NATURAL KILLER CELL PHENOTYPIC, FUNCTIONAL, AND NUTRIENT TRANSPORTER PROFILES DURING SPONTANEOUS CONTROL OF HIV-1 INFECTION IN BLACK SOUTH AFRICANS

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Despite the devastation caused by the human immunodeficiency virus (HIV) for over four decades, a subset of individuals termed HIV-1 elite controllers (ECs) can control the virus in the absence of antiretroviral therapy (ART) and may provide a model for a functional cure. This study aimed to understand the role of natural killer (NK) cells as important innate effector cells in the control of HIV-1 infection in African populations. We measured the phenotypic, functional, and nutrient transporter profiles of NK cells on cryopreserved peripheral mononuclear cells from HIV-1 ECs (n=15), viraemic progressors (VPs) (n=19), antiretroviral therapy-treated individuals (ART-treated) (n=20), and HIV-1 uninfected donors (HCs) (n=21) from Johannesburg, South Africa using multicolour flow cytometry. Functional and metabolic profiles were assessed after stimulation with a major histocompatibility complex-devoid cell line. The frequency of NK cells and their subsets in ECs were similar to HCs and ART-treated and altered compared to VPs. Total NK cells in ECs had similar expression of NKG2A (inhibition), NKG2C (activation), PD-1 (exhaustion), and CD57 (maturation) markers compared to ART-treated and increased expression of CD38 and CD69 (activation markers) compared to ART-treated individuals. CD107a (cytotoxicity) was reduced in total NK cells in all people living with HIV-1 compared to HCs, whereas IFN-γ (cytokine production) was comparable across the ECs, HCs, and ART-treated groups and significantly lower in VPs compared to the other study groups. Metabolic profiles (glucose transporter 1 (Glut1), CD98, and CD71) were similar in ECs compared to ART-treated and significantly increased in VPs compared to other study groups. Together these findings show that NK cells from ECs have an inhibitory, mature profile with low levels of immune exhaustion and reduced metabolic phenotype suggesting functional competence. These new insights could be employed in novel immunotherapeutic strategies for the treatment of HIV-1 in an African population.