Interferon Lambda 4 Variant rs12979860 Is Not Associated With RAV NS5A Y93H in Hepatitis C Virus Genotype 3a

Peiffer et al. recently reported an association between the host interferon lambda 4 (INFL4) single-nucleotide polymorphism (SNP), rs12979860, and the NS5A resistance-associated variant (RAV) Y93H in hepatitis C virus (HCV) genotype 1b (HCVg1b). This observation is intriguing because it directly links innate immunity to HCV viral drug resistance for the first time. A small cohort of (51) HCV genotype 3 (HCVg3) patients was included in the analysis; this subgroup analysis was underpowered and no association was observed in HCVg3. The association was also not observed in 259 patients with HCV subtype 1a.

HCVg3 infections are more difficult to treat with direct-acting antivirals. The reason for this is unknown, but could be explained by a distinct pattern of RAVs and an increase in the prevalence of “favorable” IFNL4 SNPs in this genotype. Here, we used a large cohort of 496 HCVg3a-infected patients (from the BOSON clinical study) and report no significant association ($P > 0.05$; Table 1). Overall, our data support the Peiffer et al. hypothesis that the association between INFL4 and Y93H is specific to HCV genotype 1b.

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