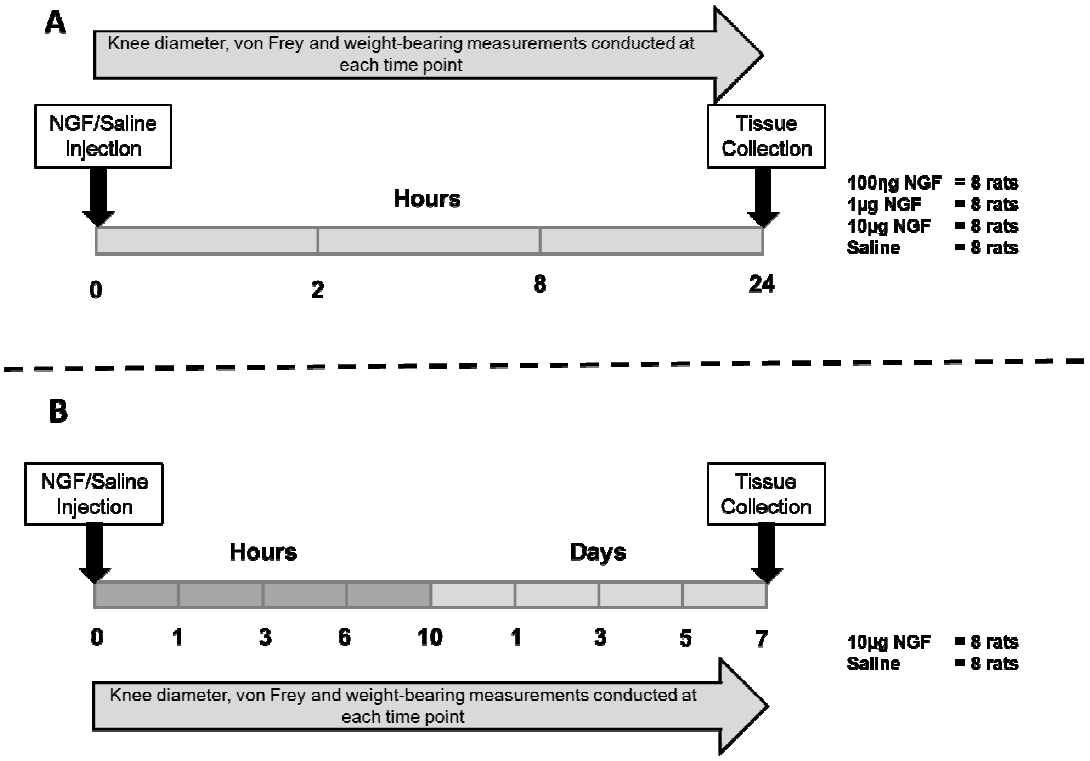
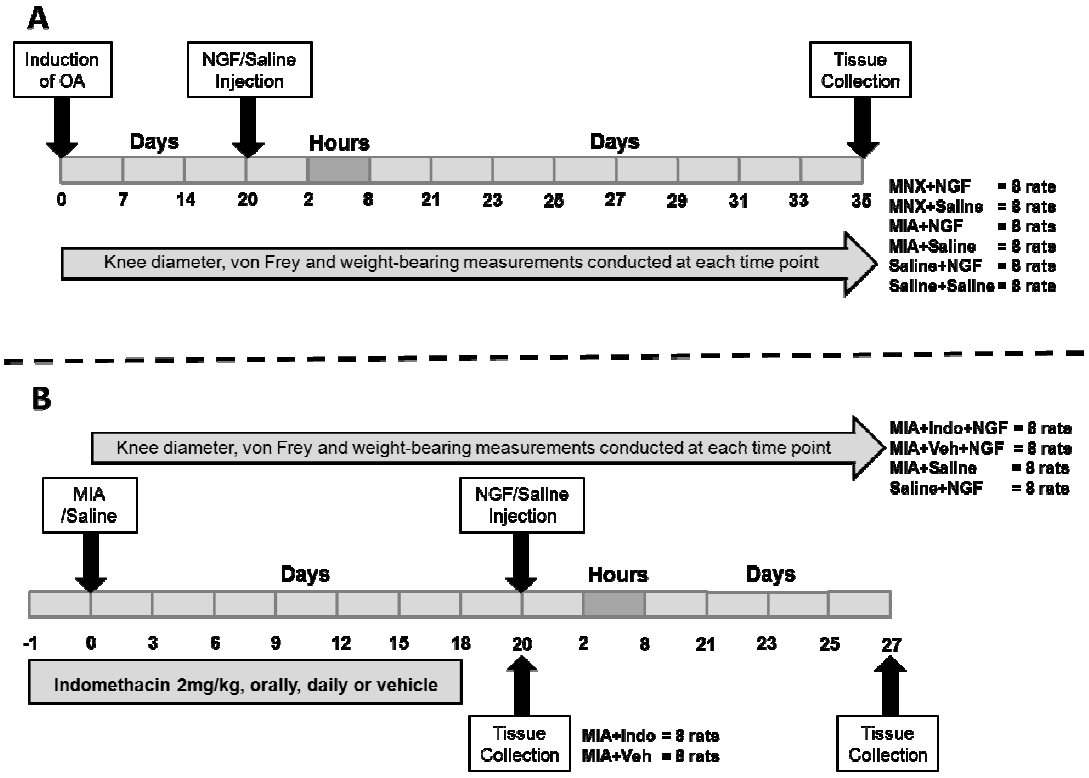
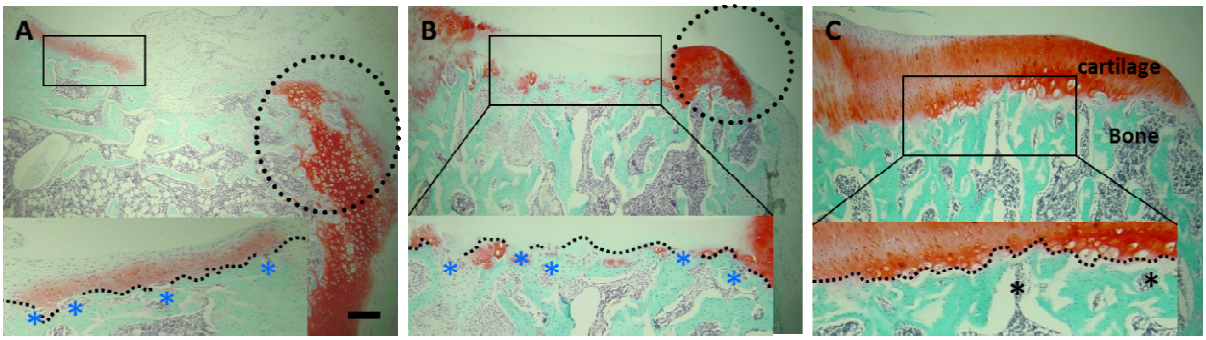
SUPPLEMENTARY FIGURES:



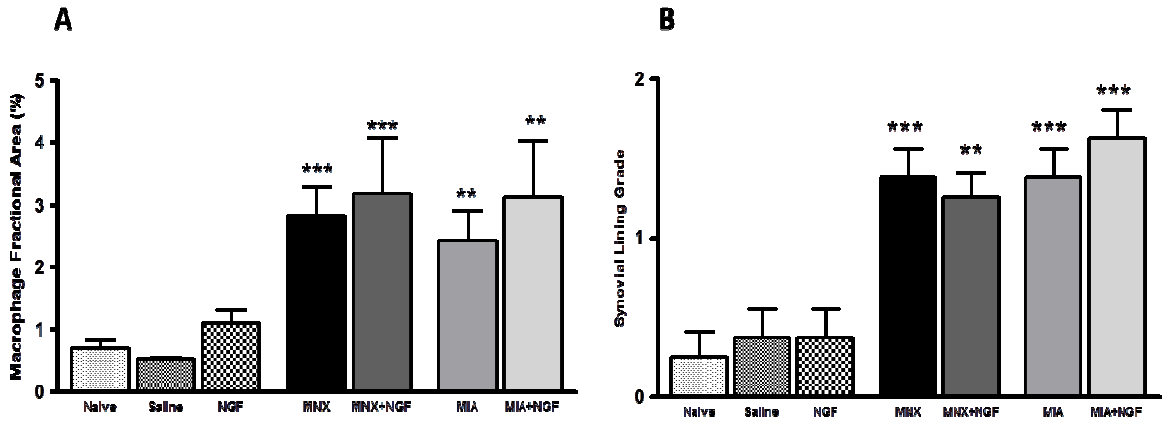
Supplementary Figure 1: Time-line and study design of the interventions in non-osteoarthritic rat knee joints. Seven week old non-osteoarthritic rats (n=8 rats/group) were initially given a single 50µl intra-articular injection of nerve growth factor (NGF) at 100ηg, 1µg, 10µg or saline control in their left knee joints on day 0 to test the dose response effect of NGF on joint swelling, pain behavior and synovitis (**A**). In a separate experiment, the highest dose of NGF at 10µg or saline control was injected in the left knee joints and the effects on joint swelling, pain behaviour and synovitis was observed for up to a week (**B**). Rats were habituated to testing equipment prior to baseline testing. Baseline measurements were taken immediately prior to intra-articular injection (day 0) and then from 1 hour onwards. Knee diameter and behavioural tests assessing changes in weight distributions and sensitivity to mechanical stimuli (von-Frey) were performed for up to one week after injection. The weight gain and general behaviour of the rats was monitored throughout the experiment. At the end of the studies, rats were killed by asphyxiation in carbon dioxide and synovia with patellae from the right and left knees were immediately harvested, embedded in OCT and snap frozen over melting isopentane.



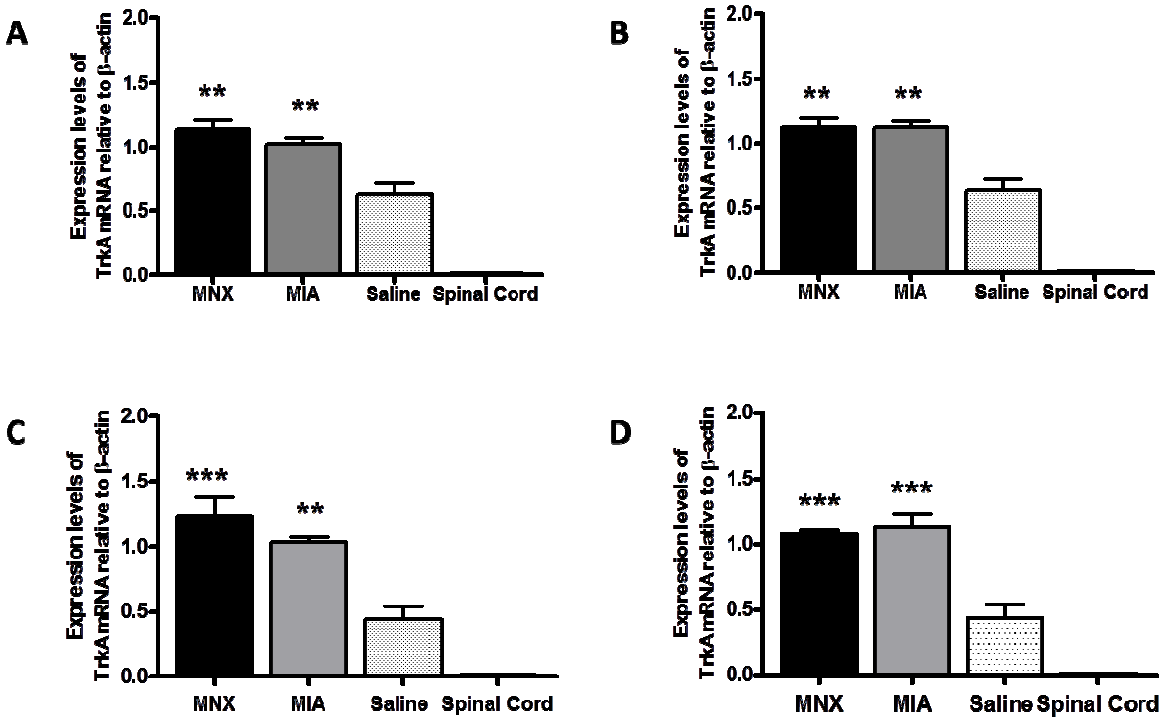
Supplementary Figure 2: Time-line and study design of the interventions in the medial meniscal transection (MNX) and monosodium-iodoacetate (MIA) models of osteoarthritis (OA). Initially the effects of intra-articular nerve growth factor (NGF) injection on OA-induced pain behaviour and pathology was assessed (**A**). In a separate study, the effects of indomethacin pre-treatment on augmented NGF-induced pain behaviour and pathology in rats with MIA-induced OA was assessed (**B**). OA was induced in the left knee joints of 7 week old rats (n=8 rats/group) by either MNX surgery or intra-articular injection of MIA (1mg/50µl saline) on day 0. Intra-articular injection (50µl) of 10µg NGF or saline control was injected in the left knee joint on day 20. Rats were habituated to testing equipment prior to baseline testing. Baseline measurements were taken immediately prior to OA induction as well as intra-articular injection of NGF. Knee diameter and behavioural tests assessing changes in weight distributions and sensitivity to mechanical stimuli (von-Frey) were performed throughout and up to the termination of the studies. The weight gain and general behaviour of the rats were also monitored throughout the studies. Pre-treatment with indomethacin (Indo) (2mg/kg, orally, daily) or saline control (vehicle [Veh]) (0.5ml) was administered from before induction of OA to day 18. At the end of the studies, rats were killed by asphyxiation in carbon dioxide and joint tissues and dorsal root ganglia harvested for processing and analysis.



Supplementary Figure 3: Histological changes (chondropathy, osteophytosis and vascular density at the osteochondral junction) of the medial tibial plateux 20 days after meniscal transection or intra-articular injection of MIA. **A**, coronal section from a MNX operated rat showing cartilage loss with a large osteophyte formed at the joint margin (**circled**) and several channels crossing into (**blue asterisk**) the articular cartilage (**dotted line; separates underlying bone from cartilage**). B, medial tibial plateau from a rat with MIA-induced OA, showing severe cartilage loss, osteophyte at joint margin and channels crossing into the cartilage. **C**, medial tibial plateau from non-arthritic control showing normal smooth cartilage and joint margins. The chondrocytes are homogenously distributed throughout the cartilage and there is neither evidence of proteoglycan loss nor channels entering the avascular cartilage (**black asterisks**). Coronal sections of the medial tibial plateau stained with Safranin-O. Scale bar = 100 µm. n=8 rats/group.



Supplementary Figure 4: NGF-induced inflammation 35 days after meniscal transection or intra-articular injection of MIA. Thirty five days after the induction of osteoarthritis (OA) by either meniscal transection surgery (MNX) or intra-articular injection of monosodium iodoacetate (MIA), there was an increase in synovial inflammation measured as macrophage infiltration (**A**) and synovial lining thickness and cellularity (**B**) in osteoarthritic rats (MNX or MIA) compared with non-osteoarthritic controls (naïve). Intra-articular injection of (nerve growth factor) NGF (10 µg) on day 20 did not increase synovial inflammation in osteoarthritic rats at day 35. ** $p<0.01$, *** $p<0.001$ versus naive controls. n=8 rats/group.



Supplementary Figure 5: Bilateral increase in TrkA expression in lumbar 1 and 2 dorsal root ganglia following induction of osteoarthritis. Ipsilateral (**A, C**) and contralateral (**B, D**) lumbar (L) 1 and 2 dorsal root ganglia (DRGs) of n=8 rats/group show a bilateral increase in TrkA mRNA at 20 (**A, B**) and 35 (**C, D**) days after induction of OA by either transection of the meniscus (MNX) or intra-articular injection of monosodium iodoacetate (MIA) compared with non-osteoarthritic control rats that received intra-articular saline injection on day 0 (saline). Spinal cord tissues (L1-6) were used as controls. TrkA mRNA is normalized to β-actin mRNA. ** $p<0.01$, *** $p<0.001$ versus non-osteoarthritic (saline-injected) rats.