

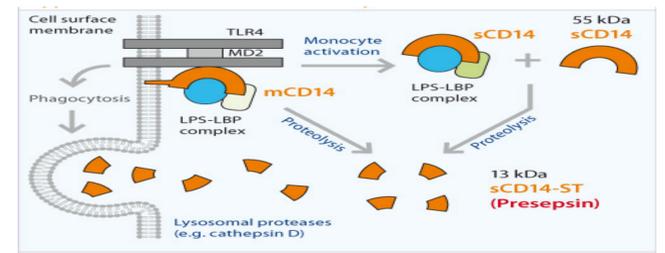
# The role of Presepsin (sCD14-ST) as an indirect marker of microbial translocation and immune activation in HIV and HIV/HCV coinfected patients

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## Background

- Presepsin, a newly discovered soluble fragment of CD14, has been studied as a sepsis biomarker.
- The mechanism of its secretion is involved in the TLR4 activation cascade and it is related to mCD14 and sCD14, which are monocyte activation markers, indirectly representing the presence of bacterial translocation<sup>(1)</sup>. Therefore Presepsin could be employed as an immune activation marker, and it could allow for the estimation of bacterial translocation rates.
- The aim of this study was to assess the correlations between Presepsin serum concentration and bacterial translocation, immune activation and fibrosis markers in subjects with HIV and HCV mono-infections and in HIV/HCV co-infection, compared to healthy controls.



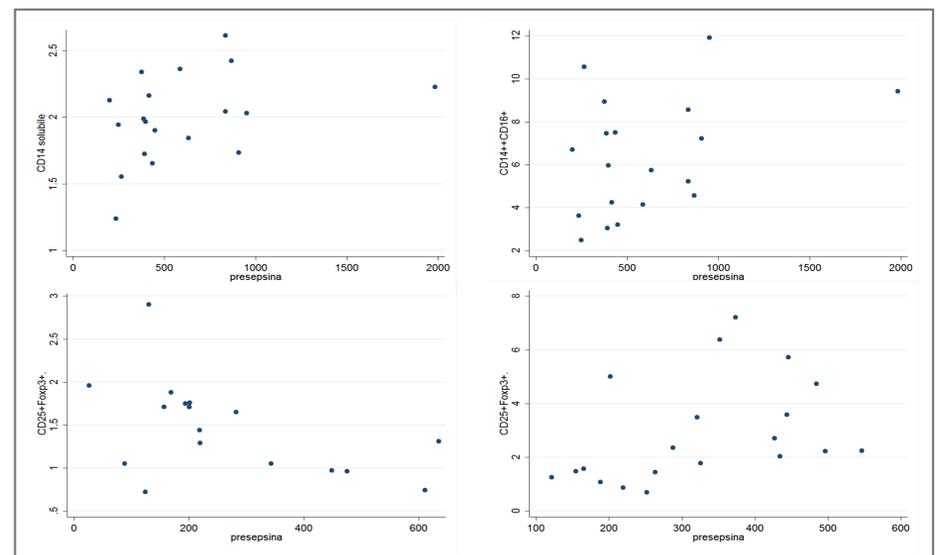
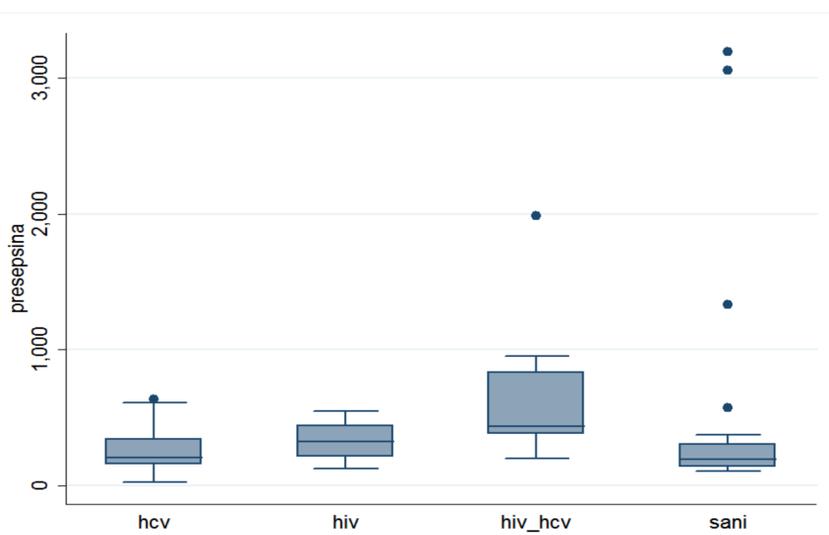
## Methods

Study population characteristics divided per groups (HIV, HCV, HIV/HCV, Healthy controls)					
Characteristics	Healthy controls n=20	HCV monoinfected n=20	HIV monoinfected n=20	HIV/HCV co-infected n=20	P
Median age (years)	37,75	56,25	46,55	48,6	0,0001
Male gender (%)	20	40	80	95	*
Median CD4+ T cell count (cells/mm <sup>3</sup> )	744,3	757,25	421,8	508,4	0,0001
Median FIB4	0,67	1,88	0,98	2,46	0,0001
Median Liver Stiffness (Kpa)	3,1	8,46	3,9	9,16	0,0001
Median serum HCV RNA (IU/ml)	0	6.303.071,1	0	1.216.752	0,523
Patients receiving HAART	0	0	20	20	*
Median plasma HIV-RNA (copies/ml)	0	0	<40**	<40**	*
Median AST level (IU/l)	18,4	48,1	26,8	55,7	*
Median ALT level (IU/l)	17,1	61,2	30,35	73,8	*
Median duration HIV infection (years)	0	0	10,55	19,35	*
Median duration HCV infection (years)	0	10,95	0	12,45	*
Genotype 1a	0	3 (15%)	0	7 (35%)	*
Genotype 1b	0	5 (25%)	0	3 (15%)	*
Genotype 1a/1b	0	2 (10%)	0	0	*
Genotype 2a	0	3 (15%)	0	0	*
Genotype 3	0	1 (5%)	0	3 (15%)	*
Genotype 4	0	1 (5%)	0	1 (5%)	*
Genotype 2a/2c	0	4 (20%)	0	2 (10%)	*
Genotype 1a ± 2a/2c	0	1 (5%)	0	0	*
Genotype 1a ± 4c/4d	0	0	0	1 (5%)	*
Genotype 1b ± 4c/4d	0	0	0	1 (5%)	*
Genotype 4c/4d	0	0	0	2 (10%)	*

- This is a cross-sectional study included 80 subjects followed up at the Department of infectious Diseases of Policlinico San Matteo, Pavia University.
- The study population included patients with HIV mono-infection (n = 20), HCVmono-infection (n = 20), HIV/HCV co-infection (n = 20), and healthy controls (n =20). Peripheral blood was analyzed to determine the levels of Presepsin, Forkhead box 3 (Foxp3+) T cells, TGF- β1, CD14 (soluble and surface isoforms), IL-17 and bacterial translocation products.
- These measurements were correlated to the severity of liver fibrosis, measured with the FIB-4 score and transient elastography.

## Results

- Presepsin concentration was significantly higher in the HIV patients (HIV monoinfected and HCV / HIV co-infected). The same group showed increased levels of sCD14 and mCD14, expression of immune activation.
- Statistical analysis show a significant correlation between presepsin and both forms of CD14 only in HIV / HCV group, where the percentage of bacterial translocation and chronic inflammation is high, as shown by the significant increase in bacterial DNA levels, sCD14, mCD14 and IL-17. Presepsin is associated to FIB4 values in the HCV group.



## Conclusion

Presepsin is a biomarker of chronic immune activation, as demonstrated by its correlations with sCD14, mCD14 and CD4+CD25+Foxp3+ lymphocytes, particularly in HIV infection. Its concentration is correlated to liver fibrosis markers, such as FIB4, particularly in HCV mono-infected patients. Considering presepsin and a direct correlation between the levels of fibrosis and an inverse correlation with Treg cells in this group, the low levels of Treg cells may be involved in increasing the state fibrosis in chronic HCV patients.

### Reference

1. Yaegashi, Y., Shirakawa, K., et al. Evaluation of a newly identified soluble CD14 subtype as a marker for sepsis. *Journal of Infection and Chemotherapy*, 11(5), 234–238. doi:10.1007/s10156-005-0400-4 (2005).