

Quasispecies evolution in NS5A region of hepatitis C virus genotype 1b during interferon or combined interferon-ribavirin therapy

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AIM: To evaluate the implication of substitutions in the hepatitis C virus (HCV) non-structural 5A (NS5A) protein in the resistance of HCV during mono-interferon (IFN) or combined IFN-ribavirin (IFN-R) therapy. Although NS5A has been reported to interact with the HCV RNA-dependent RNA polymerase, NS5B, as well as with many cellular proteins, the function of NS5A in the life cycle of HCV remains unclear.

METHODS: HCV quasispecies were studied by cloning and sequencing of sequential isolates from patients infected by HCV genotype 1b. Patients were treated by IFN-alpha2b for 3 mo followed by IFN-alpha2b alone or combined IFN-R therapy for 9 additional months. Patients were categorized into two groups based on their response to the treatments: 7 with sustained virological response (SVR) (quasispecies = 150) and 3 non-responders (NR) to IFN-R (quasispecies = 106).

RESULTS: Prior to treatment, SVR patients displayed a lower complexity of quasispecies than NR patients. Most patients had a decrease in the complexity of quasispecies during therapy. Analysis of amino acids substitutions showed that the degree of the complexity of the interferon sensitivity-determining region (ISDR) and the V3 domain of NS5A protein was able to discriminate the two groups of patients. Moreover, SVR patients displayed more variability in the NS5A region than NR patients.

CONCLUSION: These results suggest that detailed molecular analysis of the NS5A region may be important for understanding its function in IFN response during HCV 1b infection.

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