OMICS Group Conferences
Accelerating Scientific Discovery

International Conference on
Biothreats & Biodefense

October 15-17, 2012 DoubleTree by Hilton Chicago-North Shore, USA

Human monoclonal antibodies (mAb): Interrogation of the memory B cell compartment as a powerful platform for the discovery and development of superior therapeutics

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Background: Our High Throughput proprietary I-STAR™ (in-situ therapeutic antibody rescue) technology platform enables the discovery of fully human therapeutic antibody candidates eliminating the need for lengthy processes of humanization, affinity maturation and other optimization. The interrogation of the memory B cell compartment allows scanning the repertoire for antibodies in a donor and the identification of antibodies often directed against novel, rare, including conformational epitopes. Using I-STAR™ we have successfully identified the first truly broad spectrum anti-influenza virus mAb, TCN-032, and a large number of highly potent, broadly neutralizing antibodies (bNAbs) against HIV. We will present our clinical influenza program illustrating the advantages of I-STAR™.

TCN-032 is a first in class drug targeting the M2 protein with a new mechanism of action. This high affinity, high avidity fully human IgG1κ mAb demonstrates nanomolar ADCC and CDC in vitro activity. In vivo, prophylactic and therapeutic efficacy was confirmed in mice with seasonal including highly pathogenic H5N1 strains. The antibody recognizes 98% of all human, avian and swine influenza A strains sequenced to date and has a high barrier to viral escape.

Fully human mAbs present a solid approach to defend against biothreat pathogens providing a high safety margin and reasonably faster development times compared to small molecules. Theraclone's I-STAR™ technology can also contribute to vaccine engineering and the development of diagnostics.

Biography

Bonavia is currently the head of the Biology group at Theraclone Sciences, developing therapeutic antibodies for infectious diseases. Previously, Dr. Bonavia led antiviral programsfor respiratory syncytial virus, influenza virus, and Ebola virus at Novartis and Functional Genetics. He obtained his Ph.D. in microbiology at the University of Colorado Health Sciences Center and after a postdoctoral trainingin retroviruses at Johns Hopkins Medical Schoolhejoined the laboratory of viral diseases at NIH-NIAID to carry out research on HCoV-SARS. Dr. Bonavia has focused on R&D of small molecules and biologics against respiratory and biodefense viruses with an emphasis on host-targets.

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