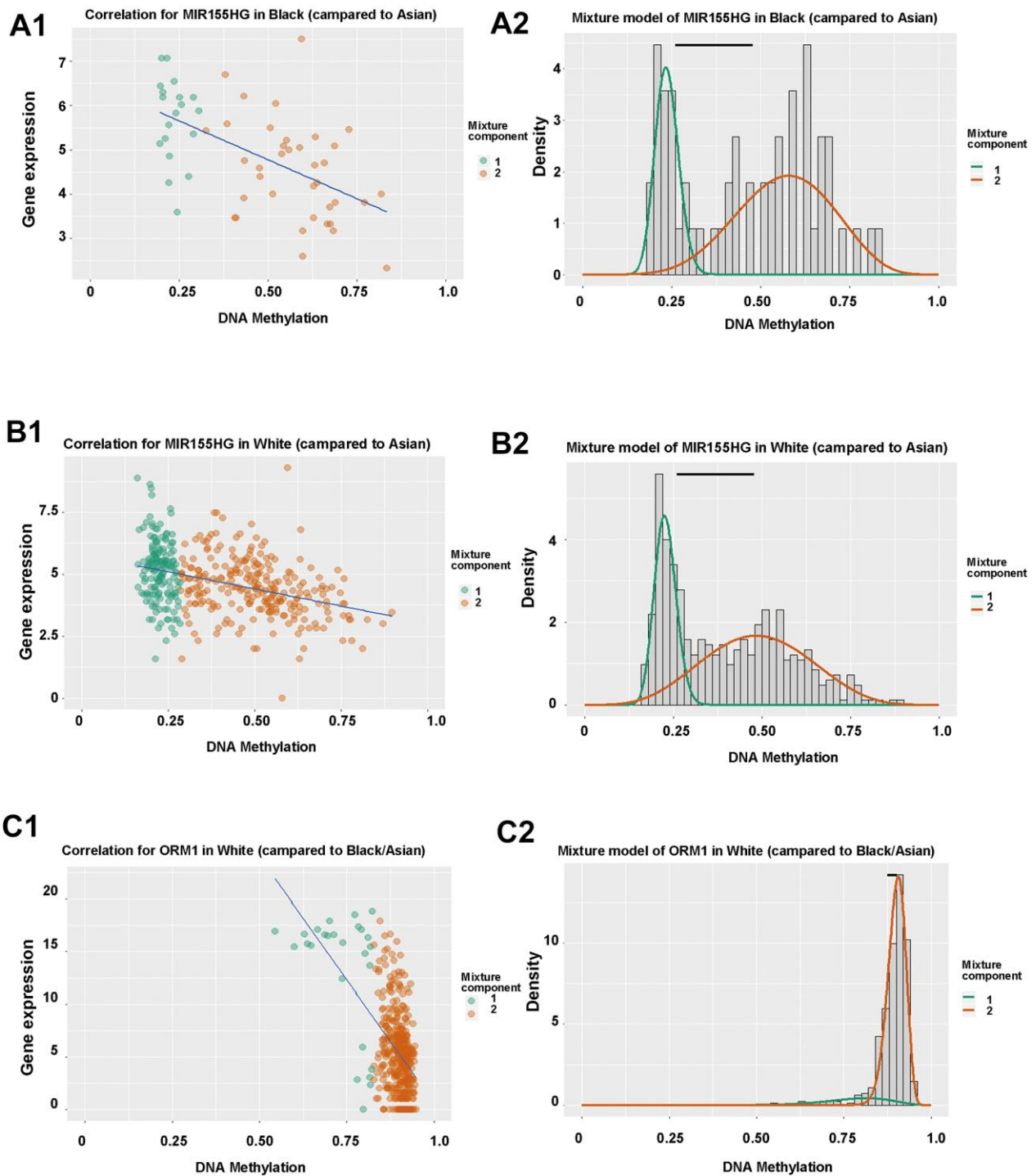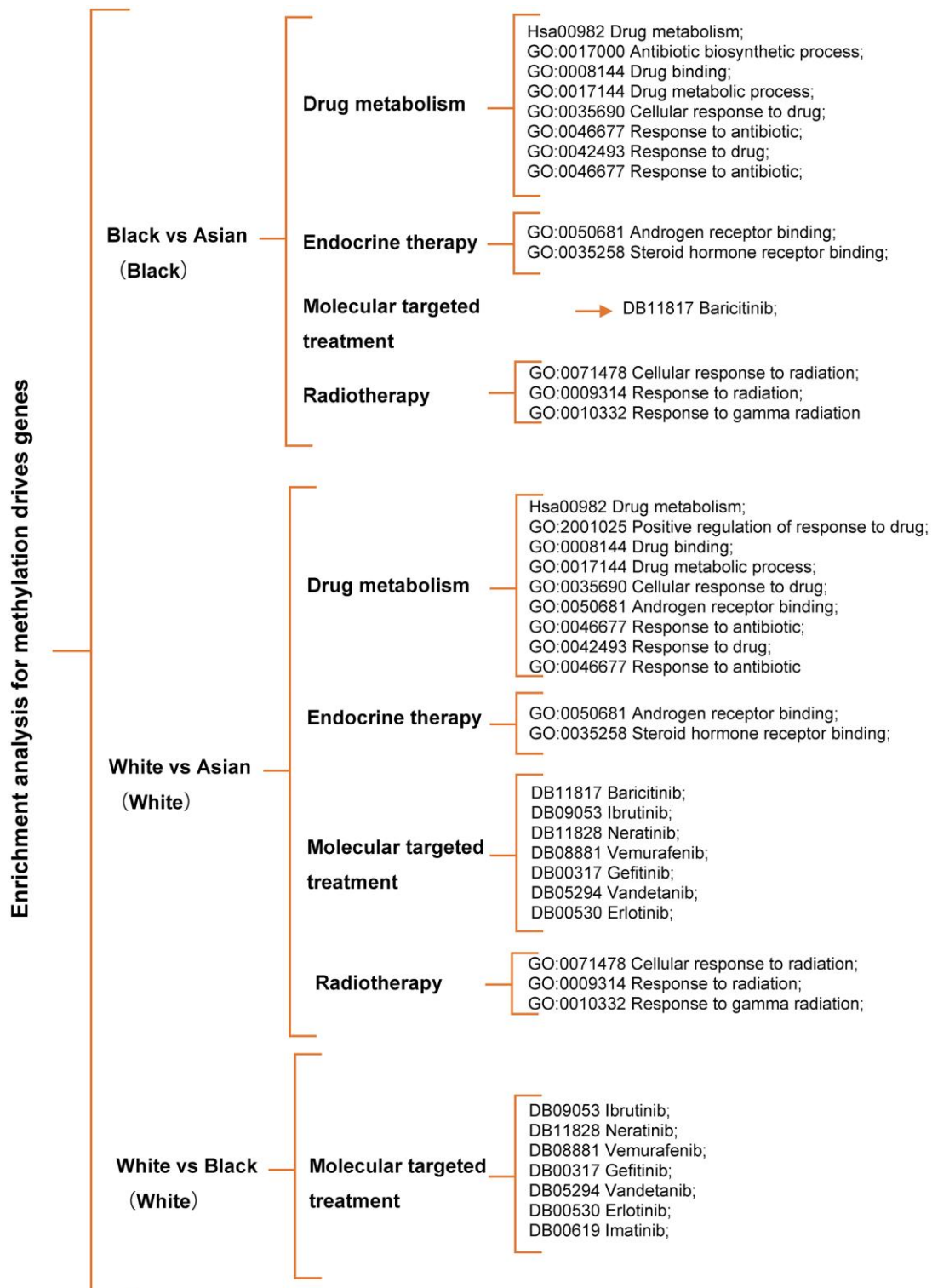Supplementary Figure 1. SNPs status differential analysis (such as mutation rate, mutation type .ect) for White people (**A**), Black people (**B**) and Asian people (**C**), respectively.

Supplementary Figure 2. Methylation drives genes of prostate cancer identified for RACES (**A–C** has shown methylation drivers genes in methylation key functional modules). (**A1**) Regression analysis between the mRNA level and DNA methylation level of *MIR155HG* in Black people; (**A2**) Differential methylation statuses for Black and Asian people. The histogram demonstrates the distribution of *MIR155HG* methylation in Black people. Beta values represent the methylation level (range from 0 to 1), and the horizontal black bar indicates the distribution of methylation values in the Asian people. (**B1**) Regression analysis between the mRNA level and DNA methylation level of *MIR155HG* in White people; (**B2**) Differential methylation statuses for White and Asian people. (**C1**) Regression analysis between the mRNA level and DNA methylation level of *ORM1*in White people; (**C2**) Differential methylation statuses for White and Black people, White and Asian people.

Enrichment analysis for methylation drives genes

Black vs Asian (Black)

- **Drug metabolism**
  - Hsa00982 Drug metabolism;
  - GO:0017000 Antibiotic biosynthetic process;
  - GO:0008144 Drug binding;
  - GO:0017144 Drug metabolic process;
  - GO:0035690 Cellular response to drug;
  - GO:0046677 Response to antibiotic;
  - GO:0042493 Response to drug;
  - GO:0046677 Response to antibiotic;
- **Endocrine therapy**
  - GO:0050681 Androgen receptor binding;
  - GO:0035258 Steroid hormone receptor binding;
- **Molecular targeted treatment**
  - → DB11817 Baricitinib;
- **Radiotherapy**
  - GO:0071478 Cellular response to radiation;
  - GO:0009314 Response to radiation;
  - GO:0010332 Response to gamma radiation

White vs Asian (White)

- **Drug metabolism**
  - Hsa00982 Drug metabolism;
  - GO:2001025 Positive regulation of response to drug;
  - GO:0008144 Drug binding;
  - GO:0017144 Drug metabolic process;
  - GO:0035690 Cellular response to drug;
  - GO:0050681 Androgen receptor binding;
  - GO:0046677 Response to antibiotic;
  - GO:0042493 Response to drug;
  - GO:0046677 Response to antibiotic
- **Endocrine therapy**
  - GO:0050681 Androgen receptor binding;
  - GO:0035258 Steroid hormone receptor binding;
- **Molecular targeted treatment**
  - DB11817 Baricitinib;
  - DB09053 Ibrutinib;
  - DB11828 Neratinib;
  - DB08881 Vemurafenib;
  - DB00317 Gefitinib;
  - DB05294 Vandetanib;
  - DB00530 Erlotinib;
- **Radiotherapy**
  - GO:0071478 Cellular response to radiation;
  - GO:0009314 Response to radiation;
  - GO:0010332 Response to gamma radiation;

White vs Black (White)

- **Molecular targeted treatment**
  - DB09053 Ibrutinib;
  - DB11828 Neratinib;
  - DB08881 Vemurafenib;
  - DB00317 Gefitinib;
  - DB05294 Vandetanib;
 - DB00530 Erlotinib;
  - DB00619 Imatinib;

Supplementary Figure 3. Metabolism pathways difference analysis according to methylation drives genes for Black and Asian people, White and Asian people, White and Black people, respectively.
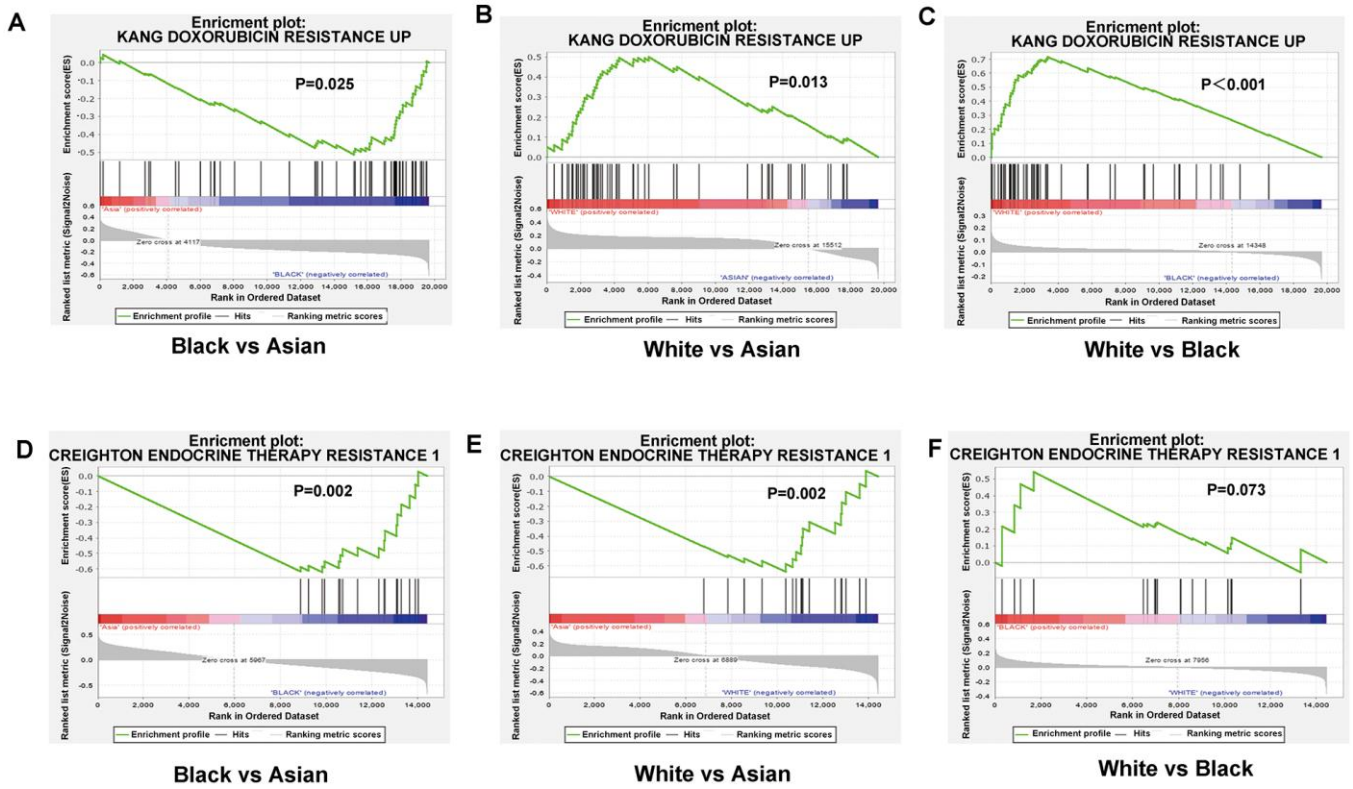
Supplementary Figure 4. GSEA metabolism pathways differences analysis for RACES. (**A**–**C**) Doxorubicin resistance differences analysis based on mRNA for Black and Asian people(p=0.025), White and Asian people (p=0.013), White and Black people(p<0.001), respectively. (**D**–**F**) Endocrine therapy resistance differences analysis based on lncRNA for Black and Asian people(p=0.002), White and Asian people(p=0.002), White and Black people(p=0.073), respectively.
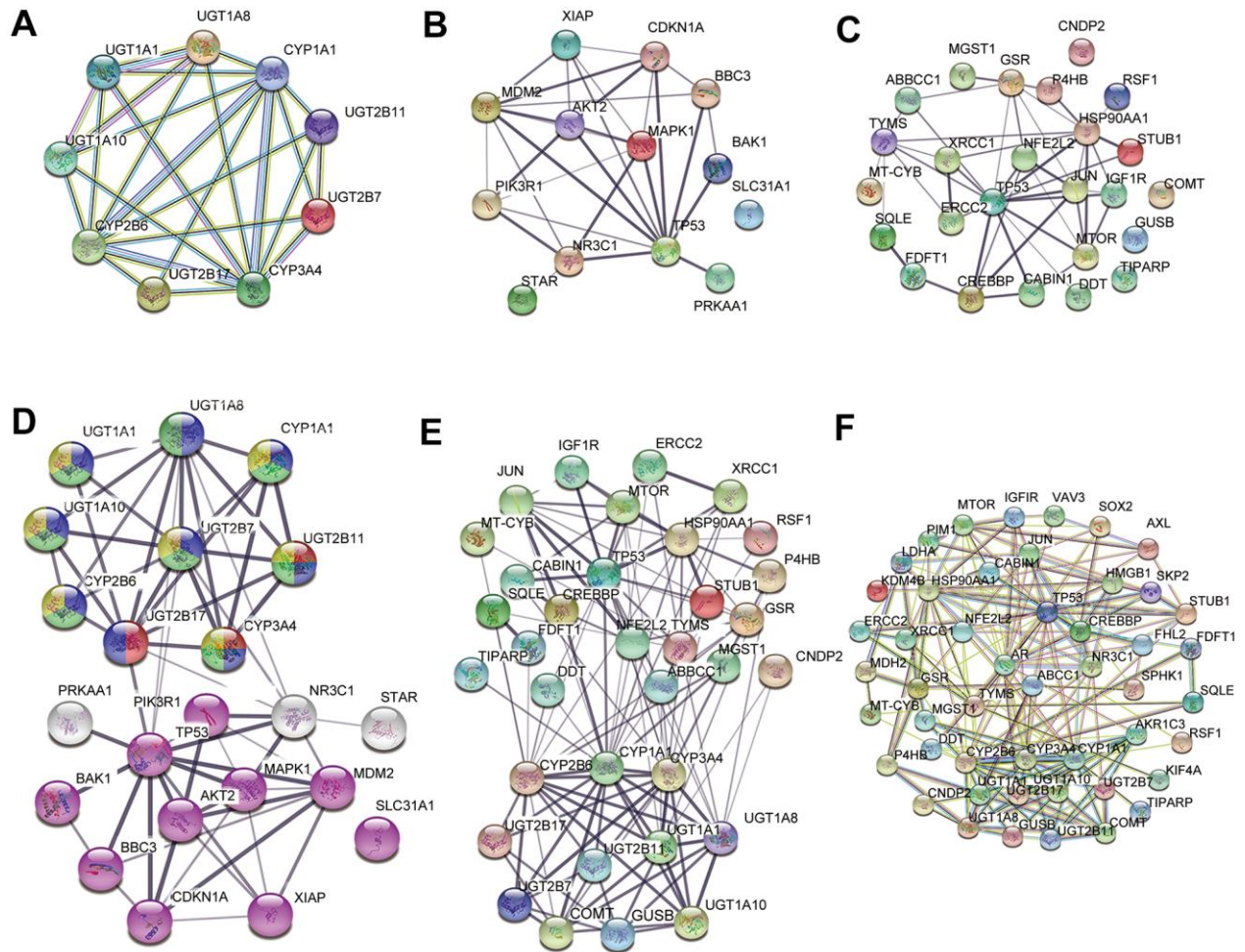
Supplementary Figure 5. Protein-protein interaction (PPI) networks for multi-omics key functional modules. (**A**) PPI network of the core mRNAs of drug metabolism functional module; (**B**) PPI network of the core miRNA target genes of platinum resistance and antineoplastic agent response functional module; (**C**) PPI network of the core lncRNA target genes of endocrine therapy resistance functional module. (**D**) PPI network for the core mRNAs of drug metabolism functional module and the core miRNA target genes of platinum resistance, antineoplastic agent response functional module. (**E**) PPI network for the core mRNAs of drug metabolism functional module and the core lncRNA target genes of endocrine therapy resistance functional module. (**F**) PPI network for the core mRNAs of drug metabolism functional module, the core miRNA target genes of platinum resistance, antineoplastic agent response functional module, the core lncRNA target genes of endocrine therapy resistance functional module and cytotoxic resistance genes (*HMGB1*, docetaxel resistance: *SKP2, AXL, MDH2, PIM1, SPHK1, LDHA, SOX2*), endocrine therapy resistance genes (*AR, FHL2, VAV3, LDHA, AKR1C3, KIF4A, KDM4B*) reported in literature.
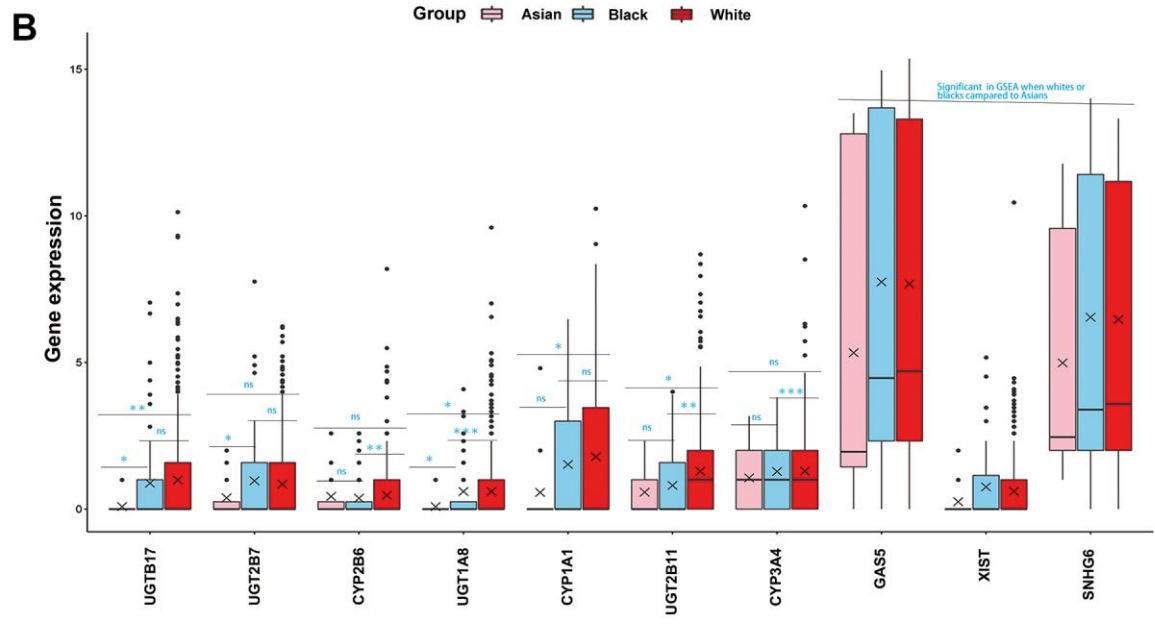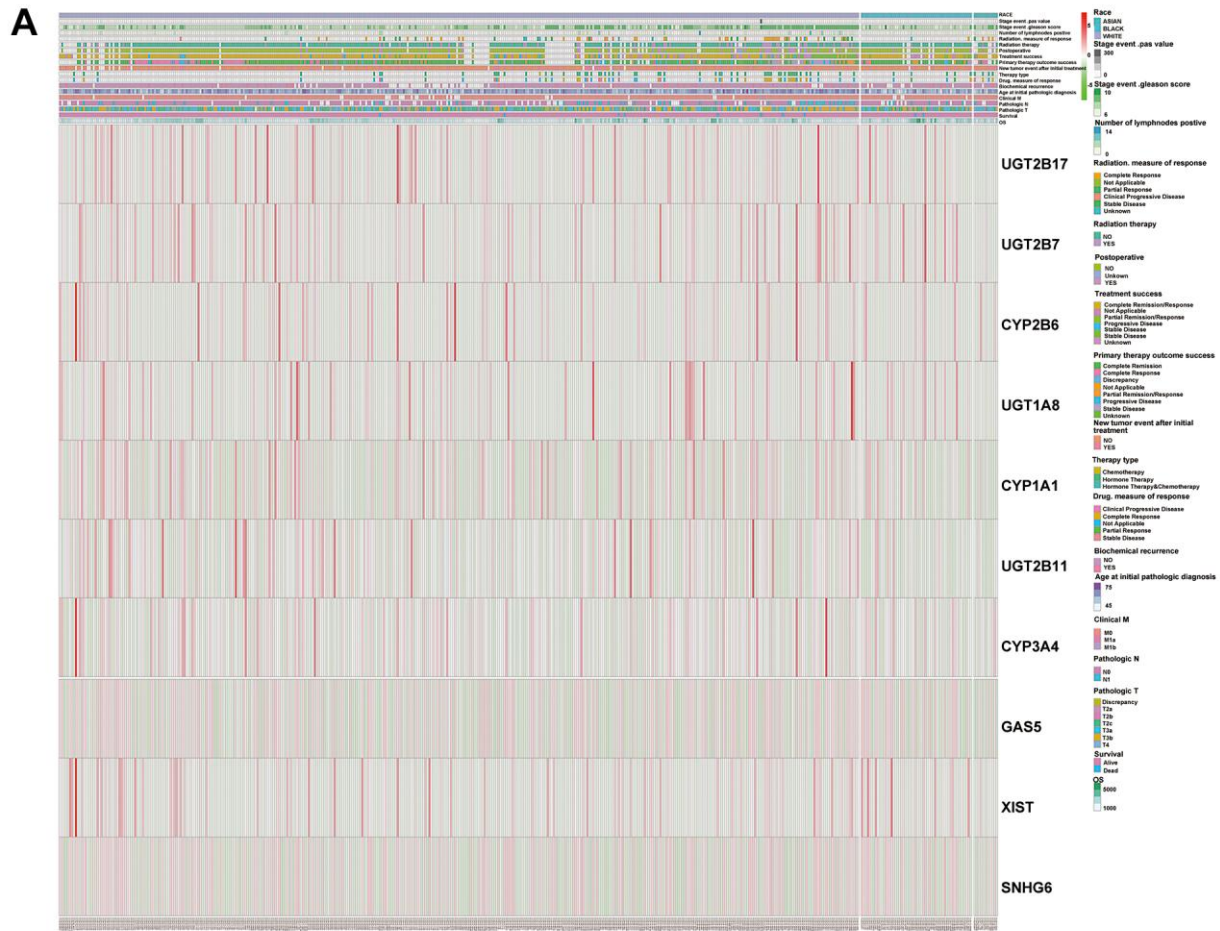
Supplementary Figure 6. The race differences analysis for drug metabolism-related core genes, which more associated with chemotherapy or endocrine therapy resistance in PCa treatment, were shown in the hot map(**A**) and box plots(**B**).