iNEXT workshop on Integrated methodologies and approaches for structural biology

Name of Speaker: **Felix Rey**
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Title of Lecture:
Widespread distribution of class II membrane fusion proteins in viruses and cells

Abstract:

Structural studies have revealed that the membrane fusion proteins used by enveloped viruses to enter cells belong to one of three structural classes (I, II and III) of homologous proteins, irrespective of the virus taxonomy based on the polymerase gene. This finding illustrates the mosaic nature of viral genomes, which are a collection of genes derived from different origins. One special case is that of the class II fusion proteins found in the *Togaviridae*, *Flaviviridae* and in several families of the newly defined *Bunyavirales* order. Class II fusion proteins were also detected in *C. elegans* retroviruses, which are otherwise clearly related to mammalian retroviruses through the Gag-Pol gene, although mammalian retrovirus have an envelope protein belonging to class I. The cell-cell fusion protein EFF-1, responsible for syncytia formation to form the skin during *C. elegans* embryogenesis, is also homologous to the class II viral proteins. More recently, the ancestral gamete fusogen HAP2 was identified as belonging to class II, and is further illustration of the impact of virus-cell genetic exchanges. This interchange appears to have been at the origin of sexual life on earth by inducing the specific merger of the plasma membranes of sperm and egg during fertilization by the same mechanism used by enveloped viruses to infect cells. In this presentation, I will review the specific features of class II fusion proteins and their mechanism of action.

Research Profile:

Felix Rey is a structural biologist studying pathogenic viruses to obtain mechanistic insight into their life cycle. One main focus is the study of viral envelope proteins, their interaction with neutralizing antibodies or with cellular receptors, and the conformational changes driving membrane fusion during entry into cells. His lab has identified that membrane fusion for virus entry is driven by proteins belonging to only three structural classes: I, II and III, irrespective of the phylogeny derived from the viral polymerase gene. His work identified that the eukaryotic proteins driving the fusion of cells, during organism development or during fertilization, are evolutionary related to the class II viral envelope proteins.

Three selected publications:

1. *A glycerophospholipid-specific pocket in the RVFV class II fusion protein drives target membrane insertion*. Guardado-Calvo P, Atkovska K, Jeffers SA, Grau N, Backovic M, Pérez-Vargas J, de Boer SM, Tortorici MA, Pehau-Arnaudet G, Lepault J, England P, Rottier PJ, Bosch BJ, Hub JS, Rey FA. ***Science***. 2017 Nov 3;358 (6363): 663-667. doi: 10.1126/science.aal2712.
2. *Structural basis of potent Zika-dengue virus antibody cross-neutralization*. Barba-Spaeth G, Dejnirattisai W, Rouvinski A, Vaney MC, Medits I, Sharma A, Simon-Lorière E, Sakuntabhai A, Cao-Lormeau VM, Haouz A, England P, Stiasny K, Mongkolsapaya J, Heinz FX, Screaton GR, Rey FA. ***Nature***. 2016 Aug 4;536(7614):48-53. doi: 10.1038/nature18938. Epub 2016 Jun 23
3. *Recognition determinants of broadly neutralizing human antibodies against dengue viruses*. Rouvinski A, Guardado-Calvo P, Barba-Spaeth G, Duquerroy S, Vaney MC, Kikuti CM, Navarro Sanchez ME, Dejnirattisai W, Wongwiwat W, Haouz A, Girard-Blanc C, Petres S, Shepard WE, Desprès P, Arenzana-Seisdedos F, Dussart P, Mongkolsapaya J, Screaton GR, Rey FA. ***Nature***. 2015 Apr 2;520(7545):109-13. doi: 10.1038/nature14130. Epub 2015 Jan 12.

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