



Supplemental Figure 1 **Identification of enhancer – promoter loops linked with osteoarthritis lead variant rs2276749 on chromosome 3**

A) Regional association plot of a ± 1 mb region surrounding the lead variant rs2276749 for the lead phenotype (total hip replacement) from Boer, Hatzikotoulas, Southam et al.³. Variants are annotated to the lead variant which is highlighted in purple. Linkage disequilibrium with the lead variant is depicted according to the colours in the legend. **B)** Plot of the identified enhancer – promoter loop associated to lead variant rs2276749. Horizontal red lines show the region of loop anchors with active promoter and enhancer regions throughout the plotting area. Horizontal dotted black lines show other identified loop anchor regions without any active enhancer/promoter region. *Hi-C matrix with TADs* shows the identified loop region as a log1p-transformed Hi-C contact matrix map showing the number of identified contacts between bins with a 10 kb bin size. Black lines shows merged topologically associated domains (TADs) calculated 50 kb bin size. Loop anchors show all identified loop anchors with the different loop calling algorithms used in this study as green bars at their respective location on the plotted chromosome region. The merged loop anchors show the region used for the final analysis after merging the several locally identified loop anchors. Putative identified loop regions are connected with a blue arc. *Genes* are the position of transcribed regions as identified in ENSEMBL genes version 110. *Osteoarthritis associated variants* are variants from the 95% credible set of a study by Boer, Hatzikotoulas, Southam et al.³ with a posterior probability of $> 3\%$ identified to reside in loop anchors called in this study. In addition, the position of the credible set variants residing in an enhancer region, rs2276749 and rs6799718 are shown in a separate track. *cCRE regulatory regions* shows all cis regulatory elements (cCRE) as identified in version3 from the ENCODE registry³⁰. ATAC Seq¹¹ (n = 8) and histone mark signal tracks for H3K4me1, H3K4me3 and H3K27ac¹² (n = 3) were averaged and merged into one track from the replicates of the public data repositories, Genomic co-ordinates (GRCh38) are given below the plot.