involving many hundreds of genes. For chondrocytes to maintain a healthy cartilage tissue requires the sustained function of many cellular processes and any decline in performance may weaken the tissue and lead to pathology. These changes may arise because of inherited susceptibilities and their interaction with environmental challenges, such as trauma, obesity and ageing.
There is much evidence that many changes occur in chondrocytes during ageing. In OA there is evidence of an age-related increase in ER stress, which may mark a decline in secretary pathway function in chondrocytes and could restrict their ability to maintain the tissue. There is also evidence of increased apoptosis in OA, which may suggest that there is an age-related decline in chondrocyte threshold for survival. This may extend to pathways, such as those involving DNA repair, resistance to oxidative stress, which may result in accumulated DNA and protein damage. It may also apply to new areas of chondrocyte biology, such as circadian clock genes, which have been detected in chondrocytes (Boot-Handford, Qing-jun Meng, personal communication). Many circadian clocks in other biological systems show age-related changes and such changes in chondrocytes may lead to impaired function. Any of these factors may be potentially damaging, because in cartilage, in contrast with most other tissues, there are no means by which dead or poorly performing cells can be replaced. It is this feature that makes chondrocytes special and cartilage the tissue in the joint most at risk of irreversible damage and loss.

I-19
NEW GENOMIC TECHNOLOGIES FOR THE STUDY OF OA

I. Meulenbelt. *LUMC, Leiden, Netherlands*

Osteoarthritis (OA) is a prevalent, disabling joint disease with a considerable, but complex, genetic component. In order to dissect underlying mechanisms of OA, many researchers have applied genetic genome wide approaches or, to explore the dynamic state of OA affected cartilage, micro array RNA expression profiling. Although robust findings have been found, major challenges remain; current OA susceptibility SNPs explain only a small part of the heritability, whereas, micro-array expression techniques have shown to have only a limited ability to catalogue and quantify the transcriptome. Given the small attributable risk of current OA susceptibility SNPs, researchers have come to the presumption that there may be many, yet undetected, rare variants and/or unconsidered non-genetic variation that could influence the complex etiology of OA.
The introduction of high-throughput next generation sequencing technologies has revolutionized both genomic and transcriptomic research. It allows whole genome and exome DNA sequencing in addition to sensitive RNA analyses through cDNA sequencing. As such, it eliminates a large part of the posed challenges. Considering the non-genetic variation, especially the epigenetic variation appears to be relevant. Epigenetic marks as reflected by methylation of cytosine's in cytosine-guanine (CpG) dinucleotides are involved in processes that require a stable control of gene expression or a selective gene-silencing. Loss of epigenetic control may result in differential gene expression and may underlie complex traits. Up until now, however, the studies aiming to explore these non-genetic variations were performed with inadequate genome coverage or failed to measure in the relevant (diseased) tissue. Recently for DNA methylation, a new technology has become available that allows high throughput typing of around 500,000 metylation sites, covering around 99 percent of RefSeq genes.
Together, these new genomic technologies may provide important additional biological insights into molecular and cellular events commencing OA onset.

I-20
CLINICAL PAIN SEVERITY AND EXPERIMENTAL PAIN SENSITIVITY IN OSTEOARTHRITIS

Y.C. Lee. *Brigham and Women's Hosp., Boston, MA*

Pain is the most common presenting symptom of osteoarthritis and an important outcome in most osteoarthritis intervention trials. However, the causes of pain among osteoarthritis patients are not well-understood, and studies of pain mechanisms have been limited. To date, most studies have relied on visual analog scales of overall pain or patient-reported pain at joint sites, but these measurements are subjective and prone to bias. Although osteoarthritis is often defined structurally by cartilage loss and joint space narrowing, population-based studies have indicated that the association between joint space narrowing and patient-reported pain is weak. Recent studies, however, suggest that correlations between structural changes and pain may be masked by other factors, such as central pain processing mechanisms, which differ between patients. To examine pain mechanisms, some studies have utilized quantitative sensory testing techniques, which rely on the application of defined, noxious, experimental stimuli to determine pain threshold and tolerance levels. These studies suggest that, compared to pain-free controls, osteoarthritis patients are more sensitive to experimental noxious stimuli at both joint and non-joint sites, indicating diffuse hyperalgesia, characteristic of central pain syndromes. Studies using quantitative sensory testing methods and functional neuroimaging have also indicated that osteoarthritis patients have impairments in conditioned pain modulation, also known as descending analgesia or diffuse noxious inhibitory controls. This talk will give an overview of the study of pain mechanisms in osteoarthritis, focusing on studies of experimental pain sensitivity in osteoarthritis patients, and the implications of these studies for future research and for the development of pain management strategies in osteoarthritis.

I-21
NEW GUIDELINES ON PUBLISHING ANIMAL STUDIES

C.B. Little. *Kolling Inst. of Med. Res., Univ. of Sydney, St Leonards, Australia*

Animal models are powerful research tools that provide a critical step not only in furthering our understanding of disease pathogenesis and potential therapeutic intervention, but also they contribute significantly to the "translatability" of drug discovery projects toward clinical realization. It is scientifically incumbent upon researchers to ensure that their experiments are well designed, controlled, powered, analyzed and reported. In the case of research involving animal models, this is true not only from the perspective of good scientific practice but also to fulfill our responsibility for the appropriate and ethical use of animals i.e. implementing the "3Rs". A critical component of reduction and refinement is ensuring that animal studies are appropriately planned, evaluated, and reported. Poor reporting is as problematic as poor experimental design in diminishing the value and validity of any scientific research. Recent reviews have highlighted the deficiencies in reporting in many studies using animal models for a variety of diseases, and those for osteoarthritis (OA) are no exception.
The ARRIVE guidelines were developed to provide a comprehensive checklist (20 items) for authors to follow (1), and their use is now a recommendation for submission of such manuscripts to OA&C. Although the emphasis is on "reporting", the ARRIVE and other guidelines, should be consulted BEFORE embarking on a study using animals, to ensure researchers control for factors that can significantly alter the experimental outcomes, and hamper or even invalidate the interpretation of the data. While applicable to all animal-based studies, the present workshop will highlight and discuss the importance of the ARRIVE guidelines as they specifically relate to OA research (2). Additionally specific issues in statistical analysis of animal studies (e.g. small "n", ordinal data etc) will be reviewed. In the long term, use of these guidelines will promote more consistent publication of animal studies, ultimately enabling better comparisons between laboratories and systematic reviews of the literature.

References

1. Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG. Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research. J Pharmacol Pharmacother. 2010 July;1 (2):94–9.
2. Percie du Sert N. Maximising the output of osteoarthritis research: the ARRIVE guidelines. Osteoarthritis Cartilage. 2012 Feb 2.

I-22
STATE OF ART IN MANAGING HAND OSTEOARTHRITIS

L. Punzi, P. Frallonardo, C. Campana, R. Ramonda. *Rheumatology Unit, Univ. of Padova, Padova, Italy*

Hand osteoarthritis (HOA) is a common disorder frequently causing pain and impaired function with subsequent reduction in health-related quality of life. Compared to other OA localisations, the management of HOA may be sometimes difficult, due to its great heterogeneity. The treatment may be influenced by many factors,