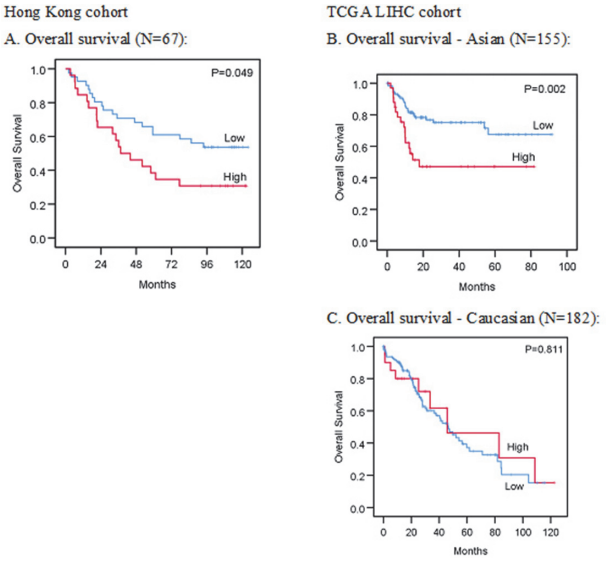
and peroxisome proliferator-activated receptor gamma (PPARγ) antagonist T0070907 were further determined. To demonstrate the clinical relevance of PPARγ, we performed scRNA-seq analysis of tumor biopsies from advanced HCC patients who received anti-PD-1 treatment.

Results We successfully established anti-PD-L1-resistance models, which were accompanied with lower $CD8^+$T cells and T helper 1 (T_H1) cells but higher exhausted T cells and myeloid-derived suppressor cells (MDSCs). Integrative gene expression analysis showed significant enrichment of PPARγ signaling in PD-L1R tumor cells. Importantly, T0070907 overcame ICB resistance in HCC, which was accompanied with enhanced cytolytic activity and reduced T cell exhaustion and decreased infiltration of MDSCs. Notably, scRNA-seq profiles of human biopsies uncovered adaptive upregulation of tumor-cell intrinsic PPARγ and re-shaping of T cell exhaustion in non-responders upon anti-PD-1 therapy.

Conclusions Taken together, hepatoma-intrinsic PPARγ activation might be associated with immune evasion and ICB resistance. Pharmacological inhibition of PPARγ sensitized tumors to anti-PD-L1 therapy, thus representing a promising strategy to overcome ICB resistance.



Abstract IDDF2020-ABS-0209 Figure 1 ABCB5 expression associated with poor survival outcomes in Asian HCC patients

IDDF2020-ABS-0209 ASIAN PREVALENT ALLELE AT ABCB5 SNP RS10254317 ASSOCIATES WITH HEPATOCELLULAR CARCINOMA (HCC) RISK AND ADVERSE CLINICAL OUTCOMES

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Background Ethnic disparities in the prevalence of hepatocellular carcinoma (HCC) continue to exist. Highest age-adjusted HCC incidence rates are recorded in East Asia, and 55% of HCC cases worldwide are from China. Meanwhile, ABCB5 has been reported to be overexpressed in HCC and associated with poor survival. To evaluate the ethnic differences, allele frequencies of ABCB5 SNP rs10254317 in the local cohort were compared with those from Chinese and Caucasian in 1000 Genomes project, and their clinical implications on HCC patients were studied.

Methods A total of 300 HCC and 300 healthy blood samples (99.3% and 94.7% Chinese respectively) were prospectively collected with informed consent. All patients had been diagnosed with primary HCC and underwent partial hepatectomy. Clinicopathological information including sex, age, tumour stage and survival outcomes were collected prospectively. Genomic DNA was extracted from blood samples and SNPs were examined. For comparison, genomics data and corresponding clinical information for HCC were obtained from The Cancer Genome Atlas (TCGA). SNP allele frequencies in different populations were obtained from 1000 Genomes Browser by NCBI.

Results Allele frequencies of rs10254317 observed in healthy local cohorts (G: 0.334 vs A: 0.666) were comparable to Northern and Southern Chinese (CHB; G: 0.311 vs A: 0.689; CHS; G: 0.286 vs A: 0.714) in 1000 Genomes project, which were significantly different from Caucasian (GBR; G: 0.615 vs A: 0.385) ($p<0.001$). Chinese-dominant allele frequency (AA/AG) associated with higher HCC risk (OR: 2.059, 95%CI: 1.16–3.67, $p=0.014$), advanced tumor stage (OR: 4.514, 95% CI: 1.02–19.96, $p=0.047$) and presence of venous infiltration (OR: 2.864, 95%CI: 1.00–8.18, $p=0.049$) from local cohort. TCGA HCC dataset also revealed a disparity in HCC survival outcomes among different populations, as elevated ABCB5 expression levels associated with poor survival in Asian HCCs but not in Caucasian HCCs (figure 1).

Conclusions Dominant allele of rs10254317 in ABCB5 among Chinese associates with risk of HCC and adverse clinical outcomes in HCC patients, which may also contribute to the ethnic disparity in HCC incidence and survival outcomes. Further investigation on SNPs of HCC-related genes with ethnic disparities are warranted.

IDDF2020-ABS-0215 ENHANCER REPROGRAMMING BY SELECTIVE HDAC8 INHIBITION POTENTIATES TUMOR REMISSION AND DURABLE BENEFIT BY PD-L1 BLOCKADE

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Background The insufficient T cell infiltration into non-inflamed tumors such as hepatocellular carcinoma (HCC) restricts the effectiveness of immune-checkpoint blockade (ICB) to a minority of patients. Epigenetic therapy provides new opportunities to rewire cancer transcriptional programs,