PhD defence Raquel Matavele

Regulatory T cells in HIV infection and in vaccinees

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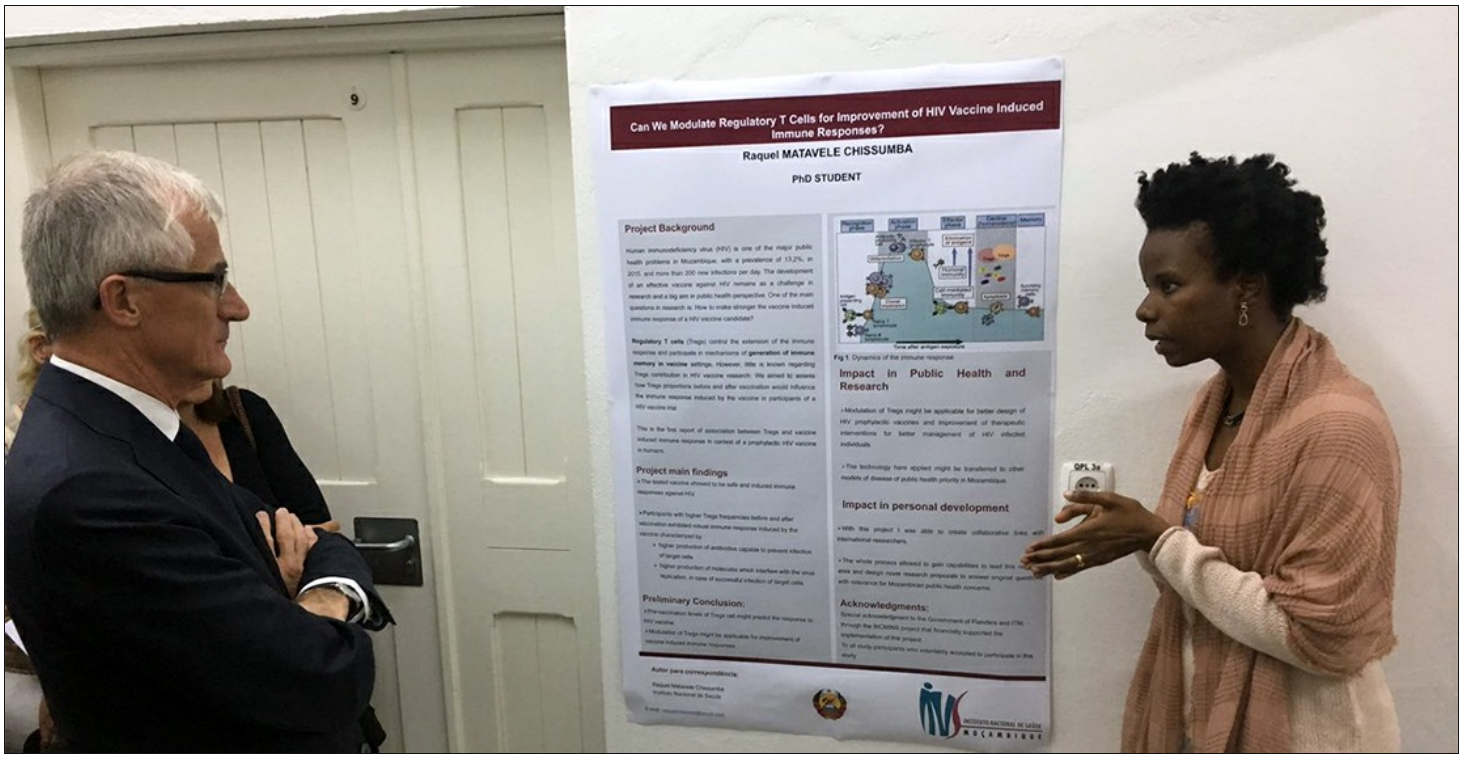

Dit is de omschrijving

Supervisors

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Abstract

The human immunodeficiency virus type 1 (HIV-1) is the causative agent of the acquired immunodeficiency syndrome (AIDS). Globally, more than 36 million individuals are infected with HIV-1. During HIV-1 infection, high levels of systemic immune activation occurs which stimulates massive viral replication. Unfortunately, there is not an effective vaccine yet against HIV-1.
Evidence from previous efficacy trials of HIV-1 vaccine candidates, shows that a good HIV-1 should induce pronounced HIV-specific memory T and B cell responses, but at the same time, needs to limit responses that favor infection. A higher risk of HIV-1 acquisition was observed in participants of a previous HIV-1 efficacy trial which was associated to higher levels of immune activation and augmented expression of HIV binding molecules in vector specific CD4 T cells. Regulatory T cells (Tregs) are a heterogeneous population of CD4 T cells with the potential to suppress exacerbated immune activation. Furthermore, Tregs also participate in mechanisms of immune memory development. However, Tregs can also suppress the development of protective antigen-specific immune responses. Little is known regarding Tregs during early infection by HIV and particularly during vaccination against HIV-1. Tregs share some differentiation pathways with Th17 cells and reciprocal development between these two CD4 T cells populations has been demonstrated.
We aimed to assess the frequencies and phenotypic alterations of Tregs, in terms of expression of activation markers, suppression markers and HIV-1 binding molecules, during HIV-infection and HIV vaccination. We also assessed how these alterations correlated with indicators of HIV disease progression and vaccine-induced immune responses.
Our findings suggest that during HIV-1 infection, an increase of Tregs in relation to total CD4 T cells correlates with systemic immune activation. Certain subsets of Tregs like those expressing the transcription factor Helios may have a beneficial role in mechanisms controlling the levels of viral replication. However higher levels of Helios expressing Tregs can be associated with deficiency in production of antibodies against HIV-1. During DNA-HIVIS/MVA-CMDR-HIV/±CN54rgp140 vaccination, pre- and post-vaccination Tregs proportions, their activation status, the Th17/Tregs ratio and other host factors affecting Tregs relative abundance, may have an impact on the magnitude of HIV vaccine-induced immune responses. Furthermore, the DNA-HIVIS/MVA-CMDR-HIV/±CN54rgp140 does not induce increased susceptibility to HIV-1 infection of Tregs and total CD4 T cells.
Therapeutic and prophylactic HIV-1 vaccine trials should consider the evaluation of Tregs for a better understanding of the mechanistic impact of these experimental interventions.