Functional cure after long term HAART initiated during early HIV infection - a comprehensive case study

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Background: Early initiation of cART during acute HIV infection can lead to control of viral replication after cessation of therapy in a rare subgroup of patients termed post treatment controllers (PTC). We set out to define immunological and virological correlates of post treatment control and to assess the potential of eradication vs. functional cure.

Methods: A 67 yrs. old male was treated with cART 3 months after HIV exposure and 1 month after seroconversion for a total of 5,5 yrs.; cART was stopped in May 2004 and the patient remained BLOD (< 20 c/ml) and shows normal T cell counts and distribution without ART since 9 years. We performed comprehensive analyses to assess the immuno-virological correlates of PTC including a humanized mouse model in this patient.

Results: CD4 count is stable between 900-1000 cells/µl, the homozygous CCR5 promoter variant A59029G but no delta 32 deletion was detected, HLA-I subtype was A 01, 02 B: 44, 52; no viral RNA or DNA was detected using ultrasensitive techniques (single copy assay, viral co-culture, DNA-PCR) in plasma, PBMC and CSF. No p24 antigen or HIV-RNA was detected in gut biopsies by immunohistochemistry or in situ hybridisation. ELISPOT revealed strong polyfunctional CTL responses against gag and nef epitopes and polyfunctional HIV specific CD4 responses and a normal distribution of TEM and TCM comparable to a control group of nine elite controllers (EC) was shown. The frequency of peripheral Treg and Th17 cells was comparable to normal controls and EC. Virus could be recovered in vivo in a humanized mouse model after transplantation of purified donor CD4 T cells and anti CD3/CD28 stimulation indicating the persistence of replication competent virus.

Conclusion: The data obtained in this unique case suggest a functional cure of this patient rather than viral eradication after early onset cART. The presence of strong HIV specific T cell responses, normal frequency of regulatory T cells and animal data suggest a strong role of preserved adaptive immune responses as a correlate of viral control in this patient arguing for adjuvant immunotherapeutic interventions (e.g. therapeutic vaccination, Il-7) in this setting.