PDL1 expression on monocytes is associated with plasma cytokines in Tuberculosis and HIV

WEGENE TAMENE[1], Meseret Abebe[2], Liya Wassie[2], Helina Mollalign[1], Katrin Bauer[3], Amha Kebede[1], Vincent Marconi[4], Rawleigh Howe[2], and Ulrich Sack[5]

[1]Ethiopian Public Health Institute
[2]Armauer Hansen Research Institute
[3]University of Leipzig Faculty of Medicine
[4]Emory University School of Medicine
[5]Leipzig University

March 07, 2024

Abstract

Introduction: PDL1 and its interaction with PD1 is implicated in immune dysfunction in TB and HIV. The expression of PDL1 on multiple subsets of monocytes as well as their associations with cytokines and microbial products have not been well studies. Method HIV (n=35), TB (n=34) and TBHIV co-infected patients (n=12), primarily treatment naïve and apparently healthy controls (n=39) were recruited. Monocyte subsets were evaluated for PDL1 expression by flow cytometry; plasma TNFα, IL6, IP10, IL10 were measured by Luminex; and cytokine mRNA from purified monocytes quantitated by qPCR. The association of PDL1 with cytokines, clinical and microbial indices, including HIV viral load, TB smear microscopy and TB urinary lipoarabinomannan (LAM) were assessed. Results: Monocyte expression of PDL1 was significantly higher in TB, HIV and TBHIV co-infected patients compared with healthy controls (p=0.0001), with the highest levels in TBHIV co-infected patients. The highest expresser of PDL1 was intermediate (CD14+CD16+) monocytes in all participant groups. PDL1 moderately correlated with viral load and smear positivity in HIV and TB respectively, whereas weakly with LAM in TBHIV co-infection. PDL1 levels strongly correlated with plasma TNFα, IL6, IP10 and IL10 level in TB subjects, and TNFα and IP10 in HIV patients. However, cytokine mRNA from purified monocytes showed no association with either plasma cytokines or monocyte PDL1, implying that if cytokines modulate PDL1, there are likely not originating from circulating monocytes themselves. These results underscore the importance of further characterization of multiple monocyte subsets and their phenotypic and functional differences in different disease states.

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