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Immune response to sequences surrounding the 12 protease cleavage sites generated during ARV treatment improved CD4 counts of SIVmac251 infected rhesus monkeys

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Background: Effective therapeutic vaccines used in combination of ARV to treat HIV infected patients can reduce drug induced toxicity, help to re-constitute immune system and achieve a functional cure. We conducted a pilot study to test the therapeutic effect of a novel HIV vaccine targeting the 12 protease cleavage sites in combination of ARV.

Methods: SIVmac251 infected rhesus monkeys were treated with a combination of FTC, PMPA and raltegravir for 49 days. Seven days after ARV initiation the monkeys in the treatment group received rVSVpcs (i.m.). Three additional therapeutic treatment with rVSVpcs (i.m.)/NANOpcs(i.n.), NANOpcs(i.n), and NANOpcs(i.n.) were carried out with 2-week intervals. ARV treatment was stopped after 49 days and viral load, CD4/CD8 counts, antibody and T cell response to PCS peptides and pooled Gag and Env peptide were analyzed.

Results: ARV treatment suppressed viral load of all macaques, but only the viral load of 6 out of 11 macaques was suppressed to non-detectable level during the treatment/ARV period. However, even with the short duration of ARV treatment and incomplete viral load suppression, the immune responses to PCS peptides were generated after 4 therapeutic treatments. The CD4 counts of PCS vaccine treated macaques were significantly improved after 35 days and 49 days of ARV treatment($p=0.027$ and 0.044), whereas there is no significant improvement in CD4 counts of monkeys only received ARV treatment despite the viral load suppression.

Conclusions: Our study showed that new immune response to PCS peptides can be generated even with incomplete viral load suppression after a short period ARV treatment. The combination of PCS vaccine treatment and ARV generated new immune response to PCS peptides, improved CD4 counts of SIVmac251 infected monkeys and can be used to improve patient care to achieve a functional cure.