhD in Cell-Matrix Biology. "The role of matrilin-1 and matrilin-3 in the pathogenesis of multiple epiphyseal dysplasia" –Faculty of Life Sciences, University of Manchester, UK. Supervised by Prof. Mike Briggs. Bsc (Hons) 1st class, Molecular biology and biochemistry with industrial placement – Durham University, UK

Additional award: Best plant physiologist 2008, final year research project: "Investigation of the biochemical response of A.thaliana to drought and salinity stress" with Prof. Marc Knight. Awards and Fellowships: International Society for Matrix Biology Travel Award winner (2013); FEBS short-term fellowship award recipient (2013).

Alex Bennett. Epsom, Surrey, UK

MSK health and OA in the UK army – the ADVANCE study (Armed Services Trauma Rehabilitation Outcome study).

Wg Cdr Alexander Bennett PhD FRCP MFSEM
Consultant in Rheumatology and Rehabilitation

Trauma is a well recognised risk factor for the future development of osteoarthritis (OA). The Armed Services Trauma and Rehabilitation outcome study (The ADVANCE study) is a 20 year cohort study comparing medical and psychosocial outcomes of military personnel both exposed and not exposed, to significant trauma.

The Bio-Mil-OA study, a sub-study of the ADVANCE study, is an ideal opportunity to investigate the predictive value of biomarkers in joint pain and osteoarthritis.

The ADVANCE study is a 20 year cohort study of 600 combat casualties and 600 matched non exposed participants investigating the predictive value of biomarkers and trauma on the long term development of pain and OA in the hip and knee. Validated serum biomarkers for OA, knee and hip radiographs and patient reported outcomes for pain and function will be taken at baseline and at 5 years.

The predictive value of the biomarkers in predicting OA development and progression and joint pain in those exposed to different levels of trauma will be investigated using quantitative immunoassays for catabolic markers of cartilage matrix degradation.

Wg Cdr Alex Bennett will give an overview of the ADVANCE Study and the Bio-Mil-OA study

Biography

Wg Cdr Alexander Bennett joined the RAF in August 2000. He has been a Consultant in Rheumatology and Rehabilitation at the Defence Medical Rehabilitation Centre, Headley Court since October 2008, the Head of the Academic Department of Military Rehabilitation Since June 2011 and is the RAF Consultant Advisor in Rheumatology and Rehabilitation.

He is also an honorary consultant at Guys and St Thomas' Teaching Hospitals and an honorary senior lecturer at Imperial College, London.

His specialist training from 2001-2008 took place in centres of excellence including Guy's and St Thomas' Hospitals London and Leeds Teaching Hospitals for Rheumatology, and for Sports Medicine at Olympic Park Sports Medicine Centre, Melbourne and the Centre for Health Exercise and Sports Medicine, University of Melbourne, Australia.

He has a keen interest in research as well as clinical aspects of Rheumatology and rehabilitation. He has published widely in Rheumatology, in particular in the fields of early diagnosis and prognosis in seronegative inflammatory arthritis/spondylitis. He has lectured on many occasions at national, European and American Rheumatology conferences.

He is a Fellow of Royal College of Physicians and a member of the British Society for Rheumatology, the Faculty of Sports and Exercise Medicine and the International Society of Assessment in Ankylosing Spondylitis (ASAS) and is the secretary to the British Society of Spondyloarthritis

He is currently overseeing all research at the Academic Department of Military rehabilitation, which focuses on Trauma rehabilitation and outcome, training injuries and outcomes and military related rheumatology. He is the lead investigator of the 20yr cohort study investigating medical and psycho-social outcomes of combat casualties.

James Bilzon. Bath, UK

The importance of translating MSK research.

Biography

Dr. James Bilzon, Senior Lecturer in Exercise Physiology
James joined the Department for Health at the University of Bath in May 2008 following a 13-year career as an Exercise Physiologist in various Ministry of Defence (MOD) departments, including the Institute of Naval Medicine and the Headquarters Army Recruiting & Training Division (ARTD). Following a 3-year period as Director of Studies for the MSc in Sport & Exercise Medicine, he became Head of Department for Health in August 2011. He currently holds a number of Honorary appointments including Honorary Civilian Consultant Advisor (HCCA) in Sport & Exercise Science to the British Army and Honorary Fellow of the Society of Sport & Exercise Medicine Malaysia (FSSEMM).
He graduated from Manchester Metropolitan University in 1994 and undertook his MSc and PhD at Loughborough University. His research interests centre around occupational and environmental exercise physiology, including injury prediction/prevention and immunological responses to exercise in extreme environments. A further strand, related to his interests in military exercise physiology, is the role of physical activity in the maintenance of health & wellbeing in persons with physical disabilities. He has now published over 30 full journal articles and attracted ~£1 million in external funding. He is currently Director of the DisAbility Sport & Health (DASH) Research Group and a member of the University's Centre for Regenerative Medicine (CRM).

ABSTRACTS

Ainslie Cahill. Arthritis Australia

Time to move.

Biography

Ainslie Cahill is Chief Executive Officer of Arthritis Australia. This national peak organisation has made significant investments in musculoskeletal research; awareness & education; and health consumer advocacy for more than 30 years. As well as being a strong and effective health consumer advocate, Ainslie has had a distinguished senior management career in publishing, film & television and vocational education.
She has fulfilled several terms on the Consumers Health Forum Board (2008-2014), including four years as Deputy Chair, and currently serves on The Life Saving Drugs Program Review Reference Group; Clinical Trials Advisory Committee; and Comcare Health Benefits of Work Advisory Group. She is currently the Secretary of Arthritis Australia.

Arthritis Australia has made significant investments in musculoskeletal research; awareness & education; and health consumer advocacy for more than 30 years. As well as being a strong and effective health consumer advocate, Ainslie has had a distinguished senior management career in publishing, film & television and vocational education. She has fulfilled several terms on the Consumers Health Forum Board (2008-2014), including four years as Deputy Chair, and currently serves on The Life Saving Drugs Program Review Reference Group; Clinical Trials Advisory Committee; and Comcare Health Benefits of Work Advisory Group. She is currently the Secretary of Arthritis Australia.

Joanne Fallowfield. Alverstoke, UK

Surgeon General's Bone Health Project: Translation of Research to Mitigate Injury Risk in Royal Marines Recruits

Biography

Dr Joanne L. Fallowfield – Head of Applied Physiology, Environmental Medicine and Sciences Division, Institute of Naval Medicine, Ministry of Defence.

Dr Fallowfield completed her PhD in nutrition and endurance exercise at Loughborough University, before taking up a university lecturing post in Exercise Physiology and Nutrition. She joined the Institute of Naval Medicine in 2006 as Head of Applied Physiology, and has led research programmes on behalf of the Surgeon General on Bone Health, Armed Forces Feeding and Casualty Nutrition. She sits on Surgeon General's Training Exercise Medical Advisory Group, the Defence Food, Nutrition and Dietary Supplements Working Group, the Royal Navy Scientific Advisory Committee and the Commando Training Centre Royal Marines Research Steering Group. She is Co-Chair of the Defence Occupational Fitness Programme Working Group, which is an intra-Government collaboration with Public Health England. She is a Visiting Research Fellow to the University of Surrey and the University of Exeter, and also provides consultative advice to the Advertising Standards Authority and the Committee of Advertising Practice.

Alexandrina Ferreira Mendes. Coimbra, Portugal

Diabetes-induced osteoarthritis: role of hyperglycemia in joint destruction

Alexandrina F Mendes1,2, Susana C Rosa1, Ana T Rufino1, Madalena Ribeiro1,2, Fernando Judas3

1Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal; 2Center for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal; 3University and Hospital Center of Coimbra, Coimbra, Portugal; 4Faculty of Medicine, University of Coimbra, Coimbra, Portugal

Recent epidemiologic and experimental data reinforced the concept that diabetes mellitus (DM) is an independent risk factor for osteoarthritis (OA). Besides a systemic inflammatory response that can affect joint tissues and contribute to OA pathogenesis, direct effects of hyperglycaemia have been shown to cause cell damage and induce inflammation by various mechanisms in several tissues associated to diabetic complications. Whether and how glucose directly affects joint tissues and cells is just beginning to be unraveled. Indirect effects of high glucose can result from enhanced formation of advanced glycation end products (AGEs) which accumulate in OA cartilage in an age-dependent manner and play a pro-inflammatory and pro-catabolic role mediated by activation of their specific receptor, RAGE, on chondrocytes and synovial cells. Some direct effects of high glucose have also been demonstrated, namely induction of IGF-1 resistance [1] and inhibition of dehydroascorbate transport which can compromise collagen synthesis [2]. Our studies have been aimed at determining whether and how hyperglycemia affects chondrocyte functions and contributes to OA development and progression. The results obtained showed that high and low glucose concentrations regulate the availability of facilitative glucose transporter (GLUT) isoforms and the glucose transport capacity of human chondrocytes. High glucose concentrations decrease the transport capacity and GLUT-1 protein content without affecting its mRNA levels, but this ability to adjust glucose transport capacity as a function of its availability is compromised in aged/OA chondrocytes leading to its intracellular accumulation [3]. The consequences of this are increased and prolonged ROS production [3] and expression of metalloproteases (MMP)-1 and -13 [4], IL-1b, TNF-a, inducible nitric oxide (NO) synthase (iNOS) and NO production, mediated by high glucose-induced NF-kB activation [5], as well as decreased responsiveness to TGF-b [4] and impaired autophagy [5]. High glucose is thus sufficient to induce an inflammatory and catabolic response in human OA chondrocytes. Furthermore, it potentiates pro-inflammatory effects of IL-1b, namely IL-6, Cciclooxigenase (Cox)-2, prostaglandin E2 (PGE2) and NO production [6]. The pro-inflammatory effects of high glucose in human chondrocytes and diabetic mice, namely induction of Cox-2, IL-6 and MMP-13 and production of PGE2, as well as decreased production of Collagen II, have also been shown to involve impairment of anti-inflammatory pathways, namely by decreasing PPAR-g expression [7].

Elucidating how high glucose modulates joint tissue homeostasis will identify novel targets for development of innovative strategies both to identify diagnostic and prognostic biomarkers of OA and to effectively modify disease progression.

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Biography

Alexandrina Ferreira Mendes graduated in Pharmaceutical Sciences in 1989, at the Faculty of Pharmacy, University of Coimbra, Portugal. For the next 4 years, she worked at the Clinical Pathology Department of the Portuguese Institute of Oncology – Coimbra Centre. In 1993, she was admitted as Teaching and Research Assistant at the same faculty and started her Ph.D. studies in 1996. Her research program was developed at the Centre for Neuroscience and Cell Biology in Coimbra and at the Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Canada, for what she received a scholarship from NATO. She completed her Ph. D. in 2003 after which she became Assistant Professor, teaching human physiology and pharmacology. Currently, she is responsible for several undergraduate courses in Human Physiology and Pharmacology and collaborates in various post-graduate programs, both as lecturer and organizer of advanced courses in immunology and joint biology, osteoarthritis and cartilage tissue engineering. She is principle investigator at the Centre for Neuroscience and Cell Biology, where, over the past 15 years, her research has been focused on chondrocyte biology and arthritis pathophysiology with an emphasis on the role of hyperglycaemia in modulating chondrocyte functions. She also has a strong interest on drug discovery for osteoarthritis, being focused in identifying disease-modifying osteoarthritis drugs among natural compounds, particularly isolated from plants of the Iberian flora. She also serves as review editor for Frontiers in Physiology and associate editor for BMC Musculoskeletal Disorders. She is also an Associate Faculty Member of F1000Prime. She is a member and expert of the Veterinary Medicines Evaluation Group of the Portuguese authority for veterinary medicines.

ABSTRACTS

Noel Fitzpatrick. Surrey, UK

An overview of a common MSK problem in dogs elbows: "Pathomechanics of developmental canine elbow disease: the implications of supraphysiological overload"

Biography

Noel Fitzpatrick, Managing Director / Duniv MVB CertVR DSAO ACVSMR MRCVS
Professor Noel Fitzpatrick, originally from Laois, Ireland, obtained his Bachelor of veterinary medicine from University College Dublin in 1990.
Following scholarships at The University of Pennsylvania and The University of Ghent, he went on to complete the RCVS certificates in small animal orthopaedics and radiology.

Noel has attained boarded specialist status by examination in both the USA and the UK, with the degrees of ACVSMR, American College of Veterinary Sports Medicine and Rehabilitation, and DSAS(Orth), the Diploma in Small Animal Surgery (Orthopaedics).

In 2005 he opened Fitzpatrick Referrals, the UK's pre-eminent and largest dedicated small animal orthopaedic and neuro-surgical facility in Surrey, employing over 140 veterinary professionals and comprising state of the art surgical, diagnostic and rehabilitation facilities.

Noel remains the clinical chair and chief surgeon at Fitzpatrick Referrals operating on a daily basis. He is particularly experienced in minimally invasive arthroscopic (keyhole) surgery, spinal disc disease, limb deformities, joint replacement and limb salvage for severe trauma or cancer.

Noel is recognised and respected globally as a true thought leader in his field of expertise.

Jim Gallagher. Liverpool, UK

What can we learn about joint degeneration from rare and orphan diseases?

J A Gallagher
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William Harvey the great English physician of the 17th century observed "Nature is nowhere accustomed more openly to display her secret mysteries than in cases where she shows tracings of her workings apart from the beaten paths; nor is there any better way to advance the proper practice of medicine than to give our minds to the discovery of the usual law of nature, by careful investigation of cases of rarer forms of disease" [1]. The history of medical science has proven Harvey correct; studying severe phenotypes of rare diseases has helped elucidate pathophysiological mechanisms of more common disorders and led to the identification of new biomarkers and therapeutic targets [2]. For example the development of bisphosphonates, the most successful class of bone active agent, owes a debt to research on hypophosphatasia. More recent research on rare bone syndromes has helped identify new targets to inhibit bone resorption and stimulate bone formation including cathepsin K and sclerostin. Drugs against both these targets are now in clinical trials

Osteoarthritis (OA) is a major cause of morbidity and disability. It is also the only major musculoskeletal disorder for which there are no effective therapies, other than pain relief and eventual joint replacement. Recent studies on rare cartilage syndromes have identified some potential therapeutic target including GDF5 and lubricin.

Research from our laboratory has focussed on the early onset, aggressive joint destruction which occurs in the osteoarthropathy of the rare disease alkaptonuria (AKU). AKU is a single gene defect in tyrosine metabolism, which is characterised by ochronosis, the deposition of pigmented polymers in connective tissues particularly cartilage. Studying tissue samples from AKU patients and from AKU mouse models has revealed significant parallels with the pathophysiology of OA. We have discovered several previously unidentified microanatomical changes in AKU joints which were subsequently recognised in joint degeneration associated with OA and ageing. Of these the most significant are high density mineralised protrusions (HDMPs). These novel micoanatomical structures arise via the extrusion of a mineralisable matrix through cracks in the subchondral plate. Formation of HDMPS constitutes a previously unrecognised mechanism of joint destruction [3].

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Biography

Jim Gallagher holds the Derby Chair of Anatomy and Cell Biology at the University of Liverpool. He obtained his PhD from Cambridge on the metabolism of vitamin D and undertook postdoctoral research with Herbie Fleisch in Bern on bisphosphonates, then Graham Russell's lab in Sheffield where they developed the first techniques to culture osteoblastic cells from human bone. Jim has published over 150 full peer-reviewed publications, 20 book chapters and 5 patents. He has supervised over 30 PhD students, 9 of whom hold academic positions in UK universities. He pioneered research on the role of extracellular nucleotides and P2 receptors in bone and skin. Recently his research group elucidated the mechanism of joint destruction in alkaptonuria.

Richie Gill. Bath, UK

Mechanisms of FAI Cartilage Damage: Experimental & Simulation Studies

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Femoral acetabular impingement (FAI) is thought to be a key underlying reason for the development of osteoarthritis of the hip. There are two main types of FAI, cam-type and pincer-type. The cam-type FAI gives rise to cartilage delamination initially thought to occur on the acetabular side of the joint. The purpose of the current study was to look at the effects of cam-type impingement on the generation of shear strains at the bone/cartilage interface, using both experimental and finite element simulation methods. Sagittal slices (n=9) of femoral porcine cartilage-bone, 10 mm thick, were loaded using a five-axis custom test machine with a curved (radius 90 mm) steel indenter. The five-axis test machine allowed the samples to be subjected to compression and mixed compression/shear loading regimens. The specimen strains were measured using two dimensional digital image correlation (DIC). Each test was also simulated using finite element analysis, and the results compared with the DIC data. The specimens were then cyclically loaded either with or without damage to the cartilage layers; damage simulated clinically reported lesions. Maximal shear strain was found at the cartilage-bone interface, and was a function of compressive loading level. The finite element predictions matched the DIC measurements. The two parameters that were most important in terms of shear strain were the cartilage thickness and contact area radius. It was found that increased cartilage thickness and increased contact radius gave rise to higher shear strains. Cyclically loading the damaged specimens produced features of cartilage delamination consistent with clinical observations. The results of this study indicate high shear strain at the bone/cartilage interface is a possible mechanism leading to cartilage delamination, and may be the mechanism behind cartilage degradation in patients with cam-type FAI.

Biography

Professor Richie Gill, BEng, DPhil, FIPEM

Richie Gill is the Professor of Healthcare Engineering at the University of Bath. His research area is Bioengineering with a particular interest in Orthopaedics.

Professor Gill completed a first degree in Aerospace Engineering and initially worked in the aerospace industry. He developed an interest in bioengineering and undertook a PhD in Orthopaedic Mechanics. He has spent over 20 years working in a mixed clinical/research environment and was the Group Head of the Oxford Orthopaedic Engineering Centre from 2001 until 2012, when he moved to the University of Bath.

He is currently on the Executive Committees of the British Orthopaedic Research Society and the European Orthopaedic Research Society, and a member of the Editorial Board of the Bone and Joint Journal.

Professor Gill has a background in both experimental and numerical methods. Much of his research has involved modelling of human musculoskeletal system, using kinematic and finite element methods. Particular areas of interest are hip and knee joint function, disease initiation and treatment. He has published over 180 peer-reviewed papers.

Yves Henrotin. Liege, Belgium

Biomarkers of prognosis and efficacy of treatment in OA.

Y Henrotin

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OA is a disease affecting the metabolism of all joint tissues leading to structural changes visible by imaging techniques. Unfortunately, features visible by imaging are in most cases irreversible and progressively moving towards worsening. One challenge for the next decade will be disease detection at the early stage when the first molecular/metabolic changes appear in joint tissues. Another challenge is to develop tools to assess the efficacy of OA treatment on the natural history of the disease. At this time, joint space narrowing measurement on standard X-ray remains the goal standard. This method has some important limitations: lack of reproducibility and sensitivity, confounded by meniscal lesions and extrusion, poorly correlated with joint function and pain. Therefore, there is an acute need for reliable biological markers that can facilitate earlier diagnosis of OA, predict the progression of the disease and evaluate the efficacy of therapeutic modalities.

A recent literature review resulted in the identification of 16 biochemical markers investigating cartilage matrix turnover. Nine concerned collagen type II degradation (Coll2-1, Coll2-1NO2, CTX-II, Helix-II, C2C, TIINE, CIIM) and synthesis (PIIANP, PIICP). Keratan sulphate, chondroitin sulphate 846 (CS846) and

ARGS-aggrecan fragment investigate proteoglycans degradation. Serum cartilage oligomeric matrix protein (COMP), deaminated-COMP (D-COMP), fibuline-3 fragments (Fib3-1 and Fib3-2) were the other biochemical markers that are considered as markers of cartilage matrix metabolism.

At this time, none of the current OA pharmacological treatment can significantly modify the natural course of OA. A significant decrease of knee joint space narrowing after a 3-year follow-up has been reported for glucosamine and chondroitin sulphate. Risedronate and strontium ranelate, two drugs currently used to treat osteoporosis decreased urinary CTX-II levels suggesting that they can modulate cartilage metabolism, even if they did not alter radiological progression. However, recently, it was demonstrated that CTX-II was more strongly associated with bone markers (i.e. uNTXI, uCTXI, serum PINP, and osteocalcin) than with other cartilage markers (PIIANP, sCS846, sCOMP), while the "other" cartilage marker markers were not so strongly associated with the bone markers. These data indicate that CTX-II might reflect bone rather than cartilage metabolism. In a exploratory study investigating the effects of three intra-articular injections of hyaluronic acid (Hylan GF-20) on the evolution of 10 biochemical markers, we have demonstrated that uCTXII, sColl2-1 and sColl2-1NO2 levels were significantly affected by treatment suggesting that these markers are sensitive to metabolic change occurring in one single joint. More recently, we have observed that three months treatment with bio-optimized curcumin significantly decreased sColl2-1 level in 24 patients with knee OA, suggesting that sColl2-1 could be a companion marker to assess curcumin efficacy at an individual level and in the next phases of its clinical development.

Although many OA-related biomarkers are currently available they exist in various states of qualification and validation. At this time, none of the existing biomarker can be considered as a surrogate marker of joint space width measurement. The biomarkers that are likely to have the earliest beneficial impact on clinical trials fall into two general categories, those that will allow targeting of subjects most likely to either respond and/or progress (prognostic value) within a reasonable and manageable time frame for a clinical study, and those that provide early feedback for preclinical decision-making and for trial organizers that a drug is having the desired biochemical effect. In this context, the recent development of large cohort designed to qualify biomarker will accelerate biochemical marker implementation in clinical research.

Biography

HENROTIN Yves is Professor of Pathology, Physical Therapy and Rehabilitation and director of the Bone and Cartilage Research Unit at the University of Liège (Belgium) www.bcru.be. He is also head of the Physical Therapy and Rehabilitation department at the Princess Paola Hospital, Marche-en-Famenne, Belgium. He is a member of the American College of Rheumatology, the Osteoarthritis Research Society International, the French Society of Rheumatology and the International Cartilage Repair Society. Between 2006 and 2013, he was a member of the board of directors the Osteoarthritis Research Society International (OARSI), the premier organization focused on the prevention, diagnosis and treatment of osteoarthritis. He was elected treasurer in 2010. He was chairmen of the world BMJD debate and consensus congress in 2010 and 2012 and chairman of the 2010 OARSI world congress. He is also the vice-president of the Spine section and the osteoarthritis section of the French Society of Rheumatology,

board member of the French Society of Rheumatology since 2011, president of the Belgium Back Society since 2000 and president of the Belgium Scientific Society of Physical Therapy since 2008. He was the Belgium delegate and board member of the COST B13 action "Low back pain: guidelines for its management" organized by European Commission Research Directorate General. He is coordinator of the WP 1 of FP-7 programme D-BOARD, a European consortium dedicated to OA biomarkers research. He is Co-President of the board of the National Council of Physical Therapy and Rehabilitation for the Belgium Health Ministry. He serves the editorial board of several scientific reviews including "Osteoarthritis and Cartilage". He is honorary editor-in-chief of International Journal of Orthopaedics. He has published over 200 scientific peer-reviewed papers and 10 chapters of book. He is the co-editor of the book "Osteoarthritis: clinical and experimental aspects" (Springer), co-editor of "Primer in OA" (edited by the OARSI) and editor of the book "Nonpharmacological modalities for the management of osteoarthritis" (Bentham). In 2005, he received a prestigious national prize (De Cooman Prize) for his contribution in the better understanding of osteoarthritis pathophysiology. He is also the founder and the chairman of the board of two spin-off company of the University of Liège: Artialis SA, a company specialized in the research and development of biological markers of musculoskeletal disorders www.artialis.com and Synolyne Pharma SA www.synolyne-pharma.com, a company developing medical device for the joint viscossuplmentation and tissue repair.

Susan Lanham-New. Surrey, UK

Vitamin D and bone health

Susan Lanham-New RNutr, FAfN, FSB
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Throughout the life-cycle, the skeleton requires optimum development and maintenance of its integrity to prevent fracture. Bones break because the loads placed upon them exceed the ability of the bone to absorb the energy involved. It is now estimated that 1:3 women and 1:12 men over the age of 55 years will suffer from osteoporosis in their lifetime and in the UK, at a cost in excess of £1.7 billion per annum to the exchequer. The pathogenesis of osteoporosis is multi-factorial. Both the development of peak bone mass and the rate of bone loss are determined by key endogenous and exogenous factors. Calcium supplements appear to be effective in reducing bone loss in late menopausal women (>5 years post-menopause), particularly in those with low habitual calcium intake (< 400mg/d). In younger postmenopausal women, who are not vitamin D deficient, vitamin D supplementation has little effect on BMD. However, vitamin D and calcium supplementation studies have been shown to reduce fracture rates in the institutionalized elderly but there remains controversy as to whether supplementation is effective in reducing fracture in free-living populations. Re-defining vitamin D requirements in the UK is urgently needed since there is evidence of extensive hypovitaminosis D in the UK. Low vitamin D status is associated with an increased risk of falling and a variety of other health outcomes and is an area that requires urgent attention. The role of other micronutrients on bone remains to be fully defined, although there are promising data in the literature for a clear link between vitamin K nutrition, dietary protein and dietary alkali on skeletal integrity including fracture reduction.

Biography

Professor Susan Lanham-New RNutr, FAfN, FSB, Professor of Human Nutrition & Department Head, University of Surrey

Professor Susan Lanham-New is Professor of Human Nutrition and Head of the Nutritional Sciences Department at the University of Surrey. Her research focuses on the area of nutrition and bone health, for which she has won a number of awards including the Nutrition Society Medal for her work on the role of the skeleton in acid-base homeostasis. She is a Member of the Scientific Advisory Committee on Nutrition (SACN) and Editor in Chief of the Nutrition Society Textbook Series (6 books, >50,000 copies sold). She is also Editor (with Professor J-P Bonjour, Geneva) of the first academic textbook on Nutritional Aspects of Bone Health. She is on the Editorial Board of Osteoporosis International and Osteoporosis Review. She has published more than 130 peer-reviewed original papers, book chapters and reviews and raised more than £5.5M in research grants. Her H index is 31. She has 15 students who have successfully completed their PhD and a further 5 students in active PhD study. She is a member of the Nutrition Forum for the National Osteoporosis Society and the Scientific Advisory Group of British Nutrition Foundation and the BNF Taskforce on Ageing and was Honorary Communications Officer of the UK Nutrition Society from 2000-2006. She has recently been awarded Fellowship status of the Society of Biology and Fellowship status of the Association for Nutrition.

Janet Lord. Birmingham, UK

Ageing in humans: separating intrinsic ageing from lifestyle effects

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We are an ageing society, with falling birth rates and increasing life expectancy. However healthy life span is not keeping pace and on average older adults can expect to be unwell for the last decade of life. Many factors influence both lifespan and healthspan but in humans one of the key factors is likely to be increasing physical inactivity. To separate out those elements of the ageing phenotype that are due to inactivity from those which are intrinsic to the ageing process, we recruited 125 adults aged 55-79 who had maintained a high level of physical activity through their adult lives. We compared these with age matched healthy older adults who were not involved in regular physical activity and healthy young subjects. The subjects were assessed for key features known to change with ageing including sarcopenia, reduced bone mineral density, adiposity, cardiovascular and lung function as well as markers of immune ageing. We have already reported the physiological data which revealed that many features of ageing including lean body mass, adiposity and muscle strength did not change with age in the physical active group, though other effects were seen such as a decline in lung capacity (FEV1) and maximal heart rate. Here we report that a comparison of immune phenotype in the exercising and non-

exercising groups showed that thymic output was significantly reduced in the inactive group compared to both appeared to both the young subjects ($p<0.002$) or the physically active older subjects ($p<0.009$). The numbers of naïve T cells was also maintained in the active elders, though the rise in the numbers of senescent T cells was not protected by an active lifestyle. We conclude that an active lifestyle through adulthood can prevent many of the physiological and immune features normally attributed to ageing.

Jean McQuade. Australia

Osteoarthritis of the Knee

Self-management programs for people with arthritis are commonplace, usually delivered by lay leaders to people with different types of arthritis or other chronic diseases. Although there is evidence for their effectiveness, systematic reviews indicate improvements are small.

The OAK program differs from other arthritis self-management programmes in a number of respects. It is disease-specific and tailored for people with Osteoarthritis of the Knee (OAK); it was developed after an ENAT survey using a collaborative approach, and a Plan, Do, Study, Act (PDSA) model; it was was planned purposely for implementation in either hospitals or community settings.

The education component of this program is detailed, for delivery by health care. Principles and theories of SM are used to promote behavioural change. In particular, exercise and disease coping strategies are promoted within a SM construct as a means of improving quality of life and general health as well as reducing pain.

The program was tested using an uncontrolled quality assurance study and the results were positive in terms of improvement in pain, quality of life and physical function.

To more rigorously test the effectiveness of the program a randomised controlled trial (RCT) was undertaken and showed statistically significant improvements compared with a control group with regard to pain, quality of life and function for participants in the OAK program on the basis of WOMAC and SF-36 measures taken 8 weeks and 6 months from baseline.

The OAK program is conducted in a group setting with six weekly sessions of 2.5 hours each. The program is designed to allow participants to progress over time by incorporating and consolidating information learned from week to week. In addition to the weekly sessions, participants are given printed information relevant to the course component discussed each week. To facilitate optimum group dynamics, the target group size is ideally 12-14 participants. The fidelity of the OAK program is maintained by the use of a scripted facilitators' manual for modules delivery each week.

The program is implemented using a holistic approach and addresses multiple aspects of care: osteoarthritis (explanation and implications), SM skills (goal-setting, problem-solving, modelling, positive thinking and improving self-efficacy), medications (types, interactions and current trends), correct use of analgesia (use, therapeutic dosing, types and side effects), pain management strategies (cognitive and pharmacologic), fitness and exercise (strength, flexibility, aerobic and balance), joint protection, nutrition

and weight control, fall prevention (balance and proprioception), environmental risks, polypharmacy and coping with negative emotions.

Following the study a health professionals training workshop was developed and the OAK program is delivered in Australia usually by physiotherapists especially those working in rural hospital or primary care settings.

To reduce costings we have recently trialled programs using self-management trained peer leaders to assist the health professional and this has worked extremely well.

Biography

Jean McQuade is Health, Education & Research Program Manager
Arthritis and Osteoporosis, Western Australia.

Margaret Rayman. Surrey, UK

Diet, nutrition and osteoarthritis

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Osteoarthritis (OA) is the fastest growing cause of disability worldwide [1]. Current treatment strategies still leave most people in pain with significant fears for the future [1]. In the absence of effective therapies, patients may wish to take some control of their own condition by making dietary changes that have the potential to ameliorate their symptoms or reduce their disease progression.

A number of dietary factors have been associated with OA symptoms or progression. Most notably, in those overweight, weight reduction of ≥10% has the potential to lead to important changes in pain and function [2]. Not only does losing weight reduce the load on weight-bearing joints, but it also reduces pain-associated inflammation [3]. Weight loss combined with physical activity, has an even greater effect on improving pain and function [4].

It has been suggested that OA is a metabolic disease in which lipids essentially contribute to the pathophysiology of cartilage degradation [5]. Dietary long-chain w-3 PUFA may affect articular cartilage composition and appear to have beneficial effects in OA [5]. Though there are no published trials on the effect of omega-3 fatty acids (alone) in OA, in vitro studies and studies in OA dogs suggest that supplementation with long-chain omega-3 PUFAs may benefit inflamed OA joints. In a US cohort of individuals with, or at high risk of, knee OA, there was a significant inverse relationship between total n-3 PUFAs and patella-femoral cartilage loss [6].

The idea that OA is a metabolic disease is supported by a number of studies that show a positive association between elevated serum cholesterol and OA. For instance, hypercholesterolemia (OR 1.61; 95% CI 1.06-2.47) and high serum cholesterol (3rd vs. 1st tertile: OR 1.73; 95% CI 1.02-2.92) were independently associated with generalized OA in
the Ulm study [7]. Hence there may be a potential benefit in adopting dietary cholesterol-lowering strategies (such as consumption of sterol/stanol spreads/drinks).

Vitamin D affects the state of multiple articular structures. A recent systematic review assessed the evidence for association between the vitamin D biomarker, serum 25(OH)D, and OA. For knee radiographic OA progression and cartilage loss, there was strong evidence for an association with low 25(OH)D [8].

Vitamin K is important in cartilage metabolism as an inhibitor of extracellular matrix calcification and a promotor of cell survival/proliferation. In the US MOST study, vitamin K deficiency was associated with incident radiographic knee OA and MRI-based cartilage lesions (RR 2.39; 95% CI, 1.05-5.40) compared with no deficiency [9].

Hence, dietary recommendations are the following:

- lose weight if overweight preferably combined with exercise;
- aim to reduce plasma cholesterol by dietary means;
- at least for a trial period, increase intake of long-chain n-3 fatty acids by eating oily fish twice a week or taking fish-oil capsules;
- aim for a safe level of sun exposure, eat rich vitamin D dietary sources or take vitamin D supplements, ≤ 25 µg/d;
- increase vitamin K intake by eating green leafy vegetables or take a vitamin K (e.g. natto) supplement.

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Biography

Professor Margaret Rayman has a doctorate in Inorganic Biochemistry from Somerville College, Oxford, and has held post-doctoral fellowships at the Institute of Cancer Research and Imperial College. Since 2007, she has been Professor of Nutritional Medicine at the University of Surrey where, in 1998, she set up the highly respected MSc Programme in Nutritional Medicine of which she is Programme Director. In 2014, she was appointed Visiting Professor at the First Affiliated Hospital Xi'an Jiaotong University School of Medicine, Xi'an, China.

Her research, which includes a number of randomised controlled trials, centres on the importance of trace elements to human health with particular emphasis on selenium and iodine in populations with marginal selenium or iodine status. She has published widely on the effects of selenium on human health including a number of highly cited reviews in The Lancet. As part of her extensive work on iodine, her group found a significant association between mild-to-moderate iodine deficiency in UK pregnant women of the ALSPAC cohort and poorer IQ and reading ability in the offspring at ages 8 and 9 (Lancet 2013).

She has authored three books: an academic book "Nutrition and Arthritis" (Blackwell Publishing) in 2006 and two evidence-based cookbooks "Healthy eating: the prostate care cookbook" in 2009 (translated into three languages), and "Healthy eating to reduce the risk of dementia" in 2015.

She has been a judge for the BBC Radio 4 Food and Farming Awards on a number of occasions.

Judi Rhys. London, UK

Living Well with Arthritis

This presentation will describe the work of the charity Arthritis Care, the UK's largest organisation working with and for all people with arthritis. The strategy and five impact goals will be considered, before a brief exploration of the main services provided by Arthritis Care across the UK and the benefits they deliver.

Biography

Judi Rhys took up her role as Chief Executive at Arthritis Care in August 2013. Arthritis Care is the UK's largest organisation working with and for all people with arthritis, empowering people through support and information, ensuring their voices are heard and their conditions more effectively managed. Judi's career to date has included the NHS, higher education and other UK health charities, including Diabetes UK and the MS Society. She holds postgraduate qualifications in public health, education, management and executive coaching, and is a keen runner.

Stephen Richardson. Manchester, UK

Development of mesenchymal stem cell-based therapies for intervertebral disc regeneration: towards a novel therapy for back pain.

Low back pain (LBP) is one of the most common musculoskeletal disorders, with an estimated 84% of the population experiencing LBP at some point in their lifetime. As with most musculoskeletal disorders, the prevalence of LBP increases with age, suggesting incidences of LBP are likely to increase in the future due to a global aging population, changes in lifestyle and occupational stresses. Although the causes of LBP are multifactorial, increasing evidence implicates intervertebral disc (IVD) degeneration as a major contributor, with loss of IVD integrity leading to the destabilization of the spinal motion segment, resulting in pain and disability.

The IVD is a complex structure that allows movement between adjacent vertebrae and sustains the load applied through the spine. It consists of the peripheral annulus fibrosus (AF), a ligamentous lamellar structure composed predominantly of type I collagen fibres, and the central nucleus pulposus (NP), a highly hydrated structure, composed of the proteoglycan aggrecan, interspersed with type II collagen fibres. Only 1% of the IVD volume is occupied by its constituent cells, but they assume a key role, as they maintain IVD homeostasis. In degeneration there is an alteration in NP cell biology leading to diminished cell numbers and altered cell function resulting in an imbalance between matrix synthesis and degradation, particularly within the NP.

Current medical treatments for IVD degeneration rely on conservative therapies (e.g. pain relief, exercise therapy) and, when these fail, surgery. Surgical treatments such as spinal fusion and disc replacement have shown satisfactory results in alleviating pain, but are not devoid of complications and long-term clinical outcomes still remain poor. Thus, there is an urgent need for alternative therapies focussed on correcting the underlying pathogenesis and aberrant cell biology of IVD degeneration. As such many researchers, including ourselves, are focussing on the development of novel cell-based therapies. However, in order for these to be successful an appropriate cell source for implantation and tissue regeneration must be identified.

This presentation will discuss the pathophysiology of IVD degeneration, efforts to elucidate the phenotype of human IVD cells and how this has allowed development of mesenchymal stem cell (MSC)-based therapies for IVD regeneration. In particular it will focus on our efforts to identify the optimal MSC

source and growth factor to direct differentiation and enhance tissue formation, as well as the influence microenvironment has on regeneration strategies.

Biography

Dr Stephen M. Richardson is a Lecturer in Cell and Tissue Engineering at the University of Manchester. Since gaining his PhD in cartilage biology in 2002, his research has focussed on mesenchymal stem cell biology and application in musculoskeletal tissue engineering and regenerative medicine therapies, with a focus on intervertebral disc regeneration as a novel treatment for low back pain. As a post-doctoral researcher he worked as part of the UK Centre for Tissue Engineering and subsequently the UK Centre for Tissue Regeneration, before securing a 5-year Research Councils UK academic fellowship. He has authored over 40 papers in the field and presented at numerous national and international conferences. His contributions to the fields of tissue engineering and regenerative medicine were recognised by the Northwest Regional Development Agency and Nature Publishing Group who named him "Northwest Young Biotechnologist of the Year 2006" and the Tissue and Cell Engineering Society who presented him with the "Early Stage Investigator Award" in 2009. He is currently an associate editor for BMC Musculoskeletal Disorders and treasurer for the UK Tissue and Cell Engineering Society (TCES).

Clare Rusbridge. Surrey, UK

Canine chondrodystrophic intervertebral disc disease (Hansen type I disc disease)

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Intervertebral disc disease (IVDD) is the most common spinal disease in dogs. Chondrodystrophic dogs, which have disproportionably short and curved limbs, are predisposed to Hansen type I IVDD and of these the miniature Dachshund is over represented [1, 2], is more likely to be presented at an earlier age [3] and is at greater risk of a severe spinal cord injury [4]. The tendency for IVDD in Dachshunds is inherited [5, 6] and a major locus on chromosome 12 harbours genetic variations affecting the development of intervertebral disc calcification [7]. Hansen type I disc degeneration is thought to occur because of loss of notochordal cells which produce proteoglycans which "hold water" in the disc. Chondrodystrophic dogs have a primary deficiency of notochordal cells, a study found that large notochordal cells in the nucleus pulposus of chondrodystrophoid dogs formed 13% of the cell population in young dogs and fell to 0.4% in adults, whereas they were the predominant cell type in the nonchondrodystrophoid dogs at all ages [8]. Thus chondrodystrophoid dogs suffer early degenerative changes in the disc and a concomitant reduction in proteoglycan content, increased collagen, and loss of water content making the discs likely to herniate [8]. Certain lifestyle factors may increase or decrease risk of IVDD and this is currently under investigation. There is a suggestion that exercise (including stair climbing) reduces the incidence of disc calcification [9]. By contrast it has been hypothesized that

obesity/lack of postural muscle strength may increase risk. Dachshunds with intervertebral disc extrusion had significantly smaller cross sectional area and greater fat infiltration in the epaxial muscles (muscles which lie dorsal to the horizontal septum of the vertebrae which mobilize and globally stabilize the trunk [10]) compared to dogs presenting with fibrocartilagenous embolism (another acute onset intervertebral disc related spinal disease)[11]. In addition chondrodystrophic dogs may have increased risk of IVVD if they have a more extreme conformation e.g. Dachshunds that have a longer back and shorter limbs are more at risk [12] and breeds with a comparatively heavy head such as the Bassett Hound may be more at risk of cervical disc disease. Breeds with a tendency for kyphoscoliosis such as the French Bulldog may be more at risk of IVDD in the IVDs adjacent to a vertebral malformation [13, 14]. This presentation details the pathogeneis, clinical presentation, diagnosis and treatment of IVDD in chondrodystrophic dogs.

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Biography

Dr Clare Rusbridge graduated from the University of Glasgow in 1991 and following an internship at the University of Pennsylvania and general practice in Cambridgeshire, she completed a BSAVA/Petsavers Residency and was Staff Clinician in Neurology at the Royal Veterinary College. She became a Diplomate of the European College of Veterinary Neurology in 1996 and a RCVS Specialist in 1999. In 2007 she was awarded a PhD from Utrecht University for her thesis on Chiari-like malformation & Syringomyelia - a painful disease occurring in some toy breed dogs. For 16 years she operated a neurology and neurosurgery referral service at the Stone Lion Veterinary Hospital in Wimbledon. In September 2013 Clare joined Fitzpatrick Referrals and the University of Surrey where she is continuing her clinical and research work. Her professional interests include neuropathic pain, inherited diseases, epilepsy and rehabilitation following spinal injury.

Nidhi Sofat. London, UK

Latest approaches on the management of OA in humans

The Sofat laboratory currently investigates the mechanisms responsible for pain and tissue damage in arthritis. Clinical studies include 'Pain management in osteoarthritis using centrally acting analgesics', funded by the Rosetrees Trust. This clinical trial is testing whether drugs that inhibit pain processing pathways in the brain can help with pain in the hand caused by osteoarthritis. Other clinical studies include the 'Pain Perception in Osteoarthritis', or PAPO study, investigating tissue damage and pain in people undergoing knee replacement surgery for osteoarthritis. Both studies are on the UK NIHR portfolio of network-adopted studies.

Our laboratory has a translational approach, with techniques including magnetic resonance imaging (MRI) to decipher regions of damage in affected joints and evaluating which brain regions are activated

by arthritis pain. We also use non-invasive quantitative sensory testing (QST) methods to identify pain pathways. QST identifies sensation and pain thresholds by stimulating the skin.

Our laboratory research uses a basic science mechanistic approach to investigate the influence of endogenous damage-associated molecular patterns (DAMPs) in driving chronic inflammation in joints. Molecules of interest include interaction of the DAMPs tenascin-C and fibronectin with oral pathogens.

Biography

Dr Nidhi Sofat is a Clinical Reader and her research interest is primarily in rheumatic diseases, osteoarthritis and pain perception. She joined St George's, University of London in 2008 as a Clinical Senior Lecturer while working to develop a translational research facility in rheumatic diseases. She has been a Consultant Rheumatologist at St George's University Hospitals NHS Foundation Trust since 2008.

Dr Sofat completed her medical training at University College London in 1996 with an Intercalated BSc in Immunology. She completed her specialist rheumatology training in 2007 and in the same year, obtained a PhD at the Kennedy Institute of Rheumatology (then part of Imperial College London). She was awarded a Clinical Research Training Fellowship by the Wellcome Trust (2003-2007) which supported her PhD training at the Kennedy Institute, where she investigated the mechanisms driving tissue damage in arthritis. She was awarded a British Society for Matrix Biology prize for her work in 2005. In 2013, Dr Sofat was awarded the Michael Mason Prize in Rheumatology by the British Society of Rheumatology (BSR) in recognition of innovative work in rheumatology research. She has served on several committees aimed at improving standards of care in musculoskeletal diseases, including the BSR External Relations Committee (concerned with influencing policy makers) and the National Institute of Health and Care Excellence (NICE) for technology appraisals in osteoarthritis. She has helped write Standards of Care documents produced by the Arthritis and Musculoskeletal Alliance (ARMA), an umbrella organisation working towards better care in the discipline.

Maria Stokes. Southampton, UK

Physical Therapy and Exercise in Osteoarthritis Prevention

Maria Stokes PhD FCSP
Faculty of Health Sciences, University of Southampton, and Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis

Exercise encompasses physical activity (habitual, sporting), and exercise programmes to improve and maintain joint heath. Clinical guidelines recommend exercise for osteoarthritis (OA) e.g. NICE, EULAR, OARSI. Benefits of moderate exercise include weight control (obesity is a known risk factor for OA) and joint health (beneficial for cartilage). Specific exercises aim to achieve optimal biomechanics to protect joints (joint alignment, load reducing strategies) and improve muscle strength, endurance, power, flexibility and co-ordination. Other physiotherapy principles include sport/task specific exercises, personalised medicine (exercises tailored for the individual) and neuromuscular control of movement (screening and retraining using specific exercises). Manual therapy techniques (pain management,

mobilisations, muscle stretching) can improve exercise outcomes. Effects of exercise on pain and function are comparable with those for non-steroidal anti-inflammatory drugs. Exercise forms part of biopsychosocial management, using tailored, patient centred interventions based on assessment, with shared decision making.

Three levels of prevention include: primary (preventing injury and onset of OA), secondary (preventing progression of OA) and tertiary (managing complicated, long-term health problems). The Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis is focussing on secondary prevention of progression of injury and/or overuse to OA. Biomechanical and neurophysiological mechanisms of abnormal movement and joint loading are investigated using 3D motion analysis and electromyographic techniques, and evidence is emerging that mechanistic-based exercises can correct abnormal movement.

Movement screening tools in clinical/field environments are used increasingly to assess movement control and functional performance, primarily in sport, to predict injury and/or inform intervention. Robustness of screening tools is variable, in terms of reliability, validity and prediction of injury risk. Consensus is needed for terminology and establishing which screening tests are appropriate for specific cohorts and movement problems.

High quality longitudinal trails are needed to ensure effective use of exercise for OA prevention. Activity needs to be maintained for long-lasting effects but adherence to changing lifestyle remains a major challenge. For exercises targeting movement problems, studies need to elucidate which elements, modes, doses, and frequency and duration of exercise are optimal for specific joints and body regions.

It remains unknown whether exercise can influence disease parthenogenesis and progression. Evidence of cost-effectiveness of exercise as a clinical intervention for OA is also needed. Understanding and overcoming barriers to exercise and enabling access will be crucial for widespread uptake of exercise. Translation research is needed to determine how to change practice and influence GP referral to exercise programmes.

Biography

Professor Maria Stokes, University of Southampton

Maria Stokes is Professor of Musculoskeletal Rehabilitation and Head of the Active Living Technologies Research Group in the Faculty of Health Sciences at the University of Southampton. She is a physiotherapist by background, with a PhD in neuromuscular physiology. She leads the Southampton arm of the Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis. Her research focuses on active living and healthy ageing, using health technologies. Themes in her research programme are: 1) mechanisms of musculoskeletal function to inform interventions across the activity spectrum from elite sport to deconditioning (frailty in older people and effects of microgravity in astronauts); 2) prevention and rehabilitation of movement impairments; 3) developing assessment tools, including rehabilitative ultrasound imaging of muscle and measuring mechanical properties of muscle using mechanomyography (MMG) and Myoton technology.

René van Weeren. Utrecht, the Netherlands

Musculoskeletal health from the "One Medicine" perspective – what can we learn from large and small animal models?

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In human medicine musculoskeletal diseases rank (together with mental disorders) first in reasons for occupational disability and have a huge impact on both quality of life and overall healthcare costs [1]. The current increase in life expectancy, together with decreasing societal acceptance of impaired mobility, have strongly pushed musculoskeletal research in recent years.

The classic animal models for research into musculoskeletal disease are small rodents, especially mice and rats. As larger species, goats and to a lesser extent sheep have been the species of choice. This choice was largely based on practical and logistical considerations such as the required size, availability, costs and ease of handling, rather than on biomedical criteria.

The growing acceptance of the "One Health, One Medicine" concept has, together with better knowledge of fundamental differences between mammalian species in articular cartilage biology and the increasing pressure to reduce, refine and replace (the three "Rs") animal experimentation, led to a change in attitude towards the use of animal models in musculoskeletal research [2]. Whereas small rodents may still be a logical step after in vitro research, the fundamental differences between articular cartilage composition of smaller species and those heavier than about 1Kg [3], together with the increasing recognition of the role of biomechanics within the joint, cast severe doubts on the validity of these species for anything but very basic work in musculoskeletal research. In contrast, within the "One Medicine" concept it is clear that in veterinary medicine there are several species featuring a high prevalence of musculoskeletal disorders that are very similar to those seen in humans. This applies to dogs with intervertebral disc disease [4] and chronic joint disorders (especially osteoarthritis (OA)) in both horses and dogs [4].

These developments have led to a gradual shift in the use of animals in musculoskeletal research. Also, regulatory bodies are making this shift of mind with the US Food and Drug Administration (FDA) now requiring preparatory work in horses before approval for certain orthopaedic devices is granted.

There is one other important aspect to this development. Whereas the classic animal models were solely used to the benefit of human research, research in dogs and horses will forcibly lead to medical improvements for these species, as they are patients too and hence not only experimental animals, but target species as well. This is an important asset for the ethical justification for the use of animals for scientific research.

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Biography

Paul René van Weeren (1957) graduated in 1983 from the Utrecht University Veterinary Faculty (The Netherlands). He became a staff member of the Department of General and Large Animal Surgery in that year and obtained his PhD degree in 1989. From 1991-1993 he worked as a visiting professor at the Escuela de Medicina Veterinaria of the Universidad Nacional in Heredia, Costa Rica. He became a diplomate of the European College of Veterinary Surgeons in 1994. He was appointed as full professor to the Chair of Equine Musculoskeletal Biology in 2007 and is now mainly involved in research with focus areas articular cartilage, tendons and biomechanics. He became Head of the Department of Equine Sciences of the Faculty of Veterinary Medicine of Utrecht University in 2012.

René van Weeren has been a supervisor of 27 PhD students, who have obtained their degree in the past years and currently supervises 10 PhD students, who will be graduating within the next few years. He is an associate editor of Equine Veterinary Journal, member of the editorial board of The Veterinary Journal, and member of the scientific board of several others. He has been, or is, guest editor of various Special Issues or Supplements of a variety of scientific journals. He has been external examiner for PhD students abroad at various occasions in Belgium, the UK, France, Austria, Sweden, Norway and Finland. He is author or co-author of more than 250 peer-reviewed scientific publications and has contributed various chapters to a variety of text books, among which the recent editions of Equine Locomotion (Eds: Back and Clayton), Equine Sports Medicine and Surgery (Eds: Hinchcliff, Kaneps and Geor) and The Athletic Horse (Eds: Hodgson, McGowan and McKeever).

Harrie Weinans. Utrecht, the Netherlands

Non-Invasive techniques for studying macrophages in joint inflammation.

Folate-based radiotracers have been used in patients with cancer and inflammatory diseases to visualize folate receptor expressing cells using PET or SPECT techniques. Activated macrophages express folate receptor beta (FR-β) and this allows specific imaging of these cells in-vivo. From previous work using SPECT imaging to visualize folate receptor expressing macrophages in both animal models and in patients with OA we know that macrophages are present in OA affected joints. However, it remains unclear what role these macrophages play in the different stages of OA and whether their role can be influenced by specific targeting.

In Wistar rats osteoarthritis was induced using a low dose of intra-articular papain injections in one knee joints combined with exposure to a moderate exercise protocol. After six weeks and twelve an in vivo folate SPECT/CT scan and micro-CT analyses were performed. Macrophages from human peripheral blood monocytes were cultured (7 days) in the presence of GM-CSF (M1 proinflammatory phenotype) or M-CSF (M2 anti-inflammatory phenotype). Subsequently the macrophages were treated with LPS, cytokines (IL-4, IL-10, IFN-y) or a corticoid steroid (triamcinolone acetonide, 1ug/ml). Folate receptor beta (FRβ) as well as other macrophage marker expressions were measured using FACS.

Intra-articular injections with triamcinolone strongly enhanced FRβ+ macrophage activation and fully prevented osteophyte formation. There were no beneficial effects of the corticoid steroid against cartilage degradation or subchondral bone sclerosis. In in-vitro cultures triamcinolone strongly induced the monocyte-macrophages differentiation towards CD163+ and FRβ+ cells, specifically in GM-CSF stimulated (M1) cultures Addition of triamcinolone to M-CSF stimulated (M2) monocytes showed enhanced IL10 expression on mRNA level.

In conclusion triamcinolone enhanced FRβ expression in monocytes that were induced to macrophage differentiation. The triamcinolone injections stimulate synovial macrophage activation and triggers the macrophages towards a more anti-inflammatory subtype.

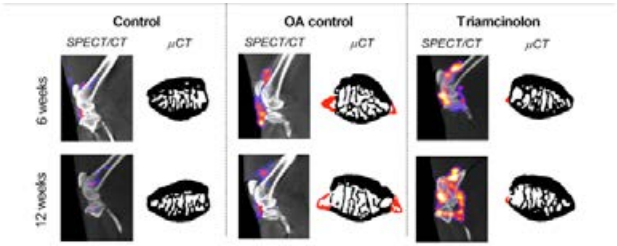

Figure 1: Macrophage activation determined after injection of 111In-DTPA-folate using SPECT/CT in Papaine induced osteoarthritis (OA) combine with moderate excercise. Representative sagittal SPECT/CT images of knee joints from representative animals per experimental group. CT images shown in black and white were used for anatomical reference, the SPECT images are shown in color. Patellar bone is shown with osteophyte formation highlighted in red.

Biography

Harrie Weinans received his PhD from the Radboud University Nijmegen in 1991 on a topic related to orthopedic implant fixation and bone regeneration. In 1994 and 1995 he was postdoc at Rush Medical Center (Chicago, USA). His current research focus involves the physical and mechanical aspects of musculoskeletal tissues in relation to the biological homeostasis in these tissues needed for proper functioning. Most of his work relates to osteoarthritis and joint homeostasis, in particular of the proteoglycan and collagen breakdown and synthesis. His research group studies joint loading, activity and (over)weight in relation to joint shape formation and cartilage degeneration. In animal models detailed imaging methods are used that enable to investigate the interaction between overloading, cartilage breakdown and aspects related to joint homeostasis such as macrophage activation in the joint. A major goal of his research is to investigate the degenerative processes of the joint and find methods to counterbalance this degeneration or even induce appropriate regeneration after the tissue is already diminished. Harrie Weinans was professor of Mechanobiology at Erasmus Medical Center from 2004 until 2013 and currently is professor of Tissue Biomechanics at TU Delft and University Medical Center Utrecht.

Jaume Bacardit. Newcastle, UK

Machine Learning for Knowledge discovery from omics/clinical OA data

Data analytics methods are becoming a bottleneck for the extraction of useful knowledge from healthcare-related data. On the one hand, classic data analysis techniques can only identify the (now scarce) "low-hanging fruits". On other hand, the state-of-the-art machine learning methods typically employ very reductionist strategies to cope with biomedical data, greatly dampening their translational potential. For the past few years we have been investigating in methodologies for the extraction of useful knowledge from biological/biomedical data by analysing and exploiting the structure of machine learning models. In this talk I will show how we can apply these methodologies to identify reduced biomarker signatures and infer functional networks from Osteoarthritis-related omics and clinical datasets.

Biography

Dr. Jaume Bacardit is Senior Lecturer in Biodata Mining at the School of Computing Science of Newcastle University his research interests include the development of machine learning methods for large-scale problems and their application to challenging problems, mostly involving biological data.

The main focus of his applied research on biological data is knowledge discovery: analyzing the structure of the data mining models to discover useful knowledge, such as (panels of) biomarkers or functional networks and in this way bring the data mining process closer to the domain experts. His methods have been applied to a variety of biological/biomedical domains: the proces of germination in plants, cancer in humans or osteoarthritis both in humans and model organisms and multiple data-generating biotechnologies: transcriptomics, proteomics, lipidomics, etc. Currently Bacardit leads data mining efforts

of the D-BOARD FP7 project that has as objective the discovery of novel biomarkers for Osteoarthritis. This project generates data of many different types, and the data mining is central to integrate all this heterogeneous information and distill biomarkers with diagnostic and prognostic power. Bacardit will also lead the data mining work of two recently awarded projects: apprOAch (Biomedical project funded by the EU under the Innovative Medicine Initiative scheme) and CRITICaL (Project on cybersecurity, funded by the UK Engineering and Physical Sciences Research Council). Bacardit has more than 50 refereed international publications, 1600+ citations, has given 10 invited talks and co-edited two books.

POSTER PRESENTERS

Andrea Darling..... Surrey, UK

Jin Luo..... Roehampton, UK

Csaba Matta..... Surrey, UK

Brigitta Matta-Domjan ..... Surrey, UK

Taryn Smith..... Surrey, UK

Laura Tripkovic ..... Surrey, UK

Louise Wilson..... Surrey, UK

Saskia Wilson-Barnes..... Surrey, UK

POSTER PRESENTERS

Andrea Darling, Surrey, UK

Increased distal radial trabecular volumetric bone mineral density with higher vitamin D status in UK dwelling postmenopausal South Asian women

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2. Specialist Assay Laboratory (Vitamin D) and Manchester Academic Health Sciences Centre, Manchester Royal Infirmary, Manchester M13 9WL, UK.

There has been little research assessing the relationship between 25-hydroxyvitamin D, (25(OH)D) and volumetric Bone Mineral Density (vBMD) in South Asians, with no data in older South Asian women. This work assessed whether serum 25(OH)D is associated with bone geometry in postmenopausal South Asians and a comparison group of Caucasian women.

In summer 2010, 18 South Asian and 48 Caucasian women (aged 58 to 75 years) had pQCT scans (Stratec X2000L) undertaken of the radius (4% and 66% sites) and tibia (4%, 14% and 38% sites). Fasting blood samples were obtained for assessment of serum 25(OH)D. Partial correlations assessed the relationship between 25(OH)D and bone geometry, adjusting for body mass index (BMI).

At the 4% (distal) radius site, in Caucasians, there was a positive correlation between 25(OH)D status and bone mineral content (BMC) ($r=0.404$ $p=0.008$), total area ($r=0.327$ $p=0.035$), and trabecular area ($r=0.327$ $p=0.034$). Asians showed a significant positive relationship between 25(OH)D concentration and trabecular vBMD ($r=0.547$ $p=0.035$) but no significant correlation between vitamin D status and any tibial bone parameter ($p>0.05$). However, at the tibial 38% site in Caucasians, there were significant correlations between 25(OH)D concentration and bone mass ($r=0.304$ $p=0.050$). There were also significant positive associations between 25(OH)D and cortical area at the 14% site ($r=0.353$ $p=0.022$) and between 25(OH)D and trabecular area at the 4% site ($r=0.336$ $p=0.029$).

Overall, in Caucasians vitamin D status appears to be positively correlated with radial and tibial bone mass and size. In South Asians, vitamin D status appears to be positively correlated with distal radial trabecular density. Further analysis is underway to assess possible explanations for these varying relationships between vitamin D status and bone geometry by ethnicity and bone site.

Jin Luo. Roehampton, UK

Difference in loading intensity of physical activity between middle-aged men and women

J Luo, J Chahal
University of Roehampton, London, UK

Physical activity is a recommended measure to prevent osteoporosis and sarcopenia. We have developed a novel method that can objectively assess the intensity of mechanical loading during everyday activities using an accelerometer attached to a person's trunk. Loading intensity at a given time is defined as the product of the magnitude and rate (frequency) of acceleration signals. The aim of this study was to investigate the difference in loading intensity of physical activity between middle-aged men and women.

Thirty three healthy women (mean age= 49.8 +/- 7.5 years) and twenty five healthy men (mean age = 49.9 +/- 7.3) were recruited. They were requested to wear an accelerometer for a period of 10 hours (from 9am to 7pm) so that their loading intensities could be recorded. On a separate day their knee extension strength was measured using an isokinetic dynamometer and bone mineral density (BMD) at the heel by an ultrasound bone scanner. The recorded 10-hour raw acceleration data were exported to computer and analysed by a customised MATLAB programme. The loading dose of physical activity was calculated at four intensity categories – very light, light, moderate, and vigorous (intensities of < 5BW/s, 5-10 BW/s, 10-15BW/s and >15BW/s) and for three frequency bands (0.1-2, 2-4, and 4-6 Hz). Independent t-test was used to examine the difference in mechanical loading, muscular strength, and BMD.

Calcaneous BMD and muscular strength were significantly different between men and women ($p<0.01$). There was no significant gender difference in duration or loading dose of physical activity spent in any loading intensity category ($p>0.05$). However, middle-aged men tended to have higher loading dose in vigorous activity ($p<0.1$).

It is concluded that loading intensity of physical activity does not differ between middle-aged men and women.

Csaba Matta, Surrey, UK

Transcriptomic and proteomic analysis of a chondrogenic progenitor cell line derived from osteoarthritic cartilage

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Osteoarthritis (OA) is one of the ten most disabling musculoskeletal conditions in developed countries. As there is currently no effective treatment for OA, there is a pressing need for the development of novel therapeutic strategies to preserve articular cartilage. In order to develop such methods a better understanding of normal and OA chondrocyte physiology is necessary. As cells in OA cartilage reside in a significantly altered, inflammatory extracellular matrix, it is logical to assume that these cells may be characterised by a transformed "membranome" – an assembly of plasma membrane ion channels and transporters. This work focuses on the analysis of mRNA and protein expression of plasma membrane proteins in a human chondrogenic cell population from OA knee cartilage with the help of transcriptomics and proteomics. Samples with enriched cell surface proteins were prepared using EZ-Link Sulfo-NHS-SS-Biotin and analysed using the short GeLC-MS/MS method on a Bruker Impact HD instrument. Approximately 25% of the proteins identified were plasma membrane proteins, which support the efficacy of the biotinylation method. In total, different 78 plasma membrane proteins were identified, some of which play important roles in chondrocyte cell biology, such as integrins, CD44, or PMCA4. To further enhance the efficacy of membrane protein enrichment, we are considering combining the biotinylation method with a Triton X-114 phase separation protocol. Correlating ion channel expression with altered function during the development of OA will provide a better understanding of pathophysiological mechanisms controlling disease progression and will contribute to the understanding of cartilage degeneration.

Brigitta Matta-Domjan. Surrey, UK

Carbon nanotubes: a promising tissue engineering approach for ex vivo cultivation & differentiation of normal & neoplastic human stem cells

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*Those two authors are equal contributors to this work

Development of biocompatible materials has great potential in biomedical engineering both for in vitro studies as well as for in vivo applications. Two- and three-dimensional carbon nanotube (CNT) substrates

imitating and providing an extracellular matrix-like structure are promising constructs as cell-supporting scaffolds. Lately, they have received considerable interest in tissue engineering cellular responses to nanoscale stimuli need to be understood.

Here, we present the preliminary results on the effect of CNT-based scaffolds on the proliferation and space arrangement of primary canine chondrocytes (PCCs) and ASPC-1 pancreatic cancer cell line. We aim to develop scaffolding materials for the in vitro cultivation of normal and neoplastic cells with the ultimate objective of using them for applications such as tissue implants in cartilage repair and tissue regeneration after surgical intervention.

In the proposed studies we aim to use an aerogel network of CNTs that has been draw from a vertically aligned array as a synthetic substrate for the growth and alignment of primary canine chondrocytes and ASPC-1 pancreatic cells. This aerogel consists of CNTs that are aligned parallel to the major axis of the CNTs, they have exceptionally low densities, are electrically and thermally conductive whilst maintaining very high tensile strength and elasticity. We are studying the cell growth, adhesion, morphology, viability and metabolism of cells seeded onto CNT substrates.

Preliminary results to date have revealed that PCCs and ASPC-1 cells are capable of proliferating on CNT-based scaffolds, although the viability of both cell types seem to be slightly decreased in comparison to the conventional 2D cell culture. Moreover, our nanosubstrates are able to induce directional cell growth of PCCs and ASPC-1 via aligning cells along CNTs. The latter is essential for in vivo application of nanosubstrates in tissue regeneration.

We are currently extending this study on CNT-based expansion of haematopoietic stem cells and differentiation towards red blood cells.

Taryn Smith. Surrey, UK

Associations between dietary intakes of vitamin d and calcium and bone parameters in UK male and female adolescents aged 14-18 years

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A large proportion of bone mass is attained during adolescence, with approximately 80-90% of peak bone mass achieved by late adolescence. The aim of this analysis was to investigate associations between dietary intakes of vitamin D and calcium and bone parameters in male and female adolescents (14-18years) recruited onto a 20 week vitamin D supplementation randomised controlled trial. A Food Frequency Questionnaire was completed by adolescents (n=113) at baseline to assess habitual intakes of vitamin D and calcium. A peripheral quantitative computed tomography (pQCT) scan of the forearm was undertaken to measure bone density at the 4% and 66% radial sites. Males (n=46) had significantly greater intakes of calcium than females (n=67) (mean 1143mg ±598 vs. 884mg ±512 respectively, p=0.004). However, vitamin D intakes were not significantly different (mean 4.8µg ±3.4 and 4.2µg ±2.9

respectively). Vitamin D intakes positively correlated with bone mass (r=0.16, p=0.096) and total cross sectional area (CSA) (r=0.20, p=0.038) at the 4% radial site. Calcium intakes were positively correlated with bone mass (r=0.31, p=0.001) and total CSA (r=0.33, p<0.001) at the 4% site. No correlations were found between intakes and any other bone parameters. When comparing the associations with vitamin D between genders, males tended to have stronger correlations (bone mass: males r=0.35, p=0.018; females r=0.25, p=0.84; CSA: males r=0.25, p=0.09; females r=0.13, p=0.29). A similar pattern was identified for calcium intakes (bone mass: males r=0.39, p=0.007; females r=0.06, p=0.62; CSA: males r=0.22, p=0.14; females r=0.12, p=0.36). Therefore, it can be seen that in this group of adolescents dietary intakes of vitamin D and calcium were associated with bone size but not bone density, and this association was stronger in males compared to females. Further analysis will investigate associations between physical activity and bone parameters to assess relative contributions of activity and diet to bone density.

Laura Tripkovic. Surrey, UK (1)

Associations between volumetric bone mineral density and dietary intake in South Asian and Caucasian women: preliminary analysis of the D2-D3 Study

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The necessity of sufficient vitamin D in order to maintain skeletal health is well established. Few foods naturally contain vitamin D; thus the majority of the UK population rely on sun exposure during the spring/summer months for endogenous vitamin D production.
The aim of this study was to draw on data obtained from the D2-D3 Study (a double blind, vitamin D RCT) to evaluate potential associations between skeletal health and dietary intake (particularly vitamin D) in South Asian (SA) and Caucasian (CA) women.
A cohort of 335 healthy women (CA n 245, SA n 90), mean age - 43.6±12.3 years; BMI - 24.1±3.8kg/m2 were recruited to the D2-D3 Study. At the baseline visit, anthropometrics and a peripheral quantitative computed tomography (pQCT) scan of the radius were completed. Subjects completed a four-day record of their dietary intake.
The pQCT data indicated that CA women had significantly greater bone mass and area (P<0.04) at the distal radius. Yet at the same site, the SA women had significantly greater volumetric bone mineral density (vBMD, P<0.009). Dietary analysis indicated that for an average daily intake, the CA and SA women consumed similar amounts of energy and vitamin D; however the CA women consumed significantly greater quantities of potassium, calcium, magnesium, phosphate and alcohol (P<0.05).
The comparison of tertiles of vitamin D intake with vBMD found no clear associations. Nor were there any correlations between vitamin D intake and vBMD. Further analysis of these diet/skeletal health associations are underway, particularly with respect to the higher vBMD detected in SA women despite a lower intake of the nutrients required for optimum skeletal health.

Laura Tripkovic. Surrey, UK (2)

Baseline 25-hydroxyvitamin D influences the total change in 25-hydroxyvitamin D in response to 15µg/600IU daily vitamin D2 or D3.

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Considerable attention has focused on the optimum dose of vitamin D required to achieve/maintain a healthy vitamin D status (25OHD), with less regard for whether there may be individual variability dependent on baseline 25OHD levels. This analysis aimed to examine response to vitamin D2/D3 within and between groups categorised by individuals' baseline 25OHD.

The D2-D3 Study is a randomised-controlled trial investigating the comparative efficacy of 15µg/600IU of vitamin D2 vs D3. Participants were assigned to D2 or D3, or placebo products daily for 12 weeks, and they gave a fasted blood sample at baseline, week 6 and week 12. A total of 291 healthy women successfully completed the study, of which 118 and 114 were assigned to the D2 and D3 groups, respectively. Of those assigned to the D2/D3 groups, baseline 25OHD was <25nmol/l in 13/15%; 25-49.9nmol/l in 38/31%; 50-74.9nmol/l in 30/35% and >75nmol/l in 19/19% of the participants.

There was a significant difference between change in 25OHD (Δ25OHD) in both the vitamin D2 and D3 groups, between those with a baseline 25OHD <25nmol/l compared to those with baseline 50-74.9nmol/l and >75nmol/l (D2: +30.4nmol/l compared to +12.9 and -11.2nmol/l respectively, D3: +48.4nmol/l compared to +24.5 and +15.1nmol/l respectively, $p<0.001$ in all cases), and those with a baseline 25OHD of 25-49.9nmol/l compared to those with baseline 50-74.9nmol/l and >75nmol/l (D2: +21.7nmol/l compared to +12.9 and -11.2nmol/l respectively, $p<0.026$; D3: +39.4nmol/l compared to +24.5 and +15.1nmol/l respectively, $p<0.007$).

This study provides evidence to show that there is individual variability in response to vitamin D2 or D3 dependent on baseline 25OHD, suggesting a non-linear relationship between intake and increase in 25OHD, which warrants further investigation in order to inform cost effective supplementation strategies.

Louise Wilson. Surrey, UK

Is vitamin D3 more effective than vitamin D2 in raising 25(OH)D status in women with osteoporosis and osteopenia?

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Establishing strategies to improve the vitamin D status in the UK is vital with the implications of a low vitamin D status known to include poor bone density. Our objective was to measure changes in serum 25(OH)D in response to 15µg/d vitamin D2 and D3 supplementation, in those with osteopenia and osteoporosis compared to those with normal bone density to investigate whether differing strategies may be needed.

Participants were recruited as part of the D2-D3 Study, and randomised to receive either 15 µg vitamin D2 (D2) or vitamin D3 (D3) daily for 12 weeks. 25(OH)D was measured at baseline and week 12. Participants were characterised as having osteoporosis/osteopenia (O) or normal bone density (N) based on a T-Score from a peripheral quantitative computed tomography (pQCT) scan of the radius. These analyses are based on four treatment groups: D2N (n39), D3N (n31), D2O (n79) and D3O (n83).

At baseline, there were no significant differences in 25(OH)D status between the four treatment groups (D2N: 52.21±36.0nmol/L, D3N: 46.09±26.27nmol/L, D2O: 55.67±28.56, D3O: 57.05±28.02nmol/L). In response to the 12-week vitamin D intervention, all four treatment groups had a significant increase in 25(OH)D status, with a higher percentage increase seen in the D3 groups (D3N: 108.86±131.41%, D3O: 103.13±139.16%) than the D2 groups (D2N: 74.09±96.84%, D2O: 46.16±63.22%). At 12-weeks the 25(OH)D status of the D30 group was significantly higher than all three other groups ($p<0.001$).

This study suggests that although both vitamin D2 and D3 significantly improve 25(OH)D status, regardless of bone density, those with osteoporosis or osteopenia may respond better to supplementation with vitamin D3.

Saskia Wilson-Barnes, Surrey, UK

Differences in bone metabolism markers in females aged 8-17 years undertaking high-impact loading physical activity.

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Weight-bearing physical activity is an important determinant of bone health across the lifespan, with adolescence being a critical time for peak bone mass (PBM) development. The aim of this study was to investigate the long-term influences of impact-loading exercise on bone turnover in young females. As part of a previous 3-year study on nutrition and bone mass* in 43 competitive gymnasts (G) and 50 controls (C) aged 8-17 years, blood and urine samples were collected at baseline, 6, 12 and 24 months for subsequent measurement of bone formation and resorption markers. Maturity status was controlled for by assessment of peak height velocity (PHV). The results showed an increase in all markers at mid-puberty (±1 year of PHV) in both groups. Longitudinally, G had significantly lower bone resorption in the early pubertal years (ANCOVA, $P<0.05$). However, by late puberty (±3 year of PHV) bone formation and resorption was higher in this group ($p<0.05$). The bone markers were strongly associated with 1-yr change in total height (r 0.47-0.76, $p<0.001$) and leg length, but weakly with 1-yr change in sitting height, TB BMC and TB BMD. High intensity, impact-loading physical activity alters bone turnover in young trained girls, with demonstration of lower bone resorption in early puberty and higher bone formation and resorption in late puberty. Although the markers were found to better reflect statural growth than growth in bone mass, these results may in part help to explain the well-documented findings of increased bone mass in physically active girls. Further research is warranted in this group, particularly with respect to vitamin D status and its role in the achievement of PBM.

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