

2006

Design clues from functional constraints and broadly neutralizing antibodies

Tongqing Zhou

Vaccine Research Center NIAID, Bethesda, Maryland

Ling Xu

Vaccine Research Center NIAID, Bethesda, Maryland

Barna Dey

Vaccine Research Center NIAID, Bethesda, Maryland

Ann J. Hessel


The Scripps Research Institute, La Jolla, California

Shahzad Majeed

Vaccine Research Center NIAID, Bethesda, Maryland,

See next page for additional authors

Follow this and additional works at: <http://digitalcommons.unl.edu/virologypub>

 Part of the [Biological Phenomena, Cell Phenomena, and Immunity Commons](#), [Cell and Developmental Biology Commons](#), [Genetics and Genomics Commons](#), [Infectious Disease Commons](#), [Medical Immunology Commons](#), [Medical Pathology Commons](#), and the [Virology Commons](#)

Zhou, Tongqing; Xu, Ling; Dey, Barna; Hessel, Ann J.; Majeed, Shahzad; Van Ryk, Donald; Xiang, Shi-Hua; Yang, Xinzhen; Zhang, Mei-Yun; Zwick, Michael B.; Arthos, James; Burton, Dennis R.; Dimitrov, Dimiter S.; Sodroski, Joseph; Wyatt, Richard; Nabel, Gary J.; and Kwong, Peter D., "Design clues from functional constraints and broadly neutralizing antibodies" (2006). *Virology Papers*. 303. <http://digitalcommons.unl.edu/virologypub/303>

This Article is brought to you for free and open access by the Virology, Nebraska Center for at DigitalCommons@University of Nebraska - Lincoln. It has been accepted for inclusion in Virology Papers by an authorized administrator of DigitalCommons@University of Nebraska - Lincoln.

Authors

Tongqing Zhou, Ling Xu, Barna Dey, Ann J. Hessel, Shahzad Majeed, Donald Van Ryk, Shi-Hua Xiang, Xinzhen Yang, Mei-Yun Zhang, Michael B. Zwick, James Arthos, Dennis R. Burton, Dimiter S. Dimitrov, Joseph Sodroski, Richard Wyatt, Gary J. Nabel, and Peter D. Kwong

Oral presentation

Open Access

Design clues from functional constraints and broadly neutralizing antibodies

Tongqing Zhou¹, Ling Xu¹, Barna Dey¹, Ann J Hessell², Shahzad Majeed¹, Donald Van Ryk³, Shi-Hua Xiang⁴, Xinzhen Yang⁴, Mei-Yun Zhang⁵, Michael B Zwick², James Arthos³, Dennis R Burton², Dimiter S Dimitrov⁵, Joseph Sodroski⁴, Richard Wyatt¹, Gary J Nabel¹ and Peter D Kwong^{*1}

Address: ¹Vaccine Research Center NIAID, Bethesda, Maryland, USA, ²The Scripps Research Institute, La Jolla, California, USA, ³Laboratory of Immunoregulation NIAID, Bethesda, Maryland, USA, ⁴Dana-Farber Cancer Institute, Boston, Massachusetts, USA and ⁵Center for Cancer Research and Nanobiology Program NCI, Frederick, Maryland, USA

* Corresponding author

from 2006 International Meeting of The Institute of Human Virology
Baltimore, USA. 17–21 November, 2006

Published: 21 December 2006

Retrovirology 2006, **3**(Suppl 1):S22 doi:10.1186/1742-4690-3-S1-S22

© 2006 Zhou et al; licensee BioMed Central Ltd.

Two strategies have been proposed for the rationale design of vaccine immunogens that elicit broadly neutralizing antibodies against HIV-1. One strategy involves exploiting functional constraints, focusing on regions of the envelope where function requires conservation and exposure. This strategy has led to the identification of coreceptor-binding-site antibodies as well as antibodies reactive with the site of T-20 binding. One drawback of this strategy, however, is the limited potency of the antibodies thus far identified. A second strategy involves the characterization of rare broadly neutralizing antibodies such as 2G12, 2F5, 4E10 and b12. Unfortunately, strains of virus resistant to these antibodies evolve with relative ease. We used X-ray crystallography to define functional constraints related to binding of the CD4 receptor and found that the site of initial CD4 contact on gp120 is the epitope for the broadly neutralizing antibody, b12. Functional analysis allowed us to transcend the particulars of b12 binding to focus on the conserved site of initial CD4 contact. The results suggest that a combination of functional analysis and potent antibody characterization may provide design clues necessary to create immunogens capable of eliciting potent broadly neutralizing antibodies.