Author's response to reviews

Title: Potential plasma markers of type 1 and type 2 leprosy reactions: a preliminary report

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Author's response to reviews: see over
**Background:** The clinical management of leprosy Type 1 (T1R) and Type 2 (T2R) reactions pose challenges mainly because they can cause severe nerve injury and disability. No laboratory test or marker is available for the diagnosis or prognosis of leprosy reactions. This study simultaneously screened plasma factors to identify circulating biomarkers associated with leprosy T1R and T2R among patients recruited in Goiania, Central Brazil. **Methods:** A nested case-control study evaluated T1R (n=10) and TR2 (n=10) compared to leprosy patients without reactions (n=29), matched by sex and age-group (+/- 5 years) and histopathological classification. Multiplex bead based technique provided profiles of 27 plasma factors including 16 pro inflammatory cytokines: tumor necrosis factor–α (TNF-α), Interferon-γ (IFN-γ), interleukin (IL)–IL12p70, IL2, IL17, IL1 β, IL6, IL15, IL5, IL8, macrophage inflammatory protein (MIP)–1 alpha (MIP1α), 1 beta (MIP1β), regulated upon activation normal T-cell expressed and secreted (RANTES), monocyte chemoattractant protein 1 (MCP1), CC-chemokine 11 (CCL11/Eotaxin), CXC-chemokine 10 (CXCL10/IP10); 4 anti inflammatory interleukins: IL4, IL10, IL13, IL1Rα and 7 growth factors: IL7, IL9, granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (GM-CSF), platelet-derived growth factor BB (PDGF BB), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF).

**Results:** Elevations of plasma CXCL10 (P=0.004) and IL6 (p=0.013) were observed in T1R patients compared to controls without reaction IL7 (p=0.039), and PDGF-BB (p=0.041) were elevated in T2R. RANTES and GMCSF were excluded due to values above and below detection limit respectively in all samples. **Conclusions:** Potential biomarkers of T1R identified were CXCL10 and IL6 whereas IL7, PDGF-BB and IL6, may be laboratory markers of TR2. Additional studies on these biomarkers may help
understand the immunopathologic mechanisms of leprosy reactions and indicate their usefulness for the diagnosis and for the clinical management of these events.

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