Supplemental Table Captions:

Supplemental Table 1. Genes differentially expressed in response to FN-f treatment.
The direction of response is indicated with "-", meaning downregulated, and "+", meaning upregulated. The most significant genes with the largest effects (adjusted p-value < 0.01 and absolute log2 fold change > 2) are denoted with "---" and "+++".
symbol: gene symbol
gene_id: gene ENSEMBL ID
padj: adjusted p-value
log2FoldChange: log2 fold change of FN-f expression relative to PBS
FNF response: direction of gene response to FN-f

Supplemental Table 2. All GO terms and KEGG pathways that are enriched in FN-f upregulated and downregulated genes.
Tables are split by GO/KEGG and Upregulated/Downregulated.
GO term columns:
TermID: GO term ID
Term: GO term name
parentTermID: GO parent term ID as determined by string similarity
parentTerm: GO parent term name as determined by string similarity
Enrichment: enrichment score
-log10pval: -log10 p-value of the GO term enrichment
Genes in Term: number of genes in that GO term
Target Genes in Term: number of genes in that term from the gene set of interest
Fraction of Targets in Term: Target Genes in Term/Total Target Genes
Total Target Genes: Number of target genes tested. This number will be the same within each dataset.
Total Genes: Number of total genes used for GO enrichment analysis. This number will be the same within each dataset.
Gene Symbols: The gene symbols of all the target genes identified with a GO term.

KEGG pathway columns:
TermID: KEGG pathway ID
Term: KEGG pathway name
Enrichment: enrichment score
-log10pval: -log10 p-value of the KEGG pathway enrichment
Genes in Term: number of genes in that KEGG pathway
Target Genes in Term: number of genes in that term from the gene set of interest
Fraction of Targets in Term: Target Genes in Term/Total Target Genes
Total Target Genes: Number of target genes tested. This number will be the same within each dataset.
Total Genes: Number of total genes used for KEGG enrichment analysis. This number will be the same within each dataset.
Gene Symbols: The gene symbols of all the target genes identified with a KEGG pathway.

Supplemental Table 3. Sex-specific genes.
symbol: gene symbol
gene_id: ENSEMBL gene ID
sex_padj_PBS: adjusted p-value of sex-specific gene in PBS
sex_log2FoldChange_PBS: log2 fold change (M/F) of gene in PBS
sex_padj_FNF: adjusted p-value of sex-specific gene in FN-f
sex_log2FoldChange_FNF: log2 fold change(M/F) of gene in FN-f
M/F: column indicating whether the gene is male-biased (M) or female-biased (F)
FNF response: direction of response of sex-specific gene to FN-f treatment. A missing value indicates the gene was not differentially expressed with FN-f. "+++": high-effect FN-f upregulation; "+": FN-f upregulation; "---": high-effect FN-f downregulation; "-": FN-f downregulation.
Change with OA: direction of expression of sex-specific gene in OA tissue. A missing value indicates the gene was not significantly expressed in OA.
OA study: the OA study the sex-specific gene was identified in, if applicable.

Supplemental Table 4. Sex-specific gene expression in multiple tissues.
This table corresponds to the heatmap in Fig 2B.
tissue_no: The number column a tissue corresponds to in the heatmap, from left to right
tissue: tissue/cell type name
gene_no: The number row a gene corresponds to in the heatmap, from top to bottom
sex: The sex the gene is associated with.
effsize: Effect size, log2 fold change
effsize_se: Standard error of effect size

Supplemental Table 5. Age-related genes.
symbol: gene symbol
gene_id: gene ENSEMBL ID
age_padj_PBS: adjusted p-value of age LRT in PBS
age_padj_FNF: adjusted p-value of age LRT in FN-f
Change with age: direction of expression change with older donors
FNF response: direction of response of age-related gene to FN-f treatment. A missing value indicates the gene was not differentially expressed with FN-f. "+++": high-effect FN-f upregulation; "+": FN-f upregulation; "---": high-effect FN-f downregulation; "-": FN-f downregulation.
Change with OA: direction of expression of age-related gene in OA tissue. A missing value indicates the gene was not significantly expressed in OA.
OA study: the OA study the age-related gene was identified in, if applicable.

Supplemental Table 6. All GO terms that are enriched in genes that increase and decrease in expression with age.
Tables are split by Up with Age/Down with Age.
TermID: GO term ID
Term: GO term name
parentTermID: GO parent term ID as determined by string similarity

parentTerm: GO parent term name as determined by string similarity
Enrichment: enrichment score
-log10pval: -log10 p-value of the GO term enrichment
Genes in Term: number of genes in that GO term
Target Genes in Term: number of genes in that term from the gene set of interest
Fraction of Targets in Term: Target Genes in Term/Total Target Genes
Total Target Genes: Number of target genes tested. This number will be the same within each dataset.
Total Genes: Number of total genes used for GO enrichment analysis. This number will be the same within each dataset.
Gene Symbols: The gene symbols of all the target genes identified with a GO term.

Supplemental Table 7. PBS and FN-f lead eQTLs and eGenes.
Conditionally independent lead eSNP-eGene pairs, separated by condition.
gene_id: eGene ENSEMBL ID
gene_name: eGene name
gene_chr: gene chromosome
gene_tss: gene transcription start site used for eQTL mapping, as defined in Methods
gene_end: gene end
gene_strand: gene strand
num_cis_variants: number of genetic variants that were *in cis* and tested for a gene
rsID: lead eSNP rsID
variantID: lead eSNP variant ID in the format "variant chromosome:variant position: allele 1: allele 2"
variant pos: lead eSNP position
beta: beta estimate of effect size
beta_se: standard error of calculated beta
nom_pval: nominal p-value
minor_allele: the minor allele, also the assessed or effect allele, for the lead eSNP. Beta estimates are relative to this allele.
MAF: minor allele frequency
eGene_nominal_threshold: the local nominal p-value significance threshold for an eGene
eGene_qval: the globally adjusted q-value for an eGene based on permutation testing
signal: iteration of conditional analysis. 0 = primary signal, 1 = secondary signal, etc.

Supplemental Table 8. Study comparisons to Steinberg et al.
eGenes and lead variants:
Comparison of eGenes and lead variants between Steinberg et al. low grade and high grade cartilage eQTL datasets and current study PBS and FN-f eQTL datasets. Steinberg et al. variant coordinates were lifted over to hg38 to match the current study. All variant IDs are in the format "chr:hg38pos:ref:alt".

gene_id: eGene ENSEMBL ID
gene_symbol: eGene name

variantID_Kramer_PBS: lead variant ID for primary eGene signal in PBS eQTL dataset
variantID_Kramer_FNF: lead variant ID for primary eGene signal in FN-f eQTL dataset
variantID_Steinberg_lowgrade: lead variant ID for eGene in Steinberg low grade cartilage dataset
variantID_Steinberg_highgrade: lead variant ID for eGene in Steinberg high grade cartilage dataset
study: Which study the eGene was identified in: Kramer, Steinberg, or both

Study Designs:
Overview of current eQTL study and Steinberg et al. OA eQTL study datasets, including sample demographics, cartilage joint site, RNA-sequencing library preparation, genotyping platform, quality control, SNP imputation, eQTL calling methods, and colocalization methods.
HWE, Hardy-Weinberg Equilibrium; MAF, minor allele frequency; HRC, Haplotype Reference Consortium; PC, principal component; FDR, false discovery rate; GWAS, genome-wide association study; PP4, posterior probability 4 obtained from coloc

Supplemental Table 9. Condition-specific eQTLs in PBS and FN-f.
All lead eSNP-eGene pairs with a significant genotype by condition interaction effect. High confidence PBS-specific and FN-f-specific eQTLs are denoted by the “high_conf” column.

gene_id: eGene ENSEMBL ID
gene_name: eGene name
gene_chr: gene chromosome
gene_tss: gene transcription start site used for eQTL mapping, as defined in Methods
gene_end: gene end
gene_strand: gene strand
rsID: lead eSNP rsID
variantID: lead eSNP variant ID in the format “variant chromosome:variant position: allele 1: allele 2”
variant pos: lead eSNP position
PBS_beta: beta estimated effect size of lead eSNP-eGene in PBS
PBS_beta_se: standard error of calculated beta in PBS
FNF_beta: beta estimated effect size of lead eSNP-eGene in FN-f
FNF_beta_se: standard error of calculated beta in FN-f
minor_allele: the minor allele, also the assessed or effect allele, for the lead eSNP. Beta estimates are relative to this allele.
MAF: minor allele frequency
interaction_pval: p-value from ANOVA testing of genotype by condition interaction
high_conf: a column indicating whether the eQTL was high confidence condition-specific. A missing value indicates it is not part of this group.

Supplemental Table 10. KEGG pathways enriched in high-confidence PBS-specific and high-confidence FN-f-response eGenes.

TermID: KEGG pathway ID

Term: KEGG pathway name
Enrichment: enrichment score
-log10pval: -log10 p-value of the KEGG pathway enrichment
Genes in Term: number of genes in that KEGG pathway
Target Genes in Term: number of genes in that term from the gene set of interest
Fraction of Targets in Term: Target Genes in Term/Total Target Genes
Total Target Genes: Number of target genes tested. This number will be the same within each dataset.
Total Genes: Number of total genes used for KEGG enrichment analysis. This number will be the same within each dataset.
Gene Symbols: The gene symbols of all the target genes identified with a KEGG pathway.

Supplemental Table 11. Differential accessible peaks.

chrom: chromosome
start: peak start
end: peak end
width: peak width
baseMean: base mean of peak counts
log2FoldChange: log2 fold change of accessibility in FN-f relative to PBS
lfcSE: standard error of log2 fold change
padj: adjusted p-value

Supplemental Table 12. Differential loops.

chrom1: chromosome of loop anchor 1
start1: start of loop anchor 1
end1: end of loop anchor 1 (10 kb from start1)
chrom2: chromosome of loop anchor 2
start2: start of loop anchor 2
end2: end of loop anchor 2 (10 kb from start2)
log2FoldChange: log2 fold change of loop contact frequency in FN-f relative to PBS
lfcSE: standard error of log2 fold change
padj: adjusted p-value
cluster: looping cluster, either gained or lost with FN-f treatment
DonorX_XXX_rX_raw: raw loop counts for a given donor sample (1-4), replicate (r1 or r2), and treatment condition (PBS or FNF)

Supplemental Table 13. Extended characterization of colocalizations between PBS and FN-f eQTL and OA GWAS signals.
OA, osteoarthritis; GWAS, Genome-wide association study; THR, Total Hip Replacement; OR, odds ratio; PBS coloc PP4, posterior probability 4 obtained from coloc testing with the PBS signal for an eQTL; FN-f coloc PP4, posterior probability 4 obtained from coloc testing with the FN-f signal for an eQTL; M vs F, male vs female

Supplemental Table 14. Donor characteristics for all collected datasets.
Ancestries for eQTL-related donors (i.e. genotyping and RNA-seq) were determined from principal component analysis with 1000 Genomes samples using EIGENSTRAT. Definitions of ancestry superpopulations are defined by 1000 Genomes.
AFR, African; AMR, Admixed American; EAS, East Asian; EUR, European; SAS, South Asian