HIV Patients Develop High Levels of Broadly Neutralizing Antibodies against Hepatitis C Virus

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INTRODUCTION

- Co-infection with HIV and hepatitis C virus (HCV) is a major health issue and may affect up to 7 million persons worldwide (Taylor LE, *Clin. Infect. Dis.*, 2012)
- The high cost of new direct-acting antivirals against HCV limit their use in countries with poor income, underscoring the urgent medical need of a HCV vaccine in HIV⁺ patients (Lambotin M, *Expert. Rev. Vaccines*, 2012)
- The impact of HIV infection on the HCV-humoral response remains unknown although it might greatly influence the design and the effectiveness of a HCV vaccine in HIV-infected patients.

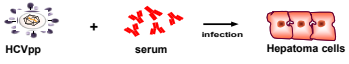
AIM: Understanding the impact of HIV infection on HCV-humoral response

➢ We aim to investigate the HCV-specific neutralizing response in HIV-infected patients.

PATIENTS

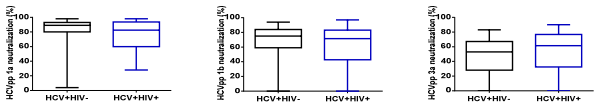
		HIV negative		HIV positive	
All patients		HIV(-) HCV(-) n = 30	HIV(-) HCV(+) n = 136	HIV(+) HCV(-) n = 70	HIV(+) HCV(+) n = 63
Sex –no. (%)	Male	22 (73%)	88 (65%)	55 (79%)	46 (73%)
	Female	8 (27%)	48 (35%)	15 (21%)	17 (27%)
Age- year	Mean	37	49.2	40.8	45.1
	Range	20 – 50	21 – 80	22 – 62	23 – 68
HIV RNA positive -no. (%)				40 (57%)	25 (40%)
HIV viral load- Log10 copies/mL					
	Mean	–	–	2.87	2.60
	Range	–	–	1.72 – 5.83	1.78 – 5.83
CD4 – cells/µL					
	Mean	–	–	550	424
	Range	–	–	77 - 1629	41 - 1770
HCV RNA positive - no. (%)		–	95 (70%)	–	36 (57%)
HCV viral load - Log10 UI/mL					
	Mean	–	5.96	–	5.83
	Range	–	4.38 – 7.15	–	1.51 – 7.24

HCVPP NEUTRALIZATION



HCV-viremic patients: similar high levels of anti-HCV nAbs in HIV⁻/HCV⁺ and HIV⁺/HCV⁺

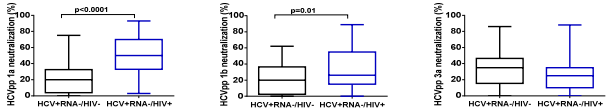
A.



HCV genotypes	G1a	G1b	G3a	G4	G2	Other
HCV+HIV- (%)	29	31	16	15	3	6
HCV+HIV+ (%)	22	22	28	22	6	

HCV-aviremic patients: higher levels of anti-HCV nAbs in HIV⁺/HCV⁺ patients

B.



Broadly nAbs anti-HCV detected in 13% HIV⁺/HCV⁻ individuals.

C.

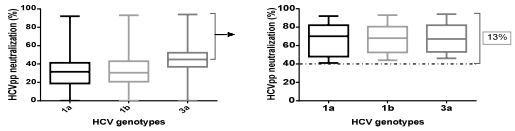
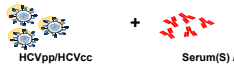


Fig. 1. Magnitude of HCV-specific neutralizing antibody-mediated response against different HCVpp genotypes. HCV pseudoparticules (HCVpp) expressing envelope glycoproteins of HCV genotypes 1a, 1b, and 3a were preincubated with patients' sera at the dilution 1:100 for 1h at 37°C and added to Huh7.5.1 cells in triplicate for 72h at 37°C. Percentage of neutralization with HCVpp genotypes 1a, 1b, and 3a are represented separately in box plot for the following populations: HCV-viremic HIV⁻/HCV⁺ and HIV⁺/HCV⁺ patients (A), HCV-aviremic HIV⁻/HCV⁺ and HIV⁺/HCV⁺ patients (B), HIV⁺/HCV⁻ patients (C). HCV genotypes of HCV viremic patients are shown.

CONFIRMATION STUDY



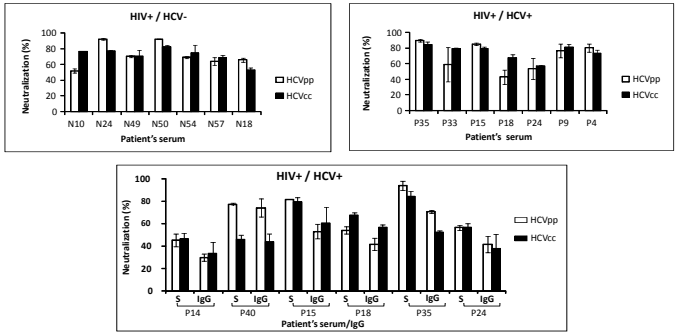


Fig. 2. Confirmation of HCVpp neutralization using the HCVcc system and purified immunoglobulins G (IgG). HCV pseudoparticules (HCVpp) expressing envelope glycoproteins of HCV genotypes 1a or cell-culture derived HCV (HCVcc) genotype 2a Jc1 were preincubated with patients' sera (S) or purified immunoglobulins G (IgG) and added to Huh7.5.1 cells for 72h at 37°C. Mean percentage of neutralization of HCVpp and HCVcc are shown for a selection of patients from the indicated populations. Mean values ± SD of three independent experiments are shown.

CONCLUSION

- ✓ HIV/HCV co-infected patients are able to develop high levels of HCV-specific broadly nAbs suggesting that HCV-humoral response is not impaired during HIV-infection
- ✓ High levels of HCV-specific nAbs persist in HCV-aviremic HIV⁺/HCV⁻ co-infected patients
- ✓ Detection of anti-HCV neutralizing activity in some HIV⁺/HCV⁻ patients suggests frequent exposure to HCV with the ability to spontaneously clear the virus
- ✓ Persistence of HCV-neutralizing response may forecast promising achievement of HCV vaccination in HIV-infected persons

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