Supplementary Methods:

Animals: Mice were kept in approved animal-care facilities and were housed 5 per cage in standard individually ventilated cages, maintained with a 12h light/dark cycle at an ambient temperature of 21°C. Animals were fed a certified mouse diet (RM3 from Special Dietary Systems, Essex, UK) and water ad libitum. Sham and PMX or sham and DMM operated animals were mixed throughout cages.

Surgical joint destabilization: All surgeries were performed according to the procedures approved by the UK Home Office (Animals Scientific Procedures Act 1986) and the guidelines issued by the International Association for the Study of Pain. 10 week-old C57BL6 or DBA1 mice (Charles River, UK), underwent surgical destabilisation by partial meniscectomy (PMX) or by destabilisation of the medial meniscus (DMM), or sham surgery of the knee joint as previously described22,23. Weights of all animals were taken at the time of surgery. Briefly, animals were placed under general anaesthesia by inhalation of Isoflurane (Vetpharma, Leeds, UK); 3% induction, 1.5-2% maintenance in 1.5-2 L/min O2. Hindlimbs were shaved and prepared for aseptic surgery. 0.3 mg/ml buprenorphine (Vetergesic Alstoe Animal Health, UK) was administered subcutaneously to all animals for analgesic purposes. For the sham operation, the knee joint was opened, the meniscotibial ligament identified and the incision was closed with sutures. For the PMX surgery, the meniscotibial ligament was transected and approximately 1 mm of the medial meniscus was removed. For the DMM surgery, the meniscotibial ligament was transected.