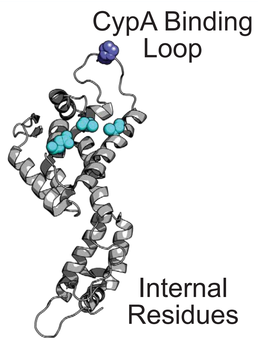
HIV-CRISPR screens reveal mechanism of TRIM5 Restriction

Isaiah Grant, Andrew Gabagat, Laura Gong, Molly Ohainle
Department of Molecular and Cell Biology, University of California, Berkeley

Does altered capsid (CA) interactions lead to changes in restriction factor sensitivity?

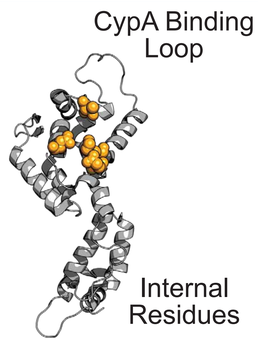
CA loss of interaction with host protein

Mutation	Type	TRIM5
P90A	CypA	⬆
N74D	CPSF6	⬆
N57A/D	CPSF6	???
A77V	CPSF6	???
A105T	CPSF6	???

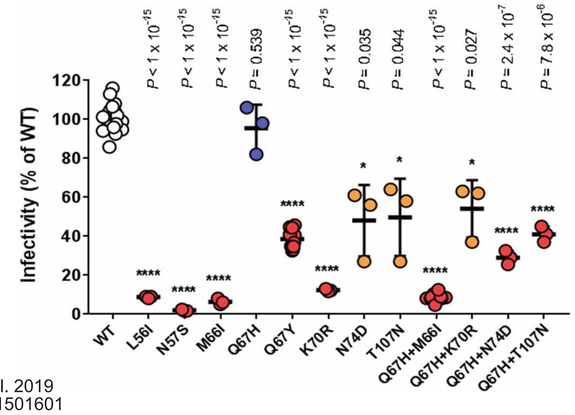


CA resistnace to antiretroviral drug (LEN)

Mutation	Type	TRIM5
N74D	LEN	⬆
N57S	LEN	???
Q67H	LEN	???
K70R	LEN	???
T107N	LEN	???



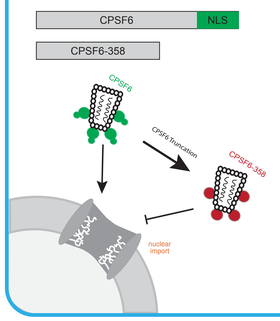
Lenacapavir resistant mutants show varying levels of infection

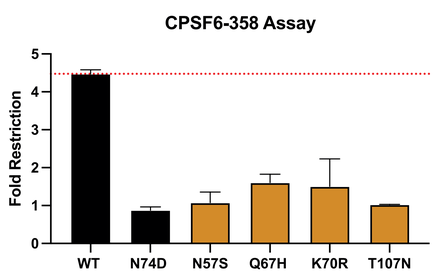


Yant et al. 2019
PMID: 31501601

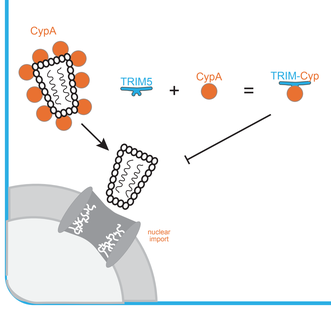
Does LEN escape alter CA-Host interactions?

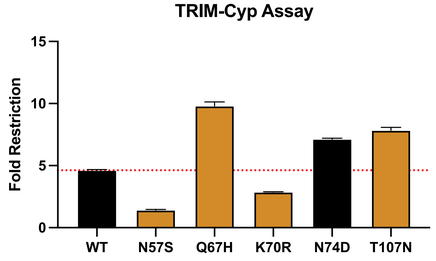
LEN resistance mutants lose CPSF6 binding



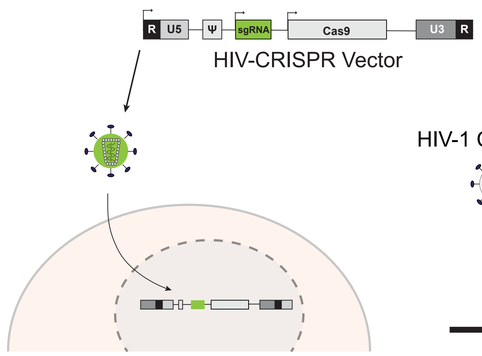


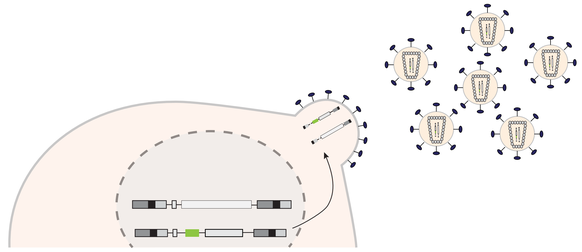
Does LEN escape affect CypA binding?





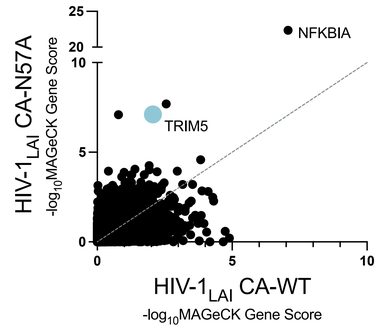
HIV-CRISPR screening allows us to elucidate differences in interactions between CA mutants and host genes

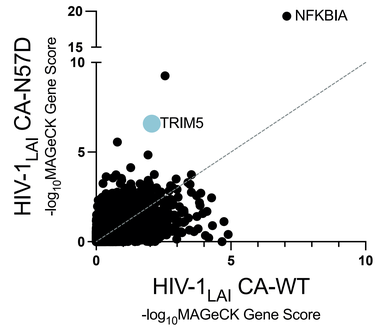


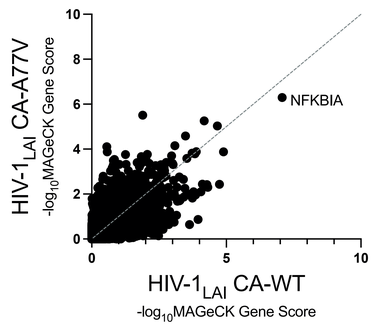


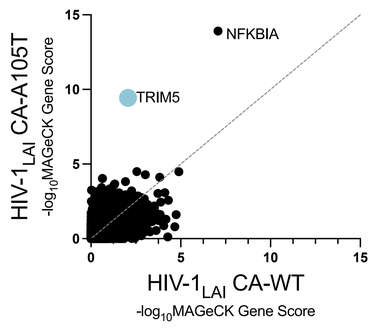
Mutation	Type	TRIM5
P90A	CypA	⬆
N74D	CPSF6/LEN	⬆
N57A/D	CPSF6	⬆
N57S	LEN	???
Q67H	LEN	???
K70R	LEN	???
A77V	CPSF6	---
A105T	CPSF6	⬆
T107N	LEN	???

TRIM5 is a hit in 3 of 4 screens, but loss of CPSF6 binding is not the only factor









OHAINLE LAB · MCB Molecular & Cell Biology · Berkeley · CHEMICAL BIOLOGY GRADUATE PROGRAM · UC BERKELEY · NIH National Institutes of Health · CHEETAH Center for the Structural Biology of HIV Infection, Restriction and Viral Dynamics