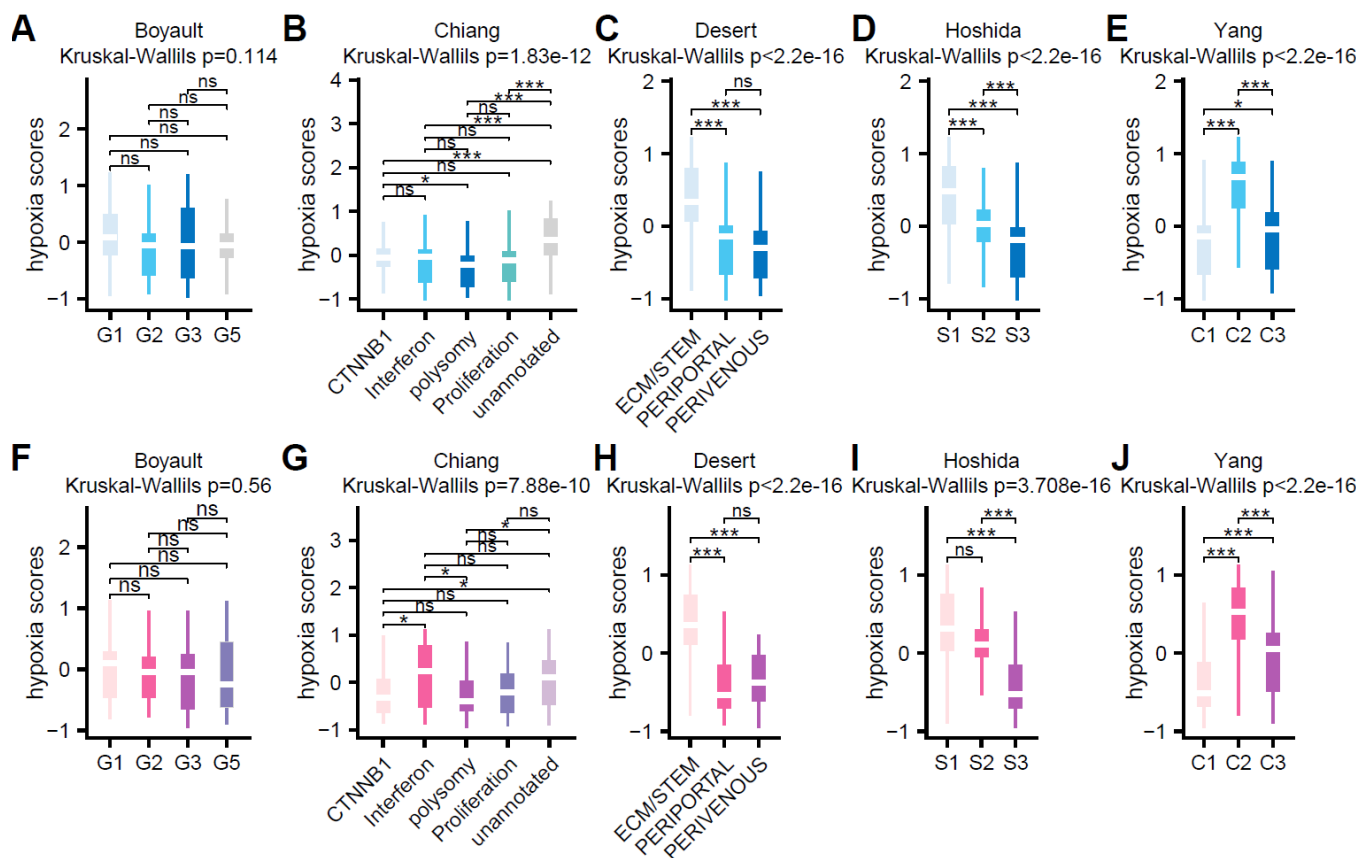**Figure S1** The association between hypoxia scores and clinical features in TCGA cohort and GSE14520 cohort. In TCGA cohort, we analyzed the association between hypoxia scores and (A) gender, (B) age, (C) child grade, (D) fibrosis ishak score, (E) stage, (F) HBV, (G) alcohol history, (H) recurrence status. In GSE145220 cohort, we analyzed the association between hypoxia scores and (I) gender, (J) age, (K) ALT level, (L) cirrhosis status, (M) stage, (N) HBV, (O) tumor size, (P) recurrence status. *, P<0.05; **, P<0.01; ***, P<0.001; ns, not significant.

Figure S2 The association between hypoxia scores and molecular subtypes in TCGA cohort and GSE14520 cohort. In TCGA cohort, we analyzed the association between hypoxia scores and (A) Boyault *et al.* classification, (B) Chiang *et al.* classification, (C) Desert *et al.* classification, (D) Hoshida *et al.* classification, (E) Yang *et al.* classification. In GSE145220 cohort, we analyzed the association between hypoxia scores and (F) Boyault *et al.* classification, (G) Chiang *et al.* classification, (H) Desert *et al.* classification, (I) Hoshida *et al.* classification, (J) Yang *et al.* classification. *, P<0.05; **, P<0.01; ***, P<0.001; ns, not significant.
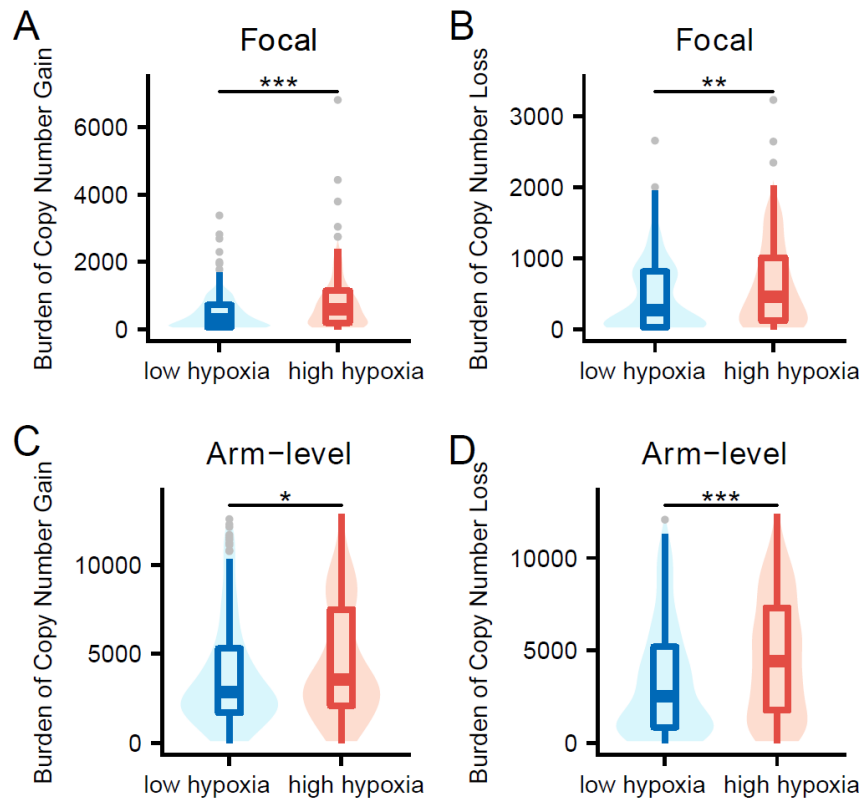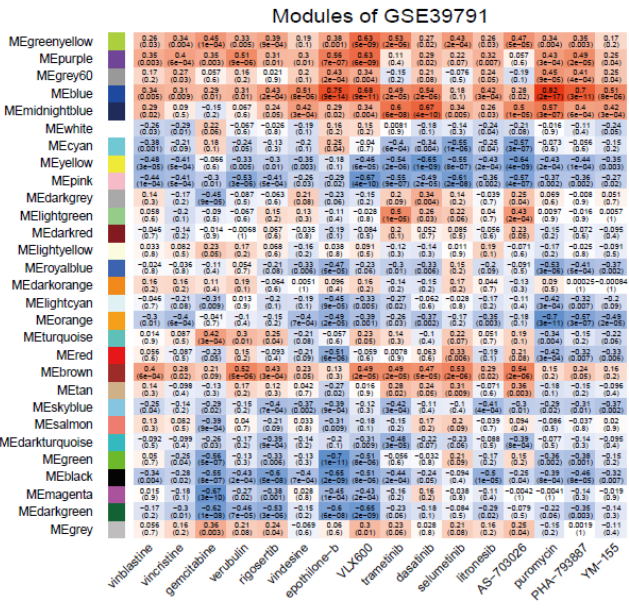
Figure S3 Distribution of copy number alterations burden between high hypoxia group and low hypoxia group. (A) Copy number gain burden in focal level. (B) Copy number loss burden in focal level. (C) Copy number gain burden in arm level. (D) Copy number loss burden in arm level. *, P<0.05; **, P<0.01; ***, P<0.001; ns, not significant.
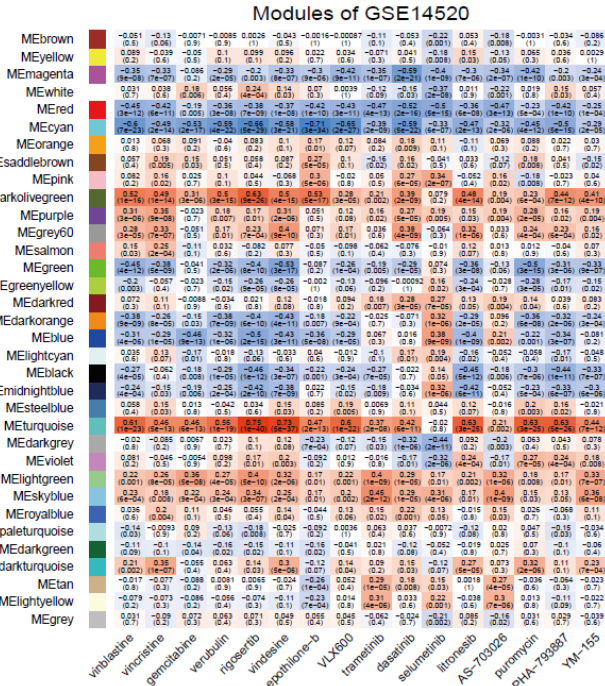
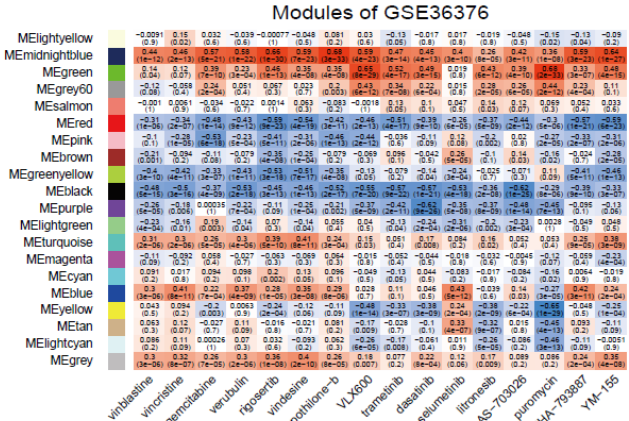**Figure S4** Identification of modules associated with the response of drugs in GSE14520 cohort, GSE36376 cohort and GSE39791 cohort. Heatmap of the correlation between the gene modules and the response of drugs in (A) GSE14520, (B) GSE39791, (C) GSE36376. Each row and column in the heatmap correspond to one gene module (labeled by color) or drug. In the heatmap, blue color represents negative correlation, while red represents positive correlation. Light color indicated lower correlation, and progressively darker color denotes higher correlation. The correlation coefficients and their P values (in brackets) had labeled in each cell.