

**Supplementary Figure 1: PCA plot of gene expression in primary human osteoblasts.** Principal component analysis of normalized expression data was performed for studies of the effect of age on global gene expression. The samples were grouped into two age groups; age group 1 representing donors born between 1913 and 1938 and age group 2 representing donors born between 1939 and 1982. NA indicates that information was not available.

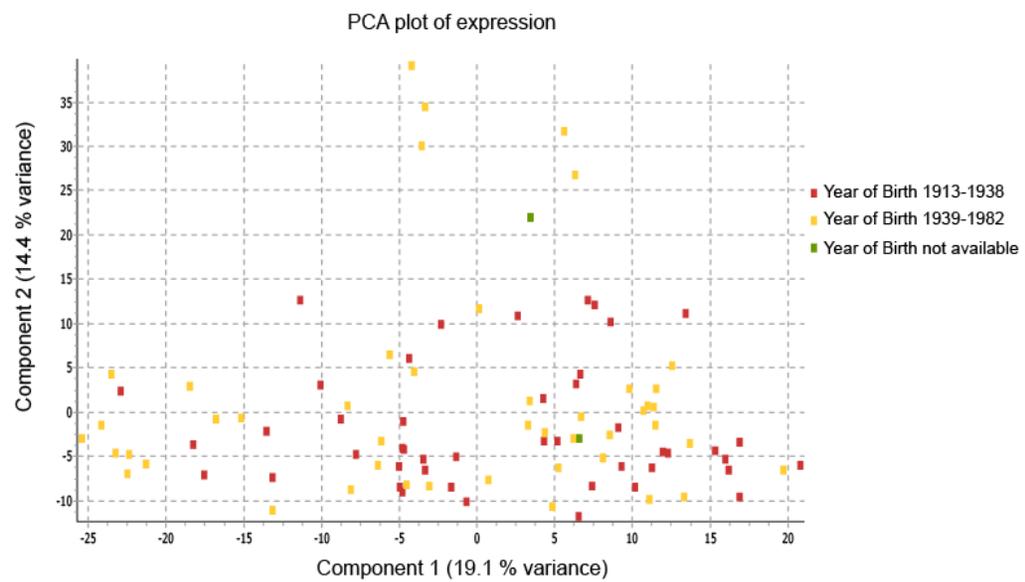
**Supplementary Figure 2: Correlation of *cis*-eQTL ranking before and after SVA-adjustments.**

Linear regression models were performed using different sets of covariates; year of birth and sex or year of birth, sex and surrogate variable identified in surrogate variable analysis. The ranking of the top 1000 *cis*-eQTLs from the first regression analysis were correlated with the corresponding ranking of the eQTLs from the analysis including the surrogate variable. The blue line represents equality of ranking between the two procedures.

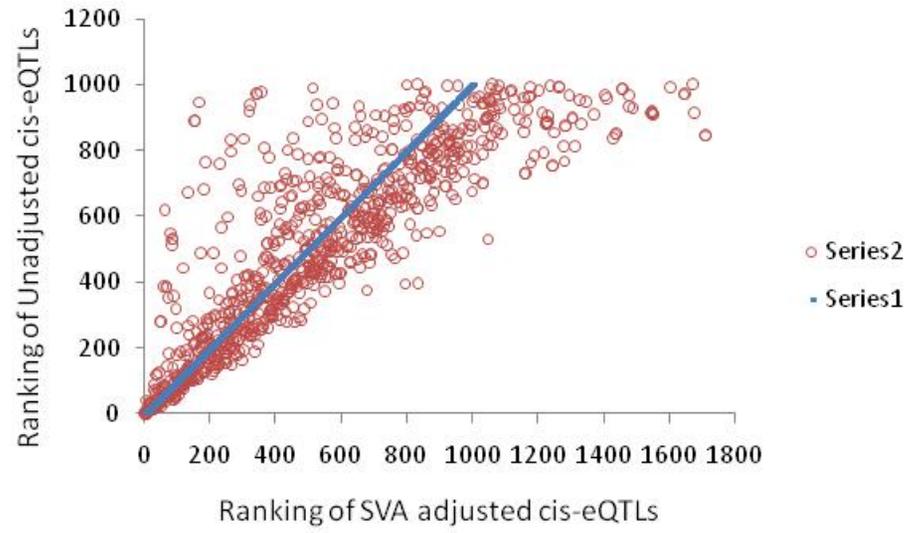
**Supplementary Figure 3: Validation of the genetic effect of *SRR* gene expression by quantitative real-time RT-PCR.** The effect of SNPs on *SRR* expression was validated by quantitative real-time PCR in HObs (n=32). The rs1885987 represent one of the top significant SNPs associated with gene expression in the microarray analysis in HObs and was used in association with the relative expression calculated using the comparative CT method using *GAPDH* as a housekeeping gene. Associations were assessed using a linear regression model. The P value and R<sup>2</sup> of the linear regression statistic are shown within the box plot.

**Supplementary Figure 4: *In vitro* transient transfection studies.** Gene reporter assays for three promoter haplotypes carrying rs408067 (G/C), rs3744270 (A/G) and rs12450028 SNPs (T/C) were performed in five different cell lines. Relative luciferase activity of the promoter haplotypes was measured following transient transfection and data is presented as mean and standard deviation of four technical replicates. The empty promoterless pGL3-Basic vector was used as negative control. Statistical significance was determined using an unpaired Student's t-test showing higher promoter activity ( $P \leq 0.01$ ) for the GAT and GGC haplotypes compared to the CGC haplotype and was reached in MG63 cells only. In the other cell types studied, the variation of promoter haplotype on reporter gene expression were insignificant ( $P > 0.05$ ).

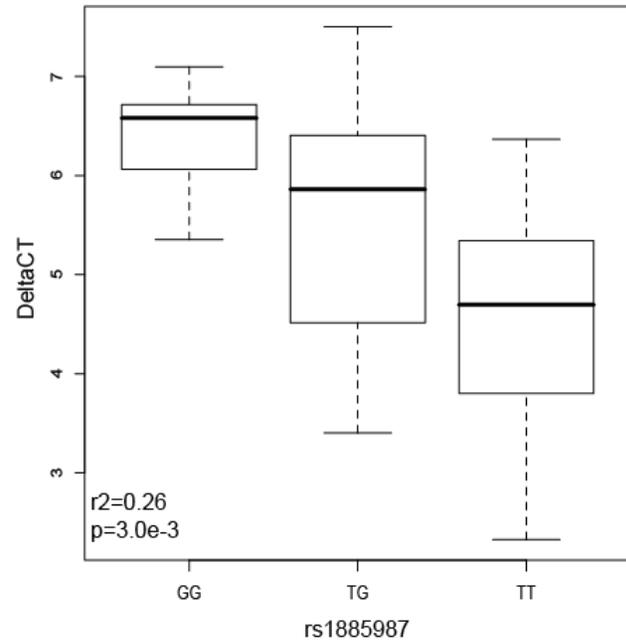
# Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure 3



### Supplementary Figure 4

SRR\_0.5Kb promoter / pGL3basic

