Online Supplementary Notes:

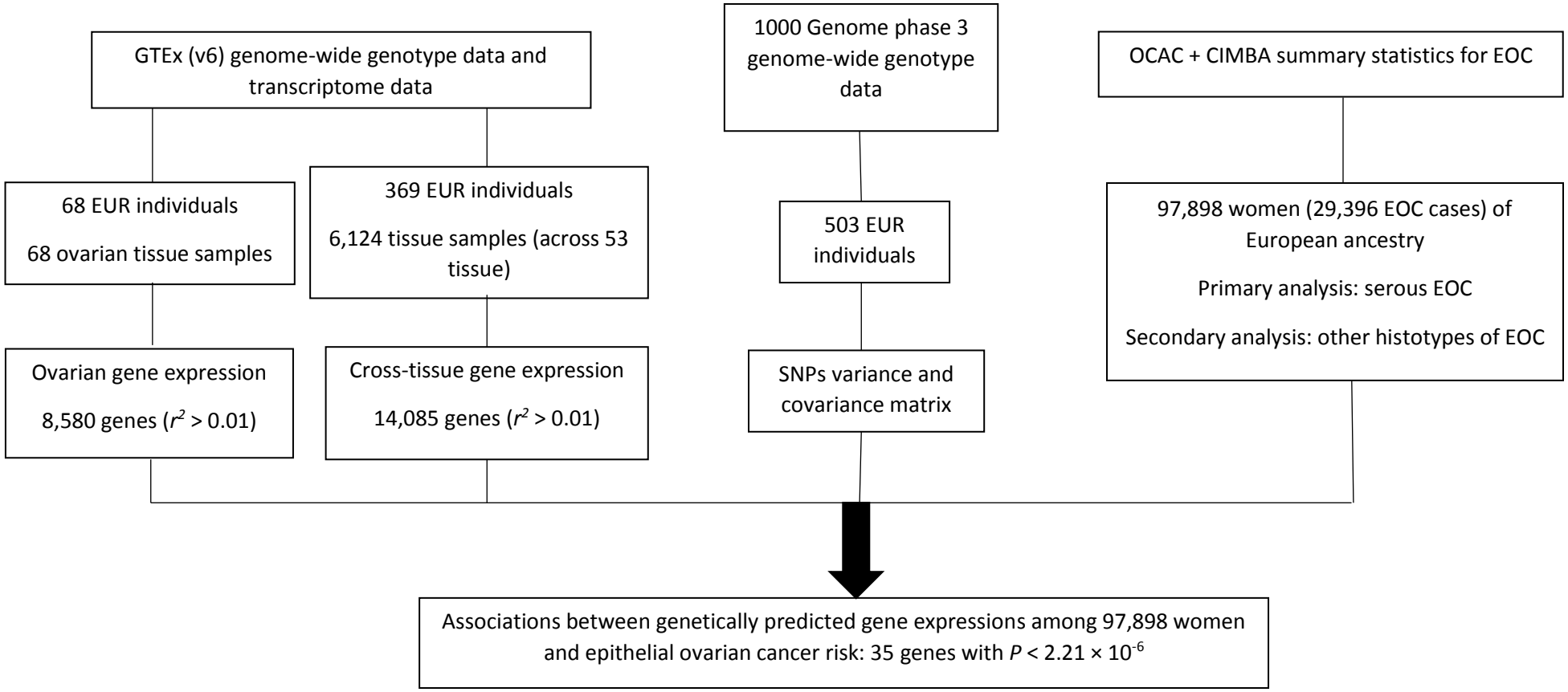
Additional Methods:

At each of four genetic loci (2q31.1, 9p22.3, 17q21.31 and 17q21.32), predicted expression levels of multiple genes were found to be associated with ovarian cancer risk (Tables 1 and 2). For Supplementary Table 5, the respective genetically predicted expression values for genes at these four loci were extracted from the glmnet model with the best lambda based on the expression dataset of Genotype-Tissue Expression project (See methods for details) and were correlated with each other at each locus. The Pearson correlation method was used. Genes with significant correlation (*P* value < 0.05) in predicted expression were highlighted in bold.

For Table S7, we defined the genomic interval based on the genes associated with epithelial ovarian cancer (EOC) at 17q21.31. The most upstream gene was *ADAM11* (Chromosome 17: 42,836,399-42,859,214; GENODE V19) and the most downstream gene was *WNT3* (Chromosome 17: 44,839,872-44,910,520, GENODE V19). All the variants that showed associations with either breast cancer or ovarian cancer with $P < 5\times10^{-8}$ and were located between 42,836,399 and 44,910,520 were extracted from the OCAC (OCAC overall invasive meta-analysis) and BCAC (OncoArray-iCOGS-GWAS meta-analysis) latest meta-analysis datasets. The effect direction of minor alleles was consistently opposite between breast cancer risk and EOC risk. The minor allele frequency for these variants is around 20%. Generally speaking, these minor alleles were associated with reduced breast cancer risk but increased EOC risk. However, there are five variants (17_43657437_A_G [MAF = 0.50], 17_43784228_T_C [MAF = 0.35], 17_43848495_G_T [MAF = 0.35], 17_44332093_G_A [MAF = 0.44] and 17_44342378_G_A [MAF = 0.44] in red) showed an opposite association pattern. These might be outlier variants based on their frequencies that deviated from the average 20%.

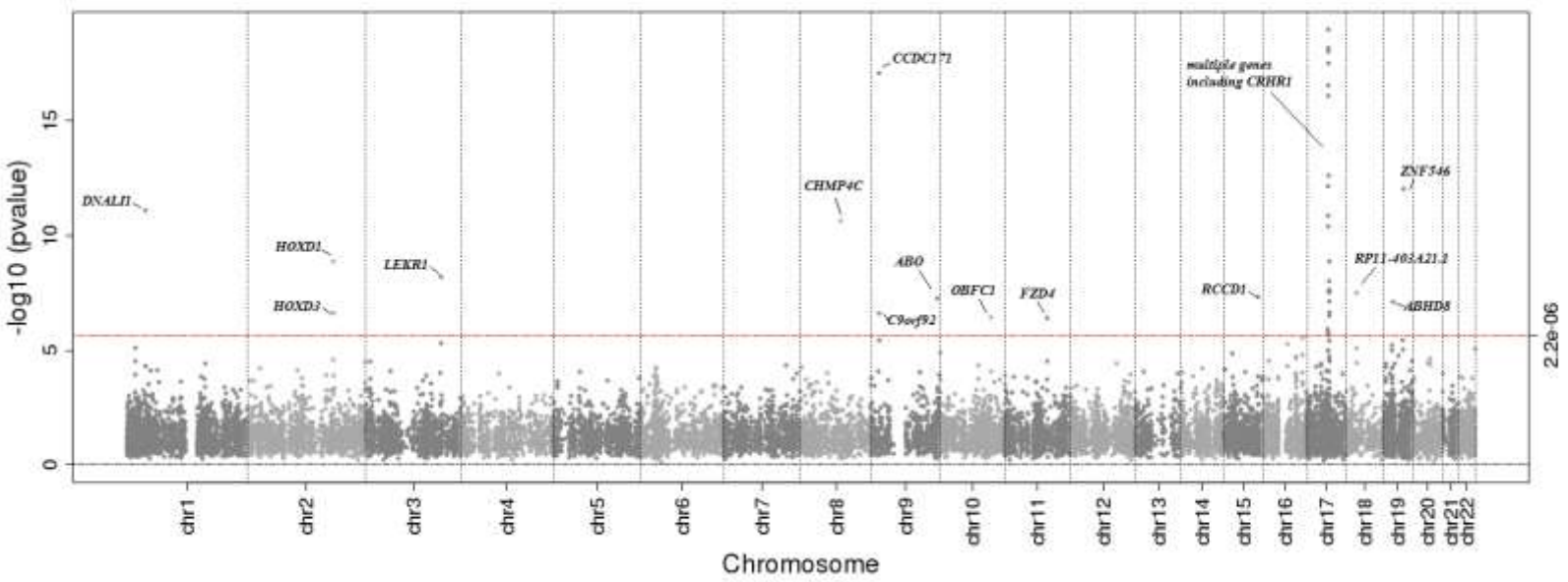
For Table S8, in the *CRHR1* cross-tissue gene expression prediction model, 467 variants were retained in the final model construction, among which 456 variants had significant associations with either breast cancer risk or epithelial ovarian cancer risk with $P < 5\times10^{-8}$ (Tables S7 and S8). The minor alleles of these 456 variants were all associated with increased *CRHR1* expression. For the other 11 variants, the minor alleles of 7 variants were also associated with increased *CRHR1* expression (rs8069296 [MAF = 0.21], rs962888 [MAF = 0.30], rs12449792 [MAF = 0.46], rs7216796 [MAF = 0.48], rs4328483 [MAF = 0.42], rs4792814 [MAF = 0.42], rs17686238 [MAF = 0.10]), and the minor alleles of other 4 variants (rs9911406 [MAF = 0.08], rs9890538 [MAF = 0.08], rs1635299 [MAF = 0.14] and rs16940742 [MAF = 0.06], highlighted in red) were associated with reduced *CRHR1* expression. The association between these four variants and either breast cancer risk or EOC risk were not strong (Table S8). Their minor allele frequencies for these four variants deviated from the overall 22% based on the 369 Europeans that were incorporated in the cross-tissue gene prediction model construction.

Supplementary Figure 1. The analysis flow chart



GTEx: Genotype-Tissue Expression project; EUR: individuals of European ancestry; OCAC: Ovarian Cancer Association Consortium; CIMBA: Consortium of Investigators of Modifiers of *BRCA1/2*; EOC: epithelial ovarian cancer. The tissue samples used in building gene expression models in GTEx (V6) came most from the people who recently died of traumatic injury (for these young donors) or cardio-cerebrovascular diseases (for the old donors). There were no overlaps between the tissues used in building gene expression models and the samples used in EOC GWAS in OCAC or CIMBA.

Supplementary Figure 2. The Manhattan plot of gene associations with epithelial ovarian cancer risk



Supplementary Figure 3. The QQ plot of gene associations with epithelial ovarian cancer risk