Osteoarthritis and Cartilage 28 (2020) S15–S19

Osteoarthritis and Cartilage

Abstracts from Invited Speakers

I-1
FROM GUT TO OA

M.J. Zuscik. *Univ. of Colorado, Anschutz Med. Campus, Aurora, CO, USA*

Purpose: As well all know, osteoarthritis (OA) is a disease of diarthrodial joints that leads to joint degeneration, inflammation, and pain. OA is the most prevalent disabling disease globally. Despite efforts to develop a disease modifying treatment, the only accepted and available clinical approaches involve palliation. While many factors contribute to the development of OA, the gut microbiome has recently emerged as an important pathogenic factor in OA initiation and progression, particularly in the context of obesity. This presentation will provide an up-to-date review of the literature regarding the link between the gut microbiome and OA.
Literature and Data to be Discussed: Studies showing correlations between serum levels of bacterial metabolites and joint degeneration were the first links connecting a dysbiosis of the gut microbiome with OA. Further investigations have demonstrated that microbial community shifts induced by antibiotics, a germ-free environment or high fat diet are important underlying factors in joint homeostasis and OA. In fact, key pro-inflammatory species have been linked to joint pain in humans with knee OA. Data will also be presented that suggests the action of 'joint protective' nutraceuticals may be via shifts in the gut microbiome. It follows that strategies to manipulate the microbiome have demonstrated efficacy in mitigating joint degeneration in OA, and may represent a new strategic approach to address disease modification for this disease.
Summary: While role of the microbiome in OA is an area of intense study, no clear mechanism of action has been determined. Increased understanding of how the two factors interact may provide mechanistic insight into OA and lead to disease modifying treatments.

I-2
WHAT RARE DISEASES CAN TELL US ABOUT OA

J.A. Gallagher. *Univ. of Liverpool, Liverpool, United Kingdom*

Purpose: Rare cartilage diseases are a neglected area of study in osteoarthritis (OA). This presentation puts forward the proposition that more emphasis on studying rare cartilage syndromes could lead to accelerated progress in understanding OA and age-related joint degeneration. OA is one of the major causes of disability globally, yet despite the resources which have been channelled into research, there are no current therapies for OA and only a limited number of biomarkers.
Methods: Research on the extreme phenotypes observed in rare diseases can help elucidate the pathogeneses of more common disorders, a phenomenon recognised by William Harvey as long ago as the 17 th century. Harvey wrote to a colleague "*⋯ 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*". In monogenic disorders, the phenotypes are often very severe and disease progress is rapid making it easy to identify pathological changes, both structural and biochemical. Several therapies for common diseases, including the blockbuster drugs statins and bisphosphonates, were discovered in part through the study of rare syndromes.
Results: Rare disease research is making a significant contribution to understanding bone turnover and to the development of new therapeutic agents to regulate bone formation and bone resorption. Whilst the potential impact on OA of studying rare cartilage syndromes has been less explored, recent research has revealed new insights into OA disease mechanisms. Analysis of rare mutations responsible for chondrodysplasias has identified genes such as GDF5, which plays a key role in skeletal development. Polymorphisms in this gene are associated with OA susceptibility. Mutation of the ANKH gene in chondrocalcinosis has highlighted the role that this gene plays in the physiological and pathological mineralisation of cartilage. The expression of ANKH, which codes for a pyrophosphate transporter is known to be dysregulated in OA. Investigation of the rare autosomal recessive disorder CACP has revealed the disease-causing mutation in the PRG4 gene which codes for the secreted mucin-like proteoglycan, lubricin.Alkaptonuria (AKU) is an autosomal recessive disease of tyrosine metabolism that inevitably leads to early onset, aggressive arthropathy. Joint destruction in AKU is caused by the deposition of ochronotic pigment in cartilage, but there are several parallels with the pathophysiology of OA. Studies on tissue samples from patients with AKU, and from mouse models of the disease, have revealed previously unrecognised microanatomical and biochemical changes in joints which have been subsequently detected in human OA. These include early changes in the integrity of collagen fibrils, the role of calcified cartilage in the initiation of OA, thinning and cracking of the subchondral plate and the formation of novel microanatomical structures including trabecular excrescences, templated by adipocytes, and high density mineralised protrusions (HDMPs). All these features are abundant and easily recognisable in the severe phenotype of AKU but have subsequently been found in common OA, where they contribute to joint destruction.
Conclusions: Studying rare cartilage diseases with extreme phenotypes can help elucidate pathophysiological mechanisms in OA.

I-3
APPLICATIONS OF RAPID MRI, HOW TO IMPROVE PATIENT CARE

B.A. Hargreaves. *Stanford Univ., Standord, CA, USA*

Magnetic resonance imaging (MRI) is routinely used in Osteoarthritis (OA) assessment, both clinically and in research studies. Numerous different MRI contrast mechanisms highlight abnormalities or changes over time, with increasing tendency toward quantitative techniques and true 3D imaging. Scan protocols can include multiple contrasts, often resulting in exam protocols of 20-30 minutes for clinical imaging, and even longer for research studies, which can limit utilization or study sizes due to cost. Rapid MRI protocols are being explored using only a few scans, to offer exam times in just 5-10 minutes, and including both knees. This has potential to rival X-ray imaging, as it can offer comprehensive joint information in a comparable time and perhaps at a comparable cost. Benefits include scanning many more subjects in studies, acquiring quantitative information in both knees in patients, and being able to scan at earlier stages of disease. Combined with advances in data science, rapid quantitative MRI protocols could offer much better understanding of the onset and progression of different OA

1063-4584/$ – see front matter