OMICS Group Conferences
Accelerating Scientific Discovery

3rd International Conference on
Vaccines & Vaccination
July 29-31, 2013 Embassy Suites Las Vegas, NV, USA

Combining next-generation sequencing and protein design-A systematic approach to vaccine development

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Elicitation of broadly neutralizing antibodies is a major goal of vaccine development. Antibody identification and immunogen design are two critical components of a rational vaccine design strategy and have become the focus of recent technology development. We demonstrated that next-generation sequencing could capture 106-107 diverse antibody sequences from peripheral blood sample of HIV-1 infected donors, thus enabling an in-depth analysis of somatic population, maturation pathway and lineage intermediates. We further extended the application of this technology, now termed antibodyomics, to the *de novo* antibody identification. Using a novel evolution-based method, we identified over a dozen of broadly neutralizing VRC01-like antibodies from a HIV-infected individual, C38. Despite their low representation in the sequenced repertoire and low homology to the known VRC-1 like antibodies, these antibodies could potently neutralize ~80% of the HIV-1 isolates. In terms of immunogen design, the concept of "epitope-scaffolds" has been recently advanced as a possible solution and showed some success in the design of epitope-specific antigens. Using a novel protein design technique of transplanting epitope onto heterologous protein scaffolds, we designed over 100 epitope-scaffold immunogens for three major epitopes on the HIV-1 viral spike - V1/V2, V3 and MPER. A subset of these designed proteins have been validated experimentally and some showed nanomolar binding affinity for the target broadly neutralizing antibodies, making these promising vaccine candidates. It is foreseeable that the combined use of antibodyomics and protein design will provide a powerful tool for vaccine development for HIV, as well as for other infectious diseases.

Biography

Jiang Zhu obtained his Ph.D. from the University of Science and Technology of China and conducted his postdoctoral work at Howard Hughes Medical Institute and Columbia University. From 2009 to 2012, he was a staff scientist at the National Institutes of Health and co-headed the bioinformatics core section in the NIH Vaccine Research Center. He is currently an Assistant Professor in the Department of Immunology and Microbial Science and a joint faculty member in the Department of Integrative Structural and Computational Biology at the Scripps Research Institute. He is also a member of the Scripps Center for HIV/AIDS Vaccine Immunology & Immunogen Discovery (CHAVI-ID).

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