Innate Immune Activation Pathways Overlap, Yet are Distinct in HCV and HIV Infection

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BACKGROUND

- Chronic innate and adaptive immune activation are well recognized during HCV and HIV infection
- Drivers of this process are less clear
- Whether the same drivers operate in each infection is unknown

AIM

Primary objective: to better understand drivers of immune activation during HCV and HIV infection

METHODS

- Plasma sCD14, IL-6, LGALS3BP (mac binding protein), LBP (LPS binding protein), I-FAB (Intestinal fatty acid binding protein), and sCD163 levels were measured by ELISA in uninfected controls, HCV infected, HCV-HIV infected and HIV infected subject not on therapy for HIV.
- HCV and HCV-HIV infected group were stratified into low vs. hi APRI score (AST/PLT ratio index, reflective of liver damage) subgroups.
- HIV infected groups were evaluated again after 3-6 months of antiretroviral therapy.
- Statistical analysis are presented as nonparametric analysis of variance comparison, with p value less than 0.05 significant.

ACKNOWLEGMENTS

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RESULTS

Figure 1: Both untreated HCV and HIV infection contribute to elevated soluble markers of immune activation

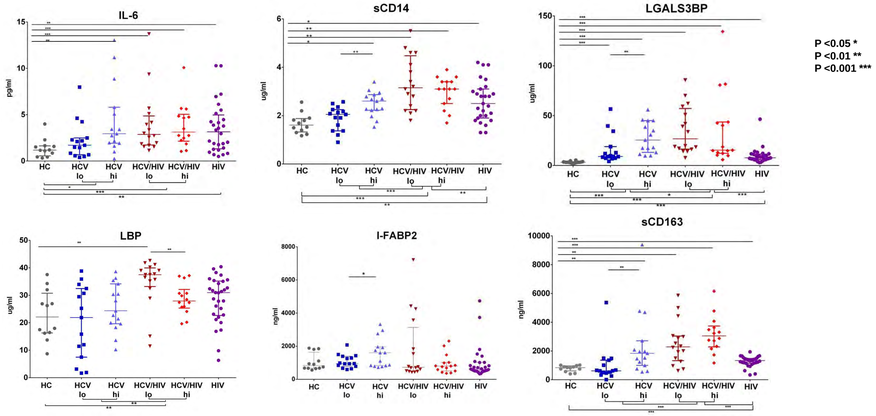


Table1: Clinical characteristics of study subject groups

Variable	UD	HCV		HCV/HIV		HIV	P
Number	12	30		30		30	
		HCVlo (15)	HCVhi (15)	HCV/HIVlo(14)	HCV/HIVhi(16)		
Age(years)	45(30,56)	55 (44,63)	54 (47,70)	48 (34,54)	46.5 (31,54)	40 (18,57)	<0.001
Race							
Caucasian	9 (75%)	5 (33.3%)	8 (53.3%)	1 (6.25%)	3 (21.4%)	10 (33.3%)	
African American	3 (25%)	7 (46.7%)	7 (46.7%)	15 (93.75%)	9 (64.3%)	17 (56.7%)	
Hispanic					2 (14.3%)	3 (10%)	
HCV (IU/mL)		1,111,840 (596327, 1943815)	547,639 (287772, 1037018)	1,349,19 (600000, 7017127)	1,750,000 (689750, 6877500)		0.040
HCV genotype (%)							
1		15 (100%)	10 (66.6%)	15 (93.72%)	12 (80%)		
2/3			5 (33.3%)				
HIV (c/mL)				54,100 (29844,299868)	1,745 (504.75, 6998)	36,491 (6795, 124622)	<0.0001
CD4 count (cells/mm³)				285 (196, 405)	278 (145, 509)	256 (114,395)	
AST (U/L)		38 (24.5, 40)	88 (51, 116.5)	36 (27.7, 47.2)	82.5(65.7, 121)	24 (19, 29)	<0.0001
ALT (U/L)		38 (26, 41)	71 (47, 121)	34 (26, 42)	97 (62, 138)	35.5 (27, 56)	<0.0001
PLT (10^3/mm³)		252 (191, 266)	155 (188, 222)	241 (216, 218)	172 (130, 194)	212.5 (162-257)	0.001
APRI score		0.3 (0.2, 0.4)	1.1 (0.85, 1.55)	0.4 (0.2, 0.47)	1.1 (0.89, 2.03)	0.2 (0.1, 0.3)	<0.0001
FIB_4 score		1.3 (0.98, 1.65)	3.1 (2.3, 4.3)	1.3 (0.9, 1.7)	2.3 (1.7, 4.0)	0.6 (0.5, 1.2)	<0.0001

RESULTS

Figure 2: Some but not all soluble markers of immune activation normalize after 3-6 months of antiretroviral therapy

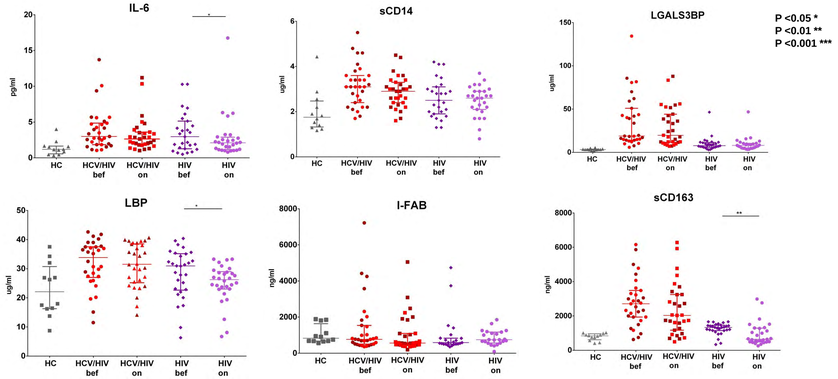


Table 2: Correlations between soluble markers of immune activation

	HCV						HCV/HIV						HIV					
	IL-6	sCD14	LBP	I-FAB	LGALS3 BP	sCD163	IL-6	sCD14	LBP	I-FAB	LGALS3 BP	sCD163	IL-6	sCD14	LBP	I-FAB	LGALS3 BP	sCD163
IL-6		r=0.341 p=0.05 *	r=0.401 P=0.028 *								r=0.415 p=0.023 *	r=0.441 p=0.015 *			r=0.772 p<0.001 ***			
sCD14	r=0.341 p=0.05 *		r=0.417 P=0.022 *		r=0.394 p=0.031 *	r=0.652 p<0.001 ***			r= 0.521 p=0.003 **		r=0.479 p=0.007 **				r=0.478 p=0.010 **		r=0.392 p=0.039 *	
LBP	r=0.401 P=0.028 *	r=0.417 P=0.022 *						r=0.521 p=0.003 **					r=0.772 p<0.0001 ***	r=0.478 p=0.010 **			r=0.489 p=0.006 **	r=0.361 p=0.05 *
I-FAB																		
LGALS3 BP		r=0.394 P=0.031 *				r=0.511 p=0.004 **	r=0.415 p=0.023 *	r=0.479 p=0.007 **				r=0.542 p=0.002 **		r=0.392 p=0.039 *	r=0.489 p=0.006 **			
sCD163		r=0.652 p<0.001 ***			r=0.511 p=0.004 **		r=0.441 p=0.015 *				r=0.542 p=0.002 **				r=0.361 p=0.05 *			

CONCLUSIONS

- Both HCV and HIV infection contribute to elevated levels of soluble markers of immune activation, with IL-6, sCD14, LGALS3BP, and sCD163 elevated during both HCV and HIV infection.
- During HCV-HIV infection sCD14 and sCD163 levels are greater than in ether monoinfection indicating an additive effect of each infection.
- Overlapping, yet distinct correlations among these markers comparing groups is consistent with common and distinct drivers of immune activation comparing HCV to HIV infection.