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ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

The Global Health Institute

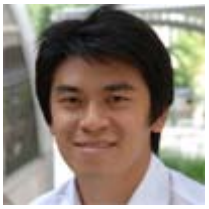
is glad to invite you to the following double seminar session on

Thursday, September 30th , 2010 - 12:15pm

Location: SV 1717A

Host : Prof. John McKinney

Professor Howard Hang
Assistant Professor - Laboratory of Chemical Biology and Microbial Pathogenesis
The Rockefeller University



Palmitoylome profiling reveals S-palmitoylation-dependent anti-viral activity of IFITM3

The identification of innate and adaptive immune effectors is crucial for dissecting mechanisms of microbial pathogenesis and development of antimicrobial therapeutics. While genome-wide screens have begun to identify host factors necessary for limiting microbial infections, posttranslational modifications that control protein activity may not be readily apparent by targeting the levels of gene expression. Here we demonstrate the antiviral activity of interferon-induced transmembrane protein 3 (IFITM3) is posttranslationally regulated by S-palmitoylation. Large-scale profiling of palmitoylated proteins in a dendritic cell line using a chemical reporter strategy revealed over 150 lipid-modified proteins with diverse roles in membrane trafficking, cell signaling, protein quality control as well as innate immunity. We discovered that S-palmitoylation of IFITM3 on membrane-proximal cysteines is required for its clustering in membrane compartments and antiviral activity against influenza virus infection. The sites of S-palmitoylation are highly conserved amongst the IFITM family of proteins in vertebrates, which suggests that S-palmitoylation of these immune effectors may be an ancient posttranslational modification that is crucial for host resistance to virus infections. The S-palmitoylation and clustering of IFITM3 will be important for the design of antiviral therapeutics based on this family of IFN-induced effectors

ofessor George Cross
Laboratory of Molecular Parasitology – The Rockefeller University

Daring to be different: unusual aspects of gene transcription in trypanosomes

I will present some contemporary observations on the regulation of gene transcription in Trypanosoma brucei — the agent of African Sleeping Sickness. We have been interested for many years in trying to elucidate the mechanisms controlling antigenic variation, a phenomenon that is unique, in its extent, to the African trypanosomes, and allows them to evade the immune response indefinitely. A key component of antigenic variation is allelic exclusion among the Variant Surface Glycoprotein (VSG) genes. Exploring chromatin structure in relation to VSG silencing and activation, and the availability of new methods for high-throughput DNA sequencing, led us to a wider study of gene expression in Trypanosoma brucei. Trypanosomes have three RNA polymerases, but that seems to be where the similarity to more intensively studied organisms ends. Evolving differently, trypanosomes have largely eschewed introns and —with a few exceptions — do not appear to regulate the initiation of RNA transcription. Differential mRNA trans-splicing and stability appear to be major determinants of mRNA abundance. We have, however, identified striking histone motifs at regions where polycistronic transcription starts and stops