INTRODUCTION It has been demonstrated the relevance of host genetic polymorphisms in IL28B as predictors of therapeutic failure during HCV treatment with pegylated interferon-ribavirin.

OBJECTIVE To better understand the genetic architecture of IL28B single nucleotide polymorphisms (SNPs) in Brazilian populations, which could result in more informative markers for drug response in HCV patients undergoing treatment.

METHODOLOGY We selected eight IL28B SNPs from literature associated with failure during HCV treatment. Two other tag-SNPs flanking IL28B were included. Data for the 10 polymorphisms was extracted from populations included in the 1000 Genomes Project European (EUR, N=503), African (AFR, N=661), Admixed (AMR, N=347), Asian (ASN, N=993) and from the three Brazilian populations included in EPIGEN Project Bambui-MG, Pelotas-RS and Salvador-BA (N=1442, 3736 and 1309 respectively). We also genotyped these 10 SNPs in a population of healthy donors from a blood bank in Rio de Janeiro (RIO, N=135) using TaqMan SNP genotyping assays (ThermoFisher Scientific, USA). Allelic discrimination was performed in StepOnePlus RealTime-PCR. Using Haploview software we determined linkage disequilibrium (LD), and populations were compared through the r² statistic and haplotype frequencies. To increase the number of potential markers of interest, annotation was performed on the SNPs genotyped in EPIGEN using MASSA tool (Multi-Agent System for SNP Annotation).
**RESULTS** Individuals from RIO had an intermediate LD pattern compared to ancestral EUR and AFR populations from 1000Genomes dataset. We observed a LD block of 5 SNPs in EUR ($r^2>0.5$) that could be inferred by rs12979860; in comparison RIO had lower values of $r^2$ between the same pairs of markers. Concordantly, $r^2$ between rs12979860 and rs8099917 in RIO was 0.34 in the same trend as for EUR ($r^2=0.42$). The most frequent haplotype was the same between RIO, 1000G and EUR (frequency between 0.20-0.28). When evaluating haplotype combinations for rs12979860/rs8099917 that simultaneously carry the alleles associated with HCV therapeutic failure (T/T), RIO population displayed higher frequency (18%) compared to 1000G and EUR (both 14%). Out of 10 SNPs, the EPIGEN dataset had information for 5 polymorphisms including rs8099917. LD patterns for Salvador showed a marked difference with lower $r^2$ values compared to Bambui and Pelotas. RIO showed similar $r^2$ values compared to Bambui and Pelotas. MASSA annotation showed other four SNPs reported in the Pharmacogenomics Knowledge Base (PKGB) associated with drug responses outcomes in HCV. Based on EPIGEN populations we observed that these candidate SNPs had no LD with rs8099917.

**CONCLUSION** Of the 10 SNPs initially evaluated, we observe that RIO has a characteristic structure that resembles with EUR, Bambui and Pelotas, but slightly differs towards Salvador, highlighting the importance of depicting genetic structure in Brazilian populations. Annotation and LD analysis suggests that other SNPs should be evaluated in the IL28B region for the brazilian population.

**KEYWORDS** IL28B, polymorphism, linkage disequilibrium, haplotype, brazilian populations.