locomotion. Ccr2 null mice were protected from these locomotion decreases, despite similar joint damage at 8 weeks post DMM, and Ccr2 null DRG did not produce MCP-1. Therefore, we sought to further investigate the expression and regulation of MCP-1 in the DMM model. The current goals were to: 1) Test whether TNF-α induces MCP-1 production in DRG cells, since it has been shown that TNF-α induces Mcp-1 mRNA in cultured DRG cell lines. 2) Analyze MCP-1 protein content in the knees of wild-type (WT) and Ccr2 null mice after DMM.

**Methods:** Knee-innervating DRG, L3-L5, were collected from 10-week old naïve C57BL/6 WT or Ccr2 null mice. Cells were isolated and cultured for 2 days in basal medium before 48 h-stimulation with 0, 25, or 100 ng/mL TNF-α; supernatants were collected for MCP-1 ELISA. Hip cartilage explants were harvested from 5-week old naïve C57BL/6 mice. Hip cartilage was used since it is not possible to culture mouse knee cartilage explants. Explants were rested overnight, stimulated with 100 ng/mL TNF-α for 48 h, and supernatants were collected for MCP-1 ELISA. DMM or sham surgery was performed in the right knees of 10-week old male C57BL/6 WT or Ccr2 null (Taconic #3736) mice. At 0, 4, and 8 weeks after surgery, whole knee joints were extracted for ELISA. At 4 and 8 weeks post surgery, DRG cells were cultured for 4 days and supernatants collected for ELISA.

**Results:** In order to test whether TNF-α is able to stimulate primary DRG cells to produce MCP-1 protein, we treated naïve WT DRG cells with TNF-α. Cultures stimulated with 25 ng/mL TNF-α produced 37-fold increased amounts of MCP-1 compared to unstimulated cells (p<0.0001); a higher concentration of 100 ng/mL TNF-α did not further increase MCP-1. This confirms earlier reports of increased Mcp-1 mRNA following TNF-α stimulation. DRG cells from naïve Ccr2 null mice responded in the same way to TNF-α.

We looked for the presence of TNF-α in cultures of DRG cells taken from WT or Ccr2 null naïve, sham, or DMM mice at 4 and 8 weeks post surgery. None of these cultures contained measurable amounts of TNF-α.

Next, we determined MCP-1 levels in whole knee joint extracts after DMM in WT and Ccr2 null mice. In WT, knee MCP-1 protein levels were elevated 4 weeks post DMM, compared to sham and naïve age-matched controls (p<0.0001); by 8 weeks post DMM, levels had returned to baseline. MCP-1 was also increased in knee extracts from Ccr2 null mice, 4 weeks after DMM, but to a lesser extent than in WT. In order to determine the potential source of MCP-1 in the knee, we began by testing whether cartilage is able to produce MCP-1. Cartilage explants stimulated with 100 ng/mL TNF-α produced 86-fold increased levels of MCP-1 compared to unstimulated explants (p=0.0008). When we looked for the presence of TNF-α in knee extracts, however, we found that DMM and naïve extracts contained similar low levels of TNF-α at 4 and 8 weeks post surgery. TNF-α levels in Ccr2 null knee extracts mirrored the WT results, with no differences at 4 or 8 weeks between DMM and naïve extracts.

**Conclusions:** These observations confirm that TNF-α can stimulate DRG neurons and cartilage explants to produce MCP-1 protein, confirming previous reports that TNF-α induces MCP-1 mRNA in these tissues. We did not, however, detect elevated TNF-α levels in the DRG or in the knee joint in situ in the DMM model at 4 or 8 weeks post surgery. It is possible that TNF-α upregulation occurs at earlier time points than the ones studied here (McNamee et al 2010 reported TNF-α mRNA in the knee at 3 days post DMM) or that other factors are driving MCP-1 production.

**FINGER LENGTH PATTERN AS A BIOMARKER FOR PRENATAL ANDROGEN EXPOSURE AND THE RISK FOR OSTEOARTHRITIS AND PAIN**


**Purpose:** The prevalence of type 3 finger length pattern, determined by a shorter 4th digit compared to the 2nd digit, is influenced by prenatal androgen exposure and has been studied previously as a biomarker for gender differences in the risk of several traits. Osteoarthritis (OA) and chronic musculoskeletal pain are both sexually dimorphic. In this study, we evaluate the association of finger length type, as a marker of prenatal androgen exposure, with the risk of osteoarthritis (OA) and chronic musculoskeletal pain.

**Methods:** Fingerlength pattern was determined in a total of 4784 participants of the prospective cohort Rotterdam Study II and III. Hand X-rays were visually classified in three different fingerlength pattern types. Logistic regression was used to analyze the association of type 3 fingerlength pattern with radiological OA of the hip, knee, and hand. A meta-analysis of previous published studies and our results was performed to evaluate the association with kneeOA. Subsequently, we studied the association of type 3 fingerlength pattern with chronic musculoskeletal pain.

**Results:** Participants with type 3 fingerlength pattern had a 64% increased risk for having handOA (OR 1.64; P-value 1.06*10^-7). This finding was independent of the severity of the disease. No associations with knee- or hipOA were found. The meta-analysis of kneeOA and type 3 fingerlength pattern showed no evidence for association, however large heterogeneity was observed, which was probably driven by differences in the OA phenotype definition. Only studies that had a clinical definition, defined by both structural damage to the knee and pain, showed an association between knee OA and fingerlength patterns. We therefore examined whether type 3 fingerlength pattern was associated with chronic joint pain and, we indeed observed that individuals with a lower 2D:4D ratio had 41% more risk for having joint pain (OR 1.41; P-value 1.4*10^-3).

**Conclusions:** Type 3 fingerlength pattern is associated with handOA, indicating prenatal androgens to contribute to the development of this disease. We additionally observed an association between low 2D:4D ratio and the risk for joint pain. Since prenatal androgens influences both the development of fingerlength pattern and the brain, a developmental cerebral susceptibility for chronic musculoskeletal pain may underlie the association found with type 3 fingerlength pattern.

**517 IN VIVO IMAGING OF NF-kB ACTIVITY AND CORRELATION TO PAIN IN A MODEL OF INFLAMMATORY ARTHRITIS**


**Purpose:** A number of pro-inflammatory and catabolic changes are observed during the progression of osteoarthritis. However, the relationship between these changes, the molecular events that regulate these changes, and the development of painful symptoms is incompletely understood. Many of the pro-inflammatory and catabolic pathways rely on the downstream effects of NF-kB activity, a key transcription factor involved in regulating inflammation. This study utilized non-invasive in vivo luminescence imaging of NF-kB activity and simultaneous measures of pain sensitivities in a mouse model of inflammatory arthritis to test for relationships between NF-kB activity and pain.

**Methods:** Transgenic mice engineered to carry cDNA for luciferase downstream of NF-kB response elements were acquired for this study (n=24, BALB/C-Tg(NF-κB A ACTIVITY AND CORRELATION TO PAIN IN A MODEL OF INFLAMMATORY ARTHRITIS)

**Abstracts / Osteoarthritis and Cartilage 21 (2013) S63-S512**

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