Novel Approaches Based on Autologous Stem Cell Engineering and Gene-Modification; Evidence for the Cure of HIV/AIDS

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Editorial

Human immunodeficiency virus-1 (HIV-1) is a retrovirus that causes reduction of CD4+ T cells by degrade of them. The restrictions of HIV-1 treatment such as Highly-Active Retroviral Therapy (HAART) are not eliminated completely; for example: Drug resistance, no eradication of virus and rebounding of its replication from latent reservoirs after stopping them [1-3]. But new approaches in HIV/AIDS therapy based on gene and cell therapies solved many problems of treatment for intractable disease [4-7]. Some polymorphisms provide nature resistance to HIV-1 or slow progression to AIDS (acquired immune deficiency syndrome) such as HLA-B27 and B57 [8] and CCR5 mutations [9]. Cc-chemokine receptor-5 (CCR5) –known as a main co-receptor in HIV-1 infection– because homozygote 32bp deletion (Δ32) in both allele of CCR5 provide natural resistance to HIV-1 infection [10-12]. This resistance was applied in Berlin patient that transplanted by allogeneic hematopoietic stem cell (HSC) from a donor with CCR5 Δ32/Δ32 genotype to HIV-1 infected patient and introduced effective cure in the absence of ART [13-17]. Afterwards, same strategy was exhibited satisfactory results for HIV-1 treatment in Boston patients [18]. Founding a suitable donor with low prevalence of target genotype (CCR5 Δ32/Δ32) and HLA-matched are main problems of HSCT strategies as allogeneic. Latest finding indicates that autologous HSCT for m303/m303 could be effective treatment for anyone HIV/AIDS affected patient worldwide [19]. It is predicted that gene therapy for HIV-1 infection can apply easier and more accessible with respect to HSCT by umbilical cord blood (CB) [20, 21]. Next approaches –cell engineering– overcome to these challenges: disruption of target gene by special enzyme [22,23]. It is showed that CCR5disruptin HIV-1 infected patient by ZFN and return modified stem cells to self-body as autologous stem cell transplantation [24]. Furthermore, another nuclease such as CRISPR/Cas9 (Clustered regularly interspersed palindromic repeats/CRISPR associated gene) could modify viral genome to inhibition of viral integration, gene expression and replication [25,26]. It is demonstrated that CRISPR/Cas9 edit CCR5gene efficacy in hematopoietic stem cells [27]. So, we can be said cell engineering with nucleases can eliminate some problems of Berlin and Boston patients. In this manner, gene therapy in HIV-1 infected patient could be more carefree. In other hand, to compare to current ART strategy, gene therapy can be cost effective in HIV infected patient lifetime [28]. So, novel strategies based on stem cell transplantation is better than retroviral drugs and they have significance positive effect in eradication or reduction of viral genome from HIV-1 infected patients. A better understanding of the host immunology and genetic factors that promote or restrict HIV-1 replication may thus lead to the development of novel therapeutics against HIV/AIDS in future.

Hopefully one day we’ll be able to say all AIDS patients become HIV negative again.

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We apologize to those colleagues whose studies could not be mentioned due to space limitation.

References


