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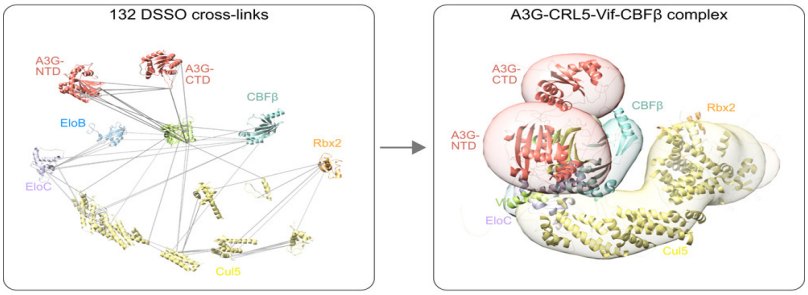
A Collaborative Research Center to Study HIV Accessory and Regulatory Complexes



[1]

Research Highlight:

Characterization of an A3G-VifHIV-1-CRL5-CBF? Structure Using a Cross-linking Mass Spectrometry Pipeline for Integrative Modeling of Host?Pathogen Complexes [1]

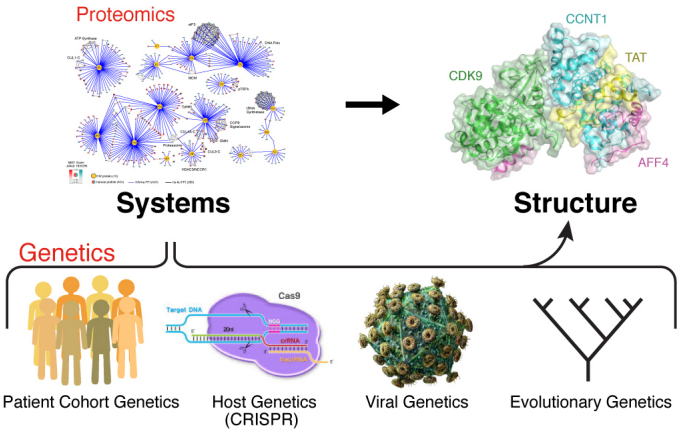
Robyn M. Kaake et al., August 2021

HARC Center Mission:

The HARC Center is an interdisciplinary research center aimed at creating a comprehensive structural picture of interactions between HIV viral proteins and key intracellular host molecules in the viral lifecycle. High-resolution structures of such complexes offer the potential for novel targeted drug design strategies in the treatment of AIDS.

The HARC Center mission is to elucidate the molecular basis of systems that are essential for, or contribute to, the pathogenesis of HIV/AIDS, including the physical/functional

interactions that occur between viral and human proteins, membranes, lipids and nucleic acids (DNA/RNA). The HIV accessory or regulatory proteins that we focus on are not currently targeted by anti-viral therapeutics, and so better molecular understanding of their functions and mechanisms may reveal new therapeutic strategies for intervention, including strategies that may escape the limitations of current drug regimens where mutations in the targeted HIV enzymes can diminish drug efficacy.



Through our powerful structure/function pipeline, now expanded to include CRISPR technology and other genetic approaches, we can gain unprecedented insight into HIV biology, new avenues to complex structures, and the potential to fundamentally alter treatment strategies by targeting key cellular processes that contribute to AIDS at interfaces where mutational resistance is highly unlikely. To accomplish this, we bring together a diverse team of investigators and collaborators that span the breadth of technologies and biological expertise needed to elucidate critical HIV-host biology at a structural level. To augment our Systems-to-Structure pipeline, we employ host genetic approaches that include: our recent advancements in CRISPR/Cas9 gene editing with a particular focus on primary cells; systematic viral genetic studies; evolutionary genetic studies to help define novel restrictions factors; and, finally, genetic information extracted from patient cohorts.

The Center is comprised of researchers from thirteen different laboratories at UCSF, Berkeley and the Fred Hutchinson Cancer Research Institute (Seattle), and is one of five Specialized Centers for Determination of Structures and HIV-host Complexes funded by the NIH AIDS-Related Structural Biology Program [2] at the National Institute of Allergy and Infectious Diseases (NIAID). Members of the HARC Center provide expertise within a comprehensive range of biochemical, molecular biological and structural methods, including mass spectrometry, x-ray crystallography, membrane expression, CRISPR, NMR and cryo-electron microscopy.

In conjunction with its research activities, the Center makes new methodologies, tools and databases available to the research community at large, and is active in creating new collaborations with outside investigators.

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