Retrovirology

Poster presentation

P17-08. Transduction of human monocyte-derived dendritic cells by recombinant adeno-associated virus

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Background

A phase I clinical trial has recently assessed rAAV serotype 2 (rAAV2) as a vector for an HIV vaccine, however disappointing immunogenicity was seen. Differences in the ability of various serotypes to transduce dendritic cells have been reported. Better defining the optimal serotype for transduction of dendritic cells may increase its utility as a T cell vaccine vector.

Methods

Six serotypes and three clones of rAAV expressing eGFP were assessed for their ability to transduce human monocytes and monocyte-derived dendritic cells (MoDCs). Transduction was assessed by flow cytometry. In addition a self-complimentary vector was compared with a conventional vector. Site-directed mutagenesis of the rAAV6 capsid was performed to further improve transduction efficiency. The immunophenotype of transduced MoDCs was assessed by flow cytometry. The ability of transduced MoDCs to stimulate a $CD8^+$ T cell clone was assessed.

Results

rAAV6 was the most efficient serotype transducing 4.3, 8.8 and 13.8 fold more MoDCs than rAAV2, rAAV5, and rAAV1 respectively; a similar pattern was seen with monocytes. Transduction of monocytes and MoDCs with rAAV6 led to similar rates of transgene expression by immature MoDCs. There was no significant difference between self-complimentary and conventional rAAV6 vectors at a range of multiplicities of infection. Mutation of a surface tyrosine of the AAV6 capsid (Y731F) improved transduction efficiency by a further 1.3 to 1.7 times. Transduction of MoDCs did not alter their immunophenotype and they were able to stimulate an antigen specific $CD8^+$ T cell clone.

Conclusion

This study extends the range of serotypes of rAAV previously examined and makes the novel finding that rAAV6 with an Y731F capsid mutation has the highest tropism for MoDCs. In addition no advantage of a self-complimentary genome was found, increasing the coding capacity of the vector. These findings may improve the utility of rAAV as a vaccine vector.