Mutations within the hepatitis C virus genotype 1b E2-PePHD domain do not correlate with treatment outcome.

Titre	Mutations within the hepatitis C virus genotype 1b E2-PePHD domain do not correlate with treatment outcome.
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Résumé en anglais	The hepatitis C virus (HCV) envelope protein 2 (E2) interacts in vitro with the interferon alpha (IFN-alpha)-inducible double-stranded RNA-activated protein kinase, suggesting a possible mechanism by which HCV may evade the antiviral effects of IFN-alpha. Variability in the part of the HCV E2 gene encoding the carboxy-terminal part of the protein, which includes the interaction domain (E2-PePHD), was explored in 25 patients infected with HCV genotype 1b and receiving IFN-alpha therapy. PCR products were generated and sequenced for 15 patients with a sustained response and for 10 patients with no virological response after treatment with IFN-alpha and ribavirin. PePHD amino acid sequences were obtained for isolates from serum collected before and during treatment, after 2 months in responders, and after 6 months in nonresponders. Quasispecies analysis of the pretreatment PePHD region was performed for isolates from patients displaying amino acid substitutions in this domain on direct sequencing. The E2-PePHD sequence was highly conserved in both resistant and susceptible genotype 1b strains and was identical to the prototype HCV type J sequence. No significant emergence of PePHD mutants during therapy was observed in our clonal analysis, and sporadic mutations and treatment outcomes were not found to be correlated. The PePHD sequence before or during treatment cannot be used to predict reliably the outcome of treatment in HCV type 1b-infected patients.
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