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Autologous immunotherapy designed to target HIV in latent reservoir

I Tcherepanova[1], J Krisko[1], J Horvatinovich[1], M DeBenedette[1], N Archin[2], J Kuruc[2], C Gay[2], D Margolis[2] and **C Nicolette[1]**
[1]Argos Therapeutics Inc., USA
[2]University of North Carolina HIV Cure Centre, USA

AGS-004 immunotherapy consists of autologous dendritic cells electroporated with four HIV RNAs encoding autologous Gag, Vpr, Rev and Nef antigens[1]. AGS-004 is undergoing testing using a kick and kill strategy in combination with the latency reversing drug, Vorinostat. To specifically target virus variants likely to emerge from a patient's latent reservoir, RT-PCR amplification protocol is applied to HIV generated in supernatants of *ex vivo* mitogen-stimulated, latently infected $CD4^+$ cells. Up to 24 replicate cultures of activated $CD4^+$ cells were established and monitored for viral outgrowth by $p24^{Gag}$ ELISA. We previously observed that the cultures became positive at different rates with variable levels of p24 measured in each culture, suggesting diversity of emerging species2. To evaluate diversity of the emerging virus, individual clones of RT-PCR-amplified target regions were sequenced using the Sanger method and analyzed by phylogenetic tree analysis. This analysis revealed that clone sequences generally grouped together by their origin culture, demonstrating similarity to one another. In contrast, the clone sequences from different individual cultures clustered separately from one another, indicating the presence of divergent viral species in independent cultures (as demonstrated in Gag example below). Therefore, diverse HIV species are being captured with RT-PCR amplification, both within as well as across the different replicate cultures of $CD4^+$ cells. Using pooled $CD4^+$ cell cultures as a substrate for amplification of RNA antigens, AGS-004 can direct the immune system to specifically target the unique autologous virus species in a patient's latent reservoir. A clinical trial testing these hypotheses is on-going.

Biography

Irina Y Tcherepanova is the Vice President of Translational Medicine at Argos Therapeutics. She has received the PhD in Molecular Pharmacology from the Albert Einstein College of Medicine and completed Post-doctoral training from the Duke University Medical Center. She has joined Argos in 2000 and was instrumental in the development of autologous RNA transfected DC immunotherapies; AGS-003 is being tested in a pivotal Phase 3 clinical trial in advanced Renal Cell Carcinoma and AGS-004 is being tested in combination with latency reversing agent Vorinostat in HIV-infected patients. She is the author of multiple peer reviewed publications and is the inventor on several patents.

itcherepanova@argostherapeutics.com

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