T cell and monocyte activation correlate and decline during HCV therapy for HCV/HIV coinfection

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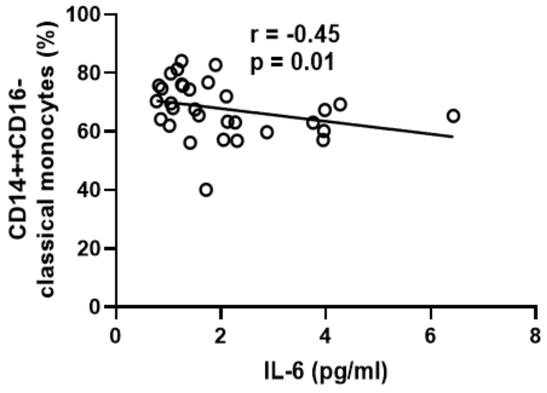
BACKGROUND

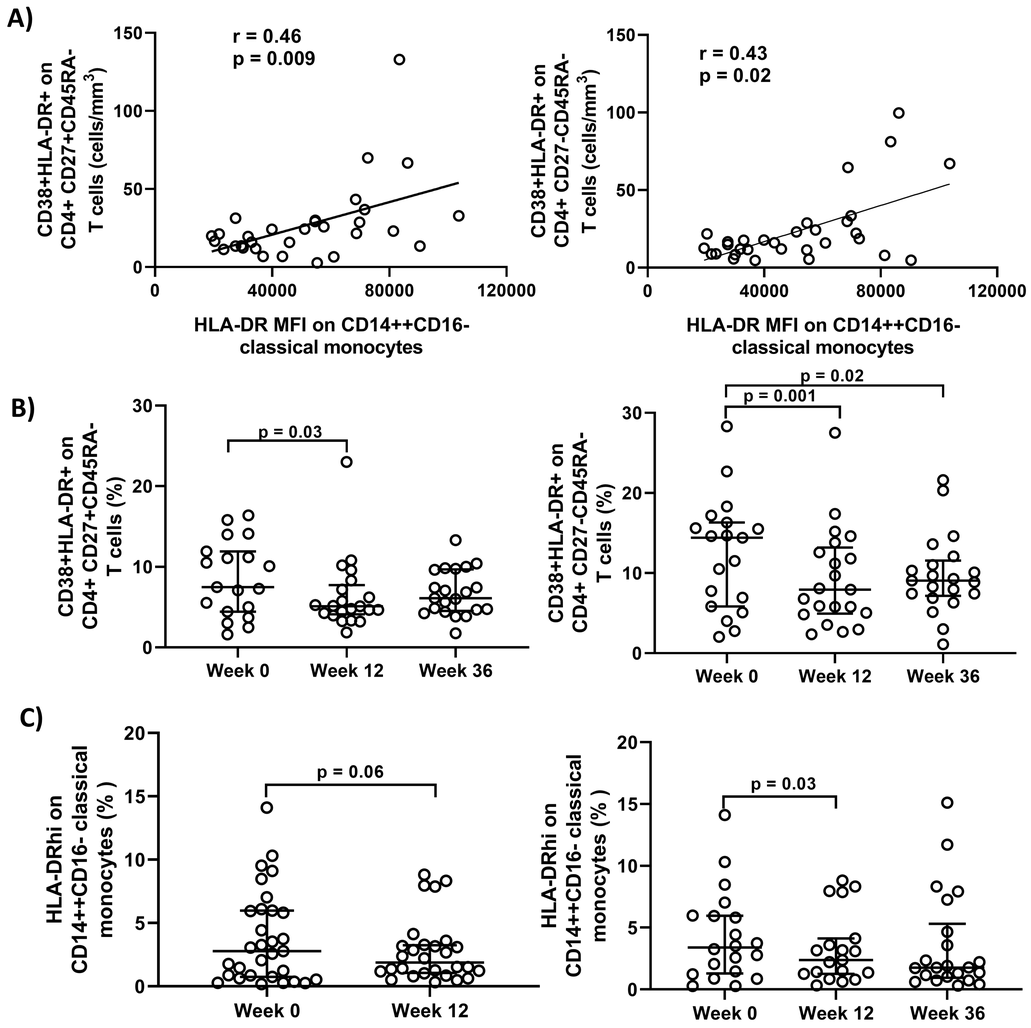
Immune activation predicts morbidity in HCV, HIV and HCV-HIV co-infection despite antiretroviral therapy (ART). HCV direct-acting antiviral (DAA) therapy is associated with partial/complete normalization of soluble markers of immune activation during HCV infection. How this extends to cellular immunity during HCV-HIV co-infection is less clear.

METHODS

We analyzed plasma and PBMC from AIDS Clinical Trials Group (ACTG) A5329, where either integrase inhibitor or protease inhibitor -based ART treated HCV/HIV co-infected participants were treated with paritaprevir/ritonavir/ombitasvir+dasabuvir+/-ribavirin for 24 (n=36) or 12 (n=9) weeks. In a subset of participants where viable samples were available ((n=21) 24 week therapy and (n=7) 12 week therapy) we performed flow cytometric analysis of T cells, central memory (CM)/effector memory (EM) subsets, monocyte subsets (CD14+CD16- classical, CD14+CD16+ inflammatory, and CD14-CD16+ patrolling), and cell activation (CD38 and HLA-DR expression) before (week 0), during (week 12) and after therapy (week 36) to assess changes (Wilcoxon Signed Rank Test) pooled over the entire sample. Spearman's correlations evaluated associations between soluble immune activation markers (plasma sCD14, sCD163, IP10 and IL-6) and T cell and monocyte subset/activation.



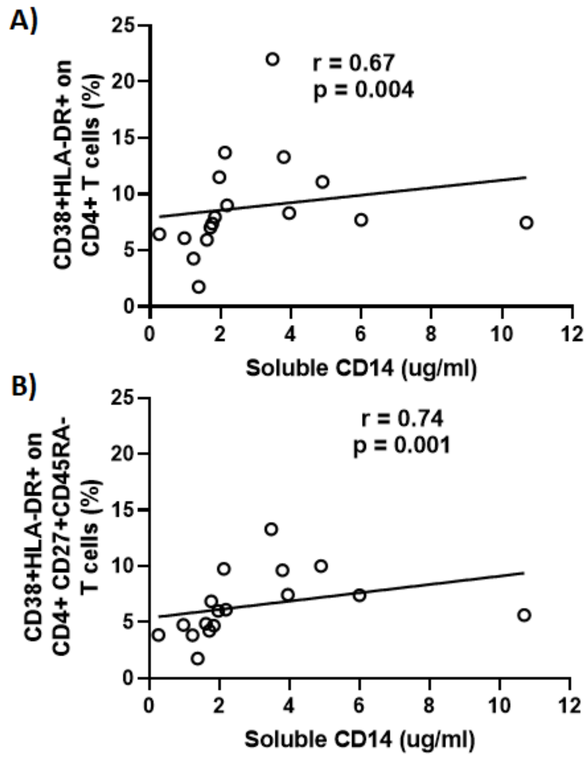
Classical monocyte frequency negatively correlates with IL-6 levels during untreated HCV in ART-controlled HCV/HIV co-infected participants at baseline.



CD38 and HLA-DR co-expression on CD4+ T cell subsets and HLA-DR expression on Monocyte subsets positively correlate during untreated HCV and decline after direct-acting antiviral (DAA) therapy in ART-controlled HCV/HIV co-infected participants.

RESULTS

CD38/HLA-DR co-expression on CD4 memory T cells decreased 12 weeks after initiation of DAA therapy (p=<0.05), and for CD4 EM (p=<0.001) at week 36(B). HLA-DRhi expressing classical monocyte frequency tended to decrease at 12 weeks (p=0.06)(C). Before therapy, HLA-DR expression on classical monocytes positively correlated with absolute counts of CD4 co-expressing CD38/HLA-DR (r=0.56, p=0.001), CD4 CM (r=0.46, p=0.009), and CD4 EM (r=0.43, p=0.02) T cells (A). Before DAA therapy IL-6 levels negatively correlated with classical monocyte frequency (r= -0.45, p=0.01), while 36 weeks after therapy initiation plasma sCD14 positively correlated with CD4 and CD4 CM T cells co-expressing CD38/HLA-DR (r=0.67, p=0.004; r=0.74, p=0.001, respectively).



CD38 and HLA-DR co-expression on CD4+ T cell subsets positively correlates with soluble CD14 after DAA therapy in ART-controlled HCV/HIV co-infected participants.

CONCLUSIONS

In this sample (n=28), memory T cell activation associated with monocyte subset activation during HCV-HIV co-infection, consistent with related underlying mechanisms. 12 weeks following therapy initiation, monocyte, CD4 and CD8 T cell activation was reduced. Residual memory CD4 T cell activation after HCV therapy associated with sCD14, potentially attributable to ART controlled HIV immune activation.

ADDITIONAL KEY INFORMATION

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