Post-liver transplantation graft biopsies should not be used to assess the *IL28B* donor genotype in HCV recipients

To the Editor:

We read with interest the article by Coto-Llerena *et al.* [1] showing that the determination of the donor interleukin 28B (*IL28B*) genotype on post-liver transplantation (LT) graft biopsies carries a high risk of misclassification, as it adds to the current debate on the clinical role of this test in LT patients. Indeed, following LT it is still somewhat unclear whether the donor, the recipient or the combination of the two *IL28B* genotypes is actually associated with the achievement of a sustained virological response (SVR) after interferon (IFN)-based treatment in HCV patients [2–6]. Clearing this matter would have important clinical implications, especially since *IL28B* genotyping of the recipient can be easily performed by DNA extraction from the blood, while on the other hand, given that donor blood is not always routinely available for clinical use, donor DNA needs to be extracted from formalin-fixed paraffin embedded (FFPE) liver tissue specimens obtained before, during or after LT. Although this is feasible from a technical standpoint, no study has shown whether the *IL28B* genotype obtained matches that obtained from peripheral blood mononuclear cells (PBMC). For this matter, the authors analyzed the *IL28B* rs12979860 donor genotype, by TaqMan real-time PCR and direct sequencing, in 56 HCV-infected LT recipients and their donors, in PBMCs and/or liver biopsies obtained at the moment of LT (reperfusion) or at any time during post-transplant follow-up. Overall, *IL28B* rs12979860 genotyping was successful in up to 98% of samples. The authors report a 100% match in *IL28B* genotype between donor PBMC and reperfusion biopsies in 36 out of 56 patients studied, while, they found a high rate of discordant results between *IL28B* genotype in donor PBMC or reperfusion liver biopsies compared to post-transplant liver biopsy specimens. To externally validate these findings, we analyzed the *IL28B* genotype of 39 liver donors by comparing DNA extracted from donor PBMC and FFPE or snap frozen post-transplant follow-up liver biopsies. *IL28B* rs12979860 genotyping was performed by TaqMan real-time PCR, and confirmed by Tetra-primers Amplification Refractory Mutation System (T-ARMS) PCR [7]. As shown in Fig. 1, we replicate Coto-Llerena's findings, since overall in 39% of cases there was a mismatch between *IL28B* genotype obtained in PBMCs and post-LT liver biopsies. Moreover, similar mismatch rates were found when *IL28B* genotype was tested from DNA extracted from snap frozen or FFPE follow-up liver biopsies (36% *vs.* 45%, $p = 0.55$). Our data therefore show that, independently from the source used to extract DNA, the use of follow-up biopsies should be discouraged as a routine test to determine donor *IL28B* genotype due to an extremely high mismatch rate.

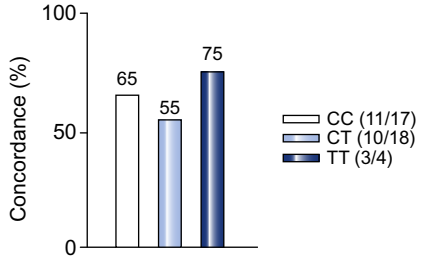

Fig. 1. *IL28B* genotype concordance between donor PBMC and post-LT liver biopsies.

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Conflict of interest

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