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P17-26. Effective Design of T-Cell Driven Vaccines Applied to the GAIA HIV Vaccine: Advances in Vaccine Design Based on Current Preclinical Success

Anne S. De Groot
University of Rhode Island, annied@uri.edu

Leonard Moise
University of Rhode Island, lmoise@uri.edu

J. Desrosiers

C. Weber

W. Martin

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AS De Groot*[1], L Moise[1], J Desrosiers[1], C Weber[2] and W Martin[1]

Address: [1]EpiVax, University of Rhode Island, Providence, RI, USA and [2]University of Freiburg, Freiburg, Germany
* Corresponding author

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Background

We continue to make progress on a multi-epitope, cross-clade GAIA HIV vaccine [De Groot, Vaccine, 2008, 26: 3059–71]. New evidence from elite controllers supports our original hypothesis that multiple, highly conserved T-cell epitopes in a single HIV vaccine construct will better control HIV infection [Davenport, Immunol Rev., April 2007; Kong, J Virol., March 2009]. We believe that T cell-mediated vaccines constructed from highly cross-conserved HIV Th and CTL epitopes will succeed with the benefit of advances in the adjuvant, formulation and delivery areas that will inform better vaccine construction. We have performed several recent studies that also support this hypothesis.

Methods

EpiVax' suite of vaccine design tools have enabled effective selection of cross-clade conserved HIV epitopes, and the delivery of those epitopes in properly designed constructs are important steps toward production of an effective vaccine.

Results

We provide three recent T-cell directed vaccination successes that illustrate the use of such vaccine design tools in preclinical challenge models and their potential for development of a protective T cell-directed HIV vaccine: (i) HLA class II conserved T-cell epitopes derived from the variola genome fully protected HLA DR3 transgenic mice from 10× LD50 vaccinia challenge without B cell priming; (ii) HLA class I and class II F. tularensis T-cell epitopes extended the mean time-to-death of A2/DR1 transgenic mice challenged with 20× LD50 attenuated F. holarctica by 53%; and, (iii) HLA class II T-cell epitopes stimulated long-lived immune responses and cleared infection in a p27 knockout mouse model of *H. pylori* infection.

Conclusion

The lessons learned from these recent studies hold promise for design of a globally relevant HIV vaccine using cross-clade HLA class I and class II T-cell epitopes, conserved over time and geography, that will be broadly immunogenic in the HLA diverse world population.