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Gene and drug discovery in chagas disease

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Abstract

Villalta will talk about the discovery of important host and *Trypanosoma cruzi* molecules that participate in the initial critical steps of infection, which are targets for intervention in Chagas heart disease.

Chagas heart disease is a deadly protozoan infection caused by *T. cruzi* that affects millions of people in endemic areas of Latin America and remains a neglected disease with no effective drugs to cure the chronic infection. Its spread from Latin America to non-endemic countries (USA, Canada, Japan, Australia, and Europe) is a new worldwide health challenge. As part of our efforts to address this serious gap in public health, we have obtained new findings on the interaction of the host and the pathogen, such as the discovery of critical host molecules (gene network *LAMC1-THBS1-GAL-3*) and *Trypanosoma cruzi* molecules (gp83, mucin, and *CKII substrate*) involved in the process of early infection by *T. cruzi*. Moreover, our group discovered two specific trypanosomal enzymes that participate in the *T. cruzi* sterol pathway essential for trypanosomal membrane structure and function and are required for the establishment of infection. These trypanosome enzymes are novel targets for effective drug development directed toward Chagas disease. Indeed, enzyme structure-based design studies generated novel selective inhibitors that clear the infection *in vitro* and *in vivo* during the acute and chronic experimental Chagas disease. Furthermore, we discovered that *defensin* a-*1*, which is regulated by the trypanosome, causes trypanosome membrane pore formation, alters trypanosome ligands, detaches the trypanosome flagellum and prevents cellular infection with a potential use for preventing transmission of the infection by blood transfusion. Thus, these results indicate that we have discovered novel targets for intervention in Chagas disease (Supported by NIH grants).

Biography

Fernando Villalta is the Chair and Professor of Immunology, School of Medicine, Meharry Medical College. He received his Ph.D. in Microbiology from the Federal University of Rio de Janeiro (1981), followed by postdoctoral training in immunology at Michigan State University (1981-1986). He is a member of the American Association of Immunologists (AAI), has chaired Symposia at several AAI meetings and received several AAI mentoring awards. He served as regular member of the Vaccines and Related Biological Products Advisory Committee of the FDA. He served on 14 NIH study sessions, including 4 for NIAID. He is serving as an editorial board member of 6 journals and reviewer for 20 journals.