Timothy Fouts, J AIDS Clin Res 2014, 5:11
http://dx.doi.org/10.4172/2155-6113.S1.009

OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
HIV/AIDS, STDs, & STIs
October 27-29, 2014 Embassy Suites Las Vegas, USA

The balance of cellular and humoral immunity determines the level of protection offered by an HIV vaccine in macaque models of HIV infection

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A guiding principle for HIV vaccine design has been that cellular and humoral immunity work together to provide the strongest degree of efficacy. However, three efficacy trials of Ad5-vectored HIV vaccines showed no protection. Transmission was increased in two of the trials, suggesting that this vaccine strategy elicited $CD4^+$ T cell responses that provide more targets for infection, attenuating protection or increasing transmission. The degree to which this problem extends to other HIV vaccine candidates is not known. Here, we show that a gp120-CD4 chimeric subunit protein vaccine (full-length single chain (FLSC)) elicits heterologous protection against SHIV or SIV acquisition in three independent rhesus macaque repeated low-dose rectal challenge studies with SHIV162P3 or SIVmac251. Protection against acquisition was observed with multiple formulations and challenges. In each study, protection correlated with antibody dependent cellular cytotoxicity (ADCC) specific for $CD4^-$ induced epitopes (CD4i) provided that the concurrent anti-vaccine T cell responses were minimal. Protection was lost in instances where T cell responses were high or when the requisite antibody titers had declined. Our studies strongly suggest that balance between a protective antibody response and antigen-specific T cell activation is the critical element to vaccine-mediated protection against HIV. Achieving and sustaining such a balance, while enhancing antibody durability, is the major challenge for HIV vaccine development, regardless of the immunogen or vaccine formulation.

Biography

Timothy Fouts is one of the founders and principle scientists at Profectus Biosciences. He directs a team of scientists in the discovery and preclinical development of vaccines, small molecule and antibody based antiviral therapies and microbicides that are within the Profectus research portfolio, in particular HIV and certain biothreat viruses. He has more than 32 scientific publications that have appeared in peer-reviewed journals and book chapters. He received his PhD in Immunology from the University of Maryland, Baltimore and did a postdoctoral fellowship at the Aaron Diamond AIDS Research Center at Rockerfeller University in NYC.

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