

POSTER 37**INHIBITION OF ARENAVIRUS INFECTION BY THIURAM AND AROMATIC DISULFIDES**

Claudia S. Sepúlveda¹, Cybele C. García¹, Jesica M. Levingston Macleod², Nora López², and Elsa B. Damonte¹

¹Laboratorio de Virología, Facultad de Ciencias Exactas y Naturales, UBA, 1428 Buenos Aires, Argentina;

²Centro de Virología Animal, I.C.T. Dr. César Milstein, CONICET, 1440 Buenos Aires, Argentina

Arenaviruses are enveloped viruses containing a bipartite, single-stranded RNA genome, with ambisense coding strategy. Five arenaviruses are known to cause severe hemorrhagic fevers in humans, but at present no reliable drug therapy is available. The presence in arenaviruses of the Z protein, containing a highly conserved RING finger motif, prompted us to initiate studies about this protein as a possible target for a new antiviral strategy. We have previously shown that antiretroviral compounds with diverse chemical structures, provided by the National Cancer Institute (USA), which target to the Zn-finger motifs in the HIV nucleocapsid protein NCp7, display antiviral and virucidal activity against arenaviruses. Here, the *in vitro* inhibitory activity of a selected group of disulfides is reported.

The thiuram disulfide **NSC14560** and the aromatic disulfide **NSC4492** were, respectively, the more potent antiviral and virucidal agents against the pathogenic arenavirus Junín, with values of antiviral effective concentration 50% (EC_{50}) of 8.5 μ M for **NSC14560**, as determined by virus yield inhibition, and inactivating concentration 50% (IC_{50}) of 0.2 μ M for **NSC4492**.

NSC14560 showed a wide spectrum of inhibitory effect against different arenaviruses in monkey and human cells. Mechanistic studies demonstrated that cell pretreatment did not affect infection. Virus adsorption and internalization were not affected. Time of addition experiments indicated that the inhibitory activity of **NSC14560** appears to target two steps of viral infection: an early step before 5 h of infection and a late stage of the cycle. **NSC4492** inactivated diverse arenaviruses, with a linear kinetics of reaction up to 45 minutes. Western blot analysis of virus-like particles released into the supernatants from cells expressing an HA-tagged version of Junin virus Z protein in presence of **NSC4492**, showed an alteration in the electrophoretic profile of Z oligomers, suggesting that the compound might induce conformational change in Z protein.

The authors acknowledge the Drug Synthesis and Chemistry Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, USA, for providing the compounds.