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Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares

Conferencia:

Structural studies of bunyavirus fusion proteins

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Aula de Seminarios do CiQUS

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Dr. Pablo Guardado Calvo obtained a Ph.D. in Structural Biology from the University of Santiago de Compostela with Dr. Mark van Raaij. During his thesis, he studied viral fibers of naked viruses, particularly reovirus and adenovirus. In 2010, he moved to the Institut Pasteur in Paris to do a postdoctoral stay with Dr. Felix Rey in the Unité de Virologie Structurale working on viral fusion proteins of retrovirus and flavivirus. Since 2015 he is a group leader in the Unité de Virologie Structurale working in the fusion proteins of bunyaviruses both from a fundamental and an applied perspective trying to understand the mechanisms of fusion and developing novel immunogens to be used in vaccines.

Abstract

Structural studies of bunyavirus fusion proteins

Infection by viruses having lipid bilayer envelopes proceeds through the fusion of the viral envelope with a membrane of the target cell, a reaction catalyzed by a family of viral proteins denominated “fusion proteins”. These proteins, which are exposed on the viral surface, are the main targets of neutralizing antibodies and the “Achilles heel” for many enveloped viruses. Structural characterization of fusion proteins has led to the development of antivirals and vaccines. Here, I will present our recent results in the structural biology of bunyaviral fusion proteins, particularly those of Rift Valley fever virus and Hantaan viruses, responsible for important epizoonoses throughout the word with devasting human and economic consequences. We will show how the structure of RVFV fusion protein (Gc) solved in complex with a lipid, combined with membrane binding experiments, site-directed mutagenesis, and molecular dynamics simulations reveal the molecular determinants of lipid specificity of class-II fusion proteins, including those of Zika, Dengue or Chikungunya viruses. Indeed, the membrane-insertion mechanism identified in this work helps us to understand the changes in cholesterol dependence linked to a serious outbreak of Chikungunya virus in 2005-2006 and the phosphatidylserine dependence of Dengue virus for entry.