**Supplemental Methods:**

**Animals.** All experimental procedures and mouse handling were done in accordance with the IACUC (University Committee on Animal Resources) at the University of Rochester in Rochester, NY. Mice purchased from The Jackson Laboratory were housed in micro-isolator cages in groups of 3. At 18 weeks of age, mice were trained for one week to consume 120 mg of hazelnut cream (Nutella, vehicle control) per day as previously described [1]. At 19 weeks of age, the hazelnut cream was supplemented with 0.31 mg/gram of body weight of glucosamine (Douglas Laboratories) or 2 μg/gram of body weight undenatured type 2 collagen (UT2C) (Douglas Laboratories) and provided to mice on ceramic tiles daily. Dosing was set up such that delivery of 100mg of hazelnut cream with with/or without supplement incorporated was provided daily for the remainder of the experiment. Following 2 weeks of supplementation, we performed a DMM surgery as previously described [2]. Briefly, mice were anesthetized via i.p. injection of 4mg/kg xylazine and 60mg/kg of ketamine and given a DMM injury. To open the joint space, a 5mm initial skin incision was established on the medial side of the knee and an incision was made on the medial side of the patellar tendon. The medial meniscotibial ligament was then transected with a # 11 scalpel. Upon the completion of the surgery, 4-0 silk sutures closed the incision site. DMM surgery was completed on the right knee and sham surgery was completed on the left knee of all mice. Sham surgeries involved the opening of the joint space, however the medial meniscotibial ligament was left unmanipulated. Analgesia was provided via i.p. injection of buprenorphine (0.5mg/kg) every 12 hours for 72 hours.

**Tissue fixation and histologic preparation.** Mice were euthanized 12 weeks post-injury in accordance with American Veterinary Medical Association Methods. Knee joints were harvested and fixed in 10% neutral buffered formalin for 72 hours. Following fixation, knee joints were placed in EDTA for a 14-day decalcification process, processed in a microwave processer and embedded in paraffin blocks. Medial compartments of knee joints were sectioned in the midsagittal plane. Each joint was sectioned at 3 levels, 15µm from the previous location. Histomorphometry and OARSI scoring was completed on 5µm Safranin/O Fast green sections of knee tissue.

**Mouse OARSI scoring.** The semiquantitative grading system established by the OARSI histopathology initiative was utilized to assess the extent of cartilage degeneration [3]. Safranin O/Fast Green stained joints were evaluated based on a 0-6 scale as previously described [4].

**Histomorphometry.** The OsteoMeasure system was utilized to quantify total tibia cartilage area, uncalcified tibia cartilage area, and Safranin O positive chondrocytes as previously described [5]. In a blinded manner, Safranin O/Fast Green stained sections were imaged with an Olympus Microscope (400x magnification). Cartilage area was outlined with the OsteoMetrics stylus pen and measurements were obtained over 3 levels for each specimen. The number of Safranin O positive chondrocytes was then counted, and all measurements were averaged across the 3 given levels for each specimen.

**16S rRNA Bacterial Sequencing.** Fresh fecal pellets were collected at 3 weeks post injury and 12 weeks post injury by scruffing mice immediately prior to sacrifice. Pellets were promptly frozen at -80°C. The ZR Fecal DNA Extraction Kit (Zymo Research) was used to isolate DNA according to manufacturer instructions. Once isolated, 16S ribosomal DNA was amplified using dual indexed V3-V4 hypervariable region primers and Phusion High Fidelity polymerase (Thermo Fisher Scientific). Pooled amplicons were pair-end sequenced using an Illumina MiSeq at the University of Rochester Genomics Research Center. For each sequencing run, a positive control consisting of a 1:5 mixture of *Staphylococcus aureus*, *Lactococcus lactis*, *Porphyromonas gingivalis*, *Streptococcus mutans*, and *Escherichia coli*. A negative control composed of sterile saline was also included. Following sequencing, raw data was converted into FASTQ format 2 x 300 paired-end sequence files with bcl2fastq, version 1.8.4; this was provided by Illumina. Format conversion without demultiplexing was performed with disabled Extended Adaptive Multi-Mode Search (EAMMS). Otherwise, default settings were used. Quantitative Insights into Microbial Ecology (QIIME) version 1.9.1 [6] was used for sequence processing and analysis of microbial composition. Reads were multiplexed as previously described [7]. Briefly, the first 12 bases of both reads in each pair consisted of a barcode, followed by a primer, a heterogeneity spacer, and the target 16S rRNA sequence. A custom Python script was employed to remove barcodes from read pairs; barcodes were then concatenated and stored in a separate file. Read pairs were assembled with fastq-join from ea-util. At least 40 bases of overlap were required, and a maximum of 10% mismatched bases were allowed. Concatenated barcode sequences were added to the beginning of corresponding assembled reads, which were together converted from FASTQ to FASTA and QUAL files for use in QIIME. During demultiplexing, barcodes, forward and reverse primer, and spacer sequences were removed. Any reads that possessed greater than 4 mismatches to the known primer sequence or greater than 3 mismatches to the barcode sequence were dropped from downstream processing and analysis. Depending on what occurred first, assembled reads were truncated at the first ambiguous base or at the beginning of the first 30-base window with a mean Phred quality score of less than 20. Any sequences containing a homopolymer greater than 6 bases or that were shorter than 300 bases were discarded. The USEARCH (version 5.2) [8] pipeline in QIIME was used to pick OTUs. The May 2013 release of the GreenGenes 99% OUT database served as the closed reference [9,10]. Paramaters for USEARCH included an indexed word length of 128 characters and default parameters. UCHIME de novo chimera detection was performed with default parameters [8]. Representative sequences used for assignment of taxonomy were chosen based on abundance and OUT clusters containing less than 4 sequences were removed. The GreenGenes reference database was used with RDP Naïve Bayesian Classifer to determine taxonomic classification, with default parameters and a minimum confidence threshold of 0.85 [11].

**OTU and Microbiome Data Selection.** Relative phyla and OTU abundances shown in Fig. 2 and 3 represent the microbiome identified from fecal pellets collected 12 weeks after injury. Individual OTUs that increased or decreased in abundance by ≥1% between vehicle control and supplement fed mice were selected for individual analysis. Data from fecal pellets collected at 3 weeks and 12 weeks post DMM were pooled and analyzed for statistical significance as described in the figure legends.

**Supplemental References:**

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