Molecular correlates of joint pain intensity in osteoarthritis

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Introduction
Chronic pain is a main symptom of osteoarthritis (OA). Patients living with OA often exhibit abnormal movement patterns primarily due to altered joint kinematics. While some of these gait changes in OA are due to deterioration in joint congruency, compensatory movement to minimize joint loading and pain is also likely to play a part. Monitoring animal movement following arthritis induction could reveal some interesting insights into pain perception. While OA is perceived as a structural disease, the underlying pathology and chronic changes occur also at a molecular level. The gene expression alterations associated with OA are important in order to understand its initiation and progression.

Materials and Methods
Intrarticular (i.a.) injection of monosodium iodoacetate (MIA, 1mg) has been used to induce OA in Wistar rats. Pain symptoms were assessed by behavioral tests: knee joint hypersensitivity test, tactile allodynia test and kinetic weight bearing (KWB), a novel instrument designed to measure time and spatial distribution of a weight bearing by each paw of a freely moving rodent. We also applied whole-transcriptome profiling study (Affymetrix GeneChip Rat Gene 2.0 ST) in order to compare data between healthy and various OA states to better understand the mechanisms underlying a disease.

Results and Discussion
KWB is a novel reliable method for pain perception studies. It allows quantification of various locomotor parameters in spontaneously moving animals. The dynamic profiles of transcriptional changes were assigned to cellular compartments of the knee joint. The presented study identified groups of co-regulated genes that share functional relationships and may play an important role in the early and intermediate stages of OA.

Conclusions
Complex description of locomotor activity of rats in MIA model of OA allows improving accurateness in rating in OA-associated pain. This might be of benefit in assessing effectiveness of novel treatments and better transitioning results from laboratory conditions to clinic. Our study provides evidence that the progression of cartilage damage is driven by complex but precise regulation of gene patterns that are induced or suppressed during various stages of cartilage damage. The results also suggest that the observed molecular alterations are located in the specific cellular compartments of the knee cartilage. The presented classification of transcriptional alterations associated with the development of cartilage degeneration provides guide the development of new therapeutic strategies.