Viral relapse is associated with the emergence of new viral strains following treatment in an HIV-positive cohort infected with acute HCV

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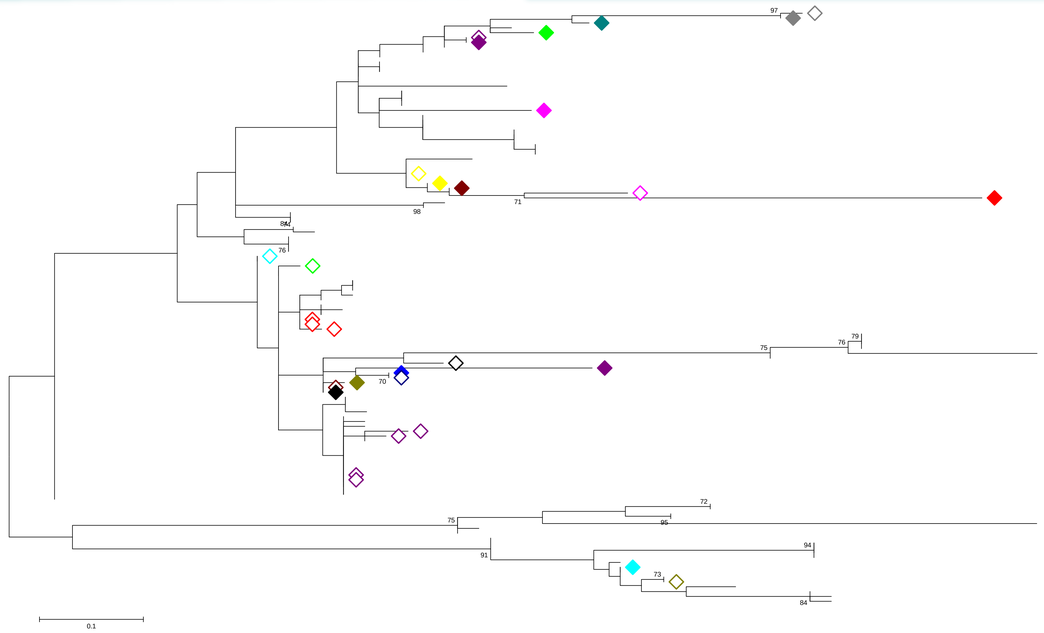
Background

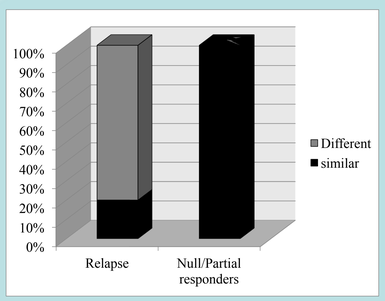
More than 1000 cases of acute hepatitis C (HCV) in HIV-positive men-who-have-sex-with-men (MSM) have recently been reported in urban centres in the Europe, Australia and the USA[1,2,3] .
Sustained virological response rates (SVR) in acutely co-infected patients are lower than in acutely mono-infected individuals (59 versus 98%) [1,4] but the reasons for this are not understood.
We carried out viral sequence analysis from pre and post treatment plasma samples taken from patients who failed therapy in an established cohort of 160 HIV-positive patients with acute HCV[5].

Methods

Viral RNA was extracted from paired plasma samples and a 220bp region of the E2 envelope gene was amplified using nested RT-PCR and a combination of genotype-specific primers. Sequences were aligned using Clustal W and a maximum likelihood phylogenetic tree constructed with MEGA 5.0 using the method and Kimura two-parameter distance for all substitutions. Genetic distance was calculated as the mean percentage difference between sequences.



Results



Of the 18 patients that failed treatment, paired samples were available from 11 (5 relapsers, 3 null responders and 3 partial responders). Viral relapse was significantly associated with the detection of new viral strains (80%; 4/5 patients) in comparison with partial and null responders (0%;0/6; p=0.015).

Figure 1: A Maximum likelihood phylogenetic tree was constructed using the Kimura-2 parameter and gamma site distribution using MEGA 5.0. Consensus sequences derived from post-treatment samples are shown as filled circles and preceding samples are shown in unfilled diamonds. Samples from relapsers are highlighted with an asterisk. Reference sequences derived from patients within the cohort and the UK were included.

Conclusions

Relapse following anti-HCV treatment in this cohort is strongly associated with the emergence of new viral strains. Further analysis is required using superior methodology such as next generation sequencing to differentiate between reinfection and emerging dominance of pre-existing minority strains

References

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