Anton M Sholukh, J Antivir Antiretrovir 2014, 6:2
http://dx.doi.org/10.4172/1948-5964.S1.020

OMICS Group Conferences
Accelerating Scientific Discovery

4th World Congress on
Virology

October 06-08, 2014 Hilton San Antonio Airport, TX, USA

IgG dose dictates outcome for passive immunization of macaques with polyclonal anti-SHIV IgG against challenge with heterologous tier 2 SHIV

Anton M Sholukh
Texas Biomedical Research Institute, USA

An ultimate goal for HIV vaccine design is the induction of cross-reactive neutralizing antibodies (nAbs). The exceptional diversity of HIV makes it impossible for any AIDS vaccine recipient to be exposed to virus strains exactly matching the immunogen given. For that reason, heterologous SHIV challenges are essential for realistic vaccine efficacy testing in primates. We sought to test whether passive immunization with SHIVIG, defined as polyclonal IgG raised in rhesus monkeys (RMs) with chronic clade C SHIV infection, could protect against multiple low-dose intrarectal challenges with a tier 2 SHIV-2873Nip carrying an HIV-C envelope that was heterologous to any viruses or envelopes against which the IgG responses had been elicited.

SHIVIG demonstrated binding to HIV Gag, Tat and Env of different clades and competed with the broadly neutralizing antibodies b12, VRC01, 4E10, and 17b. SHIVIG neutralized tier 1 and tier 2 viruses, including SHIV-2873Nip the heterologous challenge virus. NK-cell depletion decreased the neutralizing activity of SHIVIG 20-fold in PBMC assays. Although SHIVIG neutralized SHIV-2873Nip in vitro, this polyclonal IgG preparation failed to prevent acquisition after repeated intrarectal low-dose virus challenges, but at a dose of 400 mg/kg, it significantly lowered peak viremia (P=0.001). Surprisingly, single-genome analysis revealed a higher number of transmitted variants at the low dose of 25 mg/kg, implying increased acquisition at low SHIVIG levels. In vitro, SHIVIG demonstrated complement-mediated Ab-dependent enhancement of infection (C'-ADE) at concentrations similar to those observed in plasmas of RMs treated with 25 mg/kg of SHIVIG at the time of virus exposure.

These primate model data suggest a dual role for polyclonal anti-HIV-1 Abs depending on plasma levels upon virus encounter.

Biography

Sholukh, a native of Belarus, completed his PhD in 2002. His PhD work was devoted to study the regulation of intracellular signaling and transduction of light signals in the retinal photoreceptor. Since 2004 Dr. Sholukh's research interests have broadened to immunology and antibody engineering. His work also included the discovery of an important soluble CXC chemokine receptor 2. In 2009, Dr. Sholukh joined the laboratory of Dr. Ruprecht at the Dana-Faber Cancer Institute (Harvard Medical School) and in 2013 he moved to Texas Biomedical Research Institute. His current interests are focused on dissecting the humoral immune response to HIV and HIV vaccine candidates as well as on the vaccine design.

asholukh@txbiomed.org