

HelmholtzZentrum münchen

German Research Center for Environmental Health

HIV Full-Replication Technology for Identification of novel HIV Inhibitors from Multiple Sources

HIV/AIDS: A major global health problem

The statistics for 2007

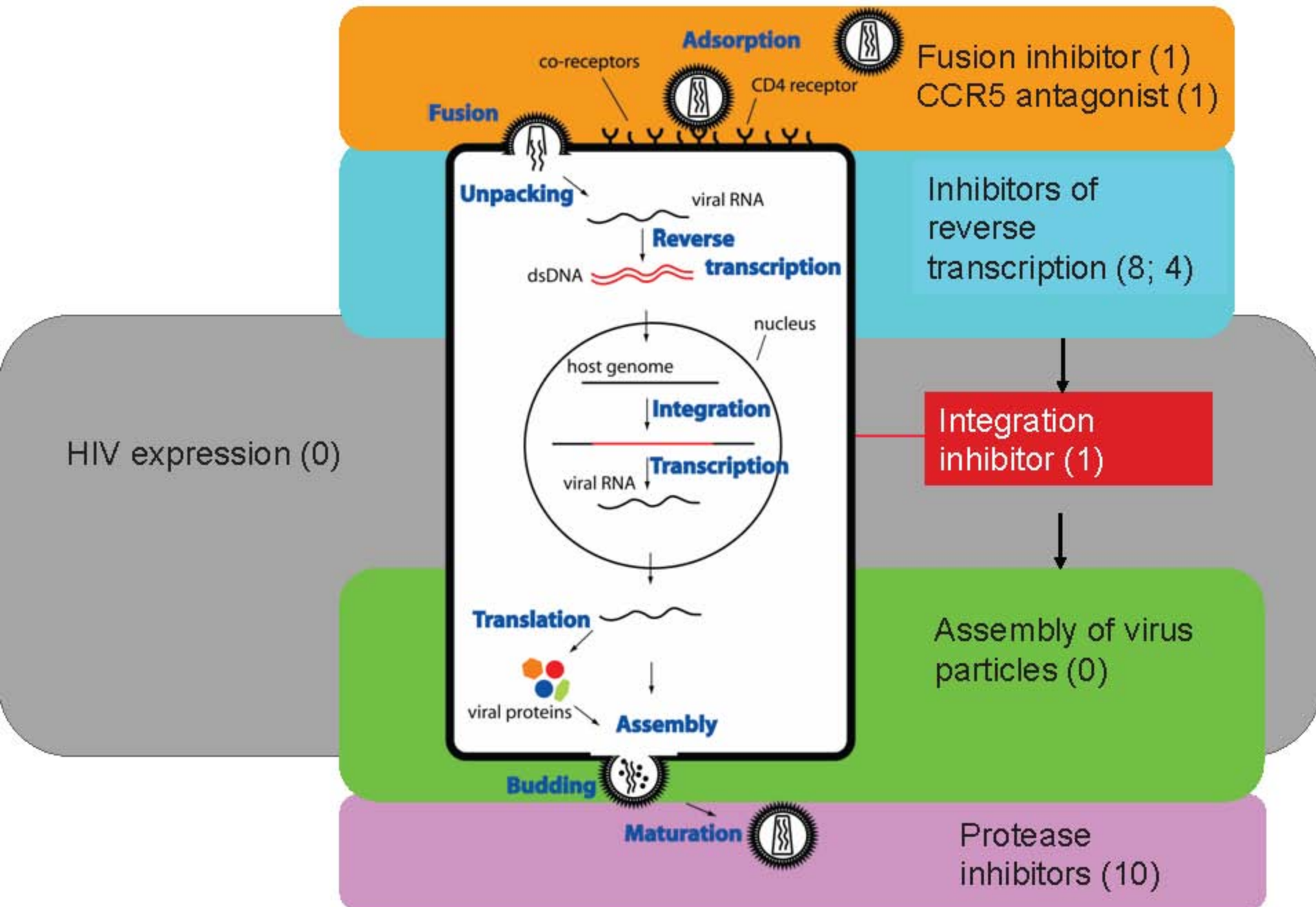
(UNAIDS, 2008 report on the global AIDS epidemic)

- 33 million people currently living with HIV;
- 2.7 million new HIV infections in 2007;
- 2.0 million deaths due to AIDS in 2007

Projected to be the third leading cause of death in 2030

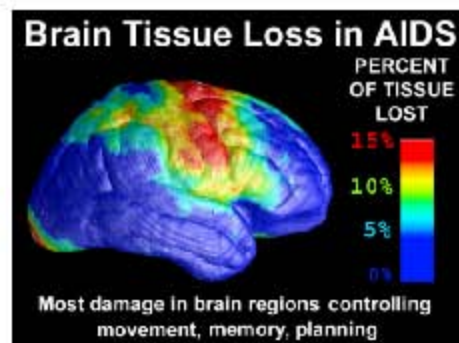
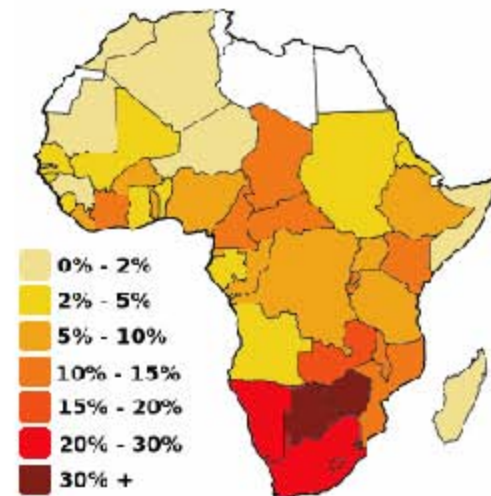
Prevention of disease requires continuous treatment with inhibitors of HIV replication

25 FDA-approved anti-HIV drugs

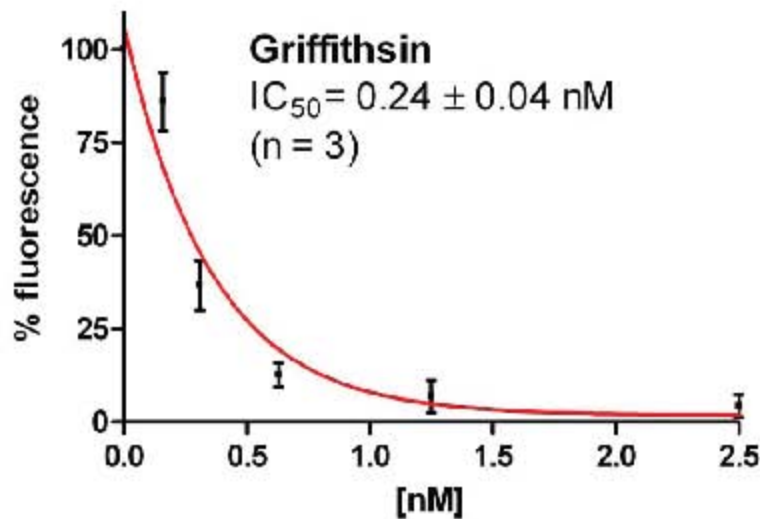
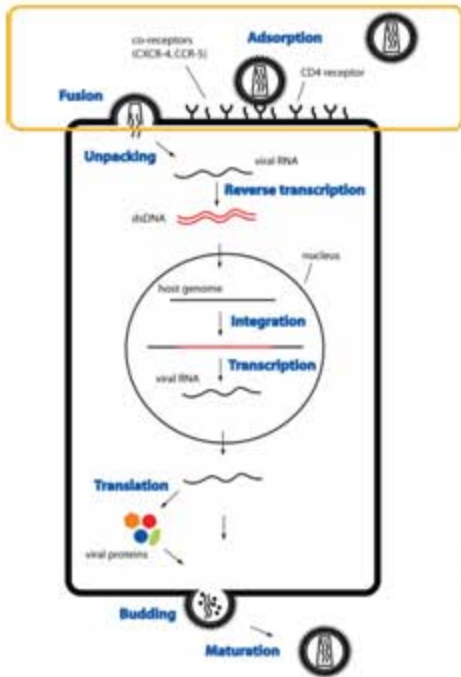


Why do we need new anti-HIV therapies?

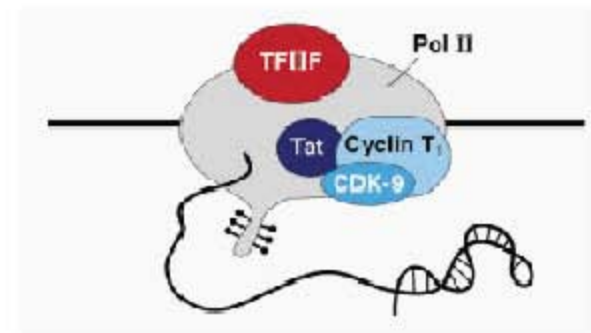
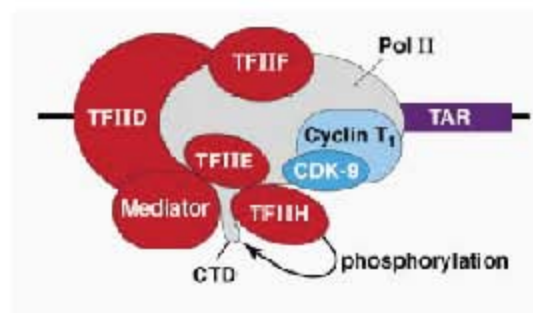
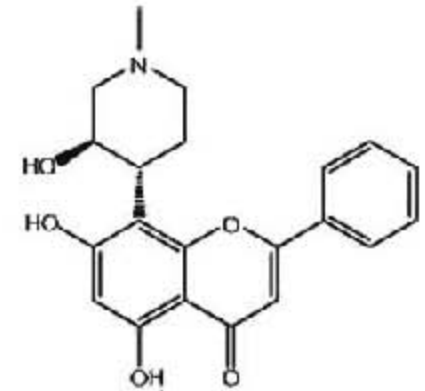
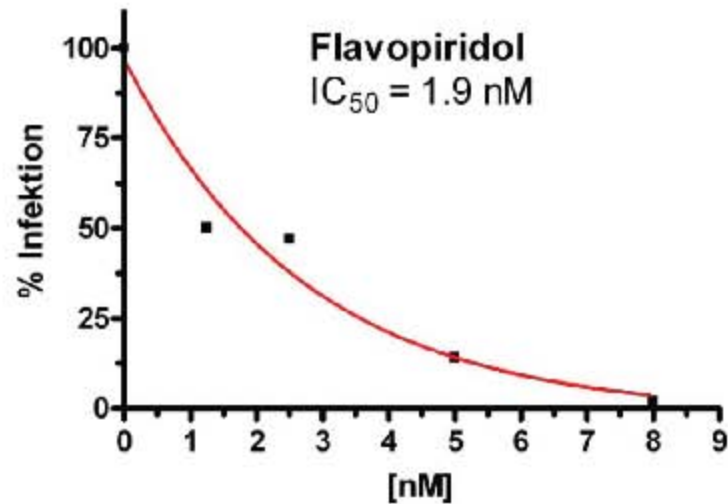
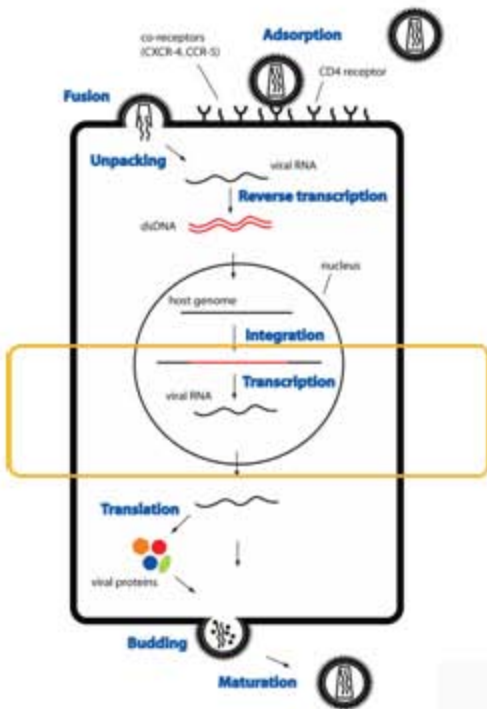
- **Drug resistance: battling HIV variability**
- **Providing treatment for people in resource limited settings**
- **Silencing the virus in cellular reservoirs**



Natural products as HIV inhibitors: attachment

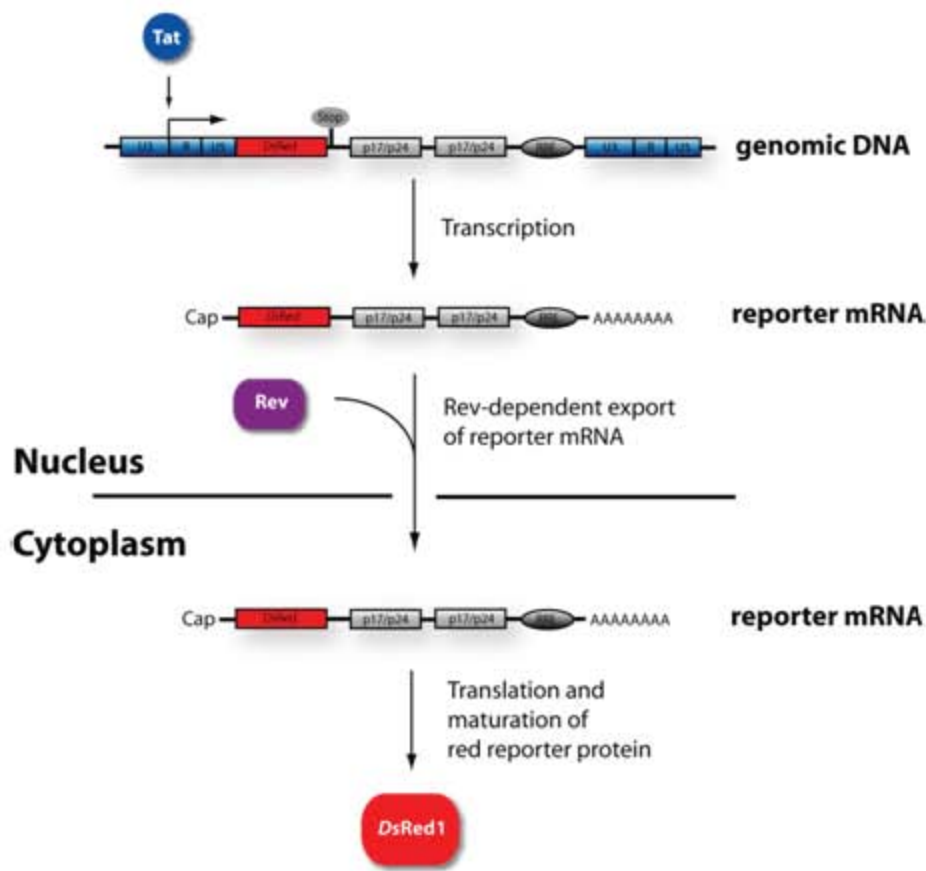


Natural products as HIV inhibitors: gene expression



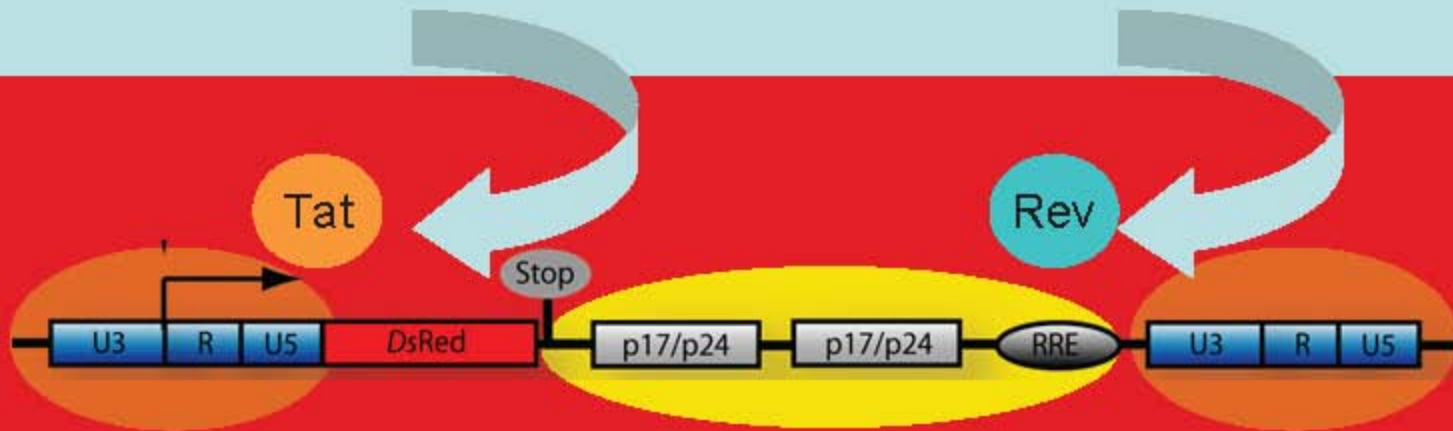
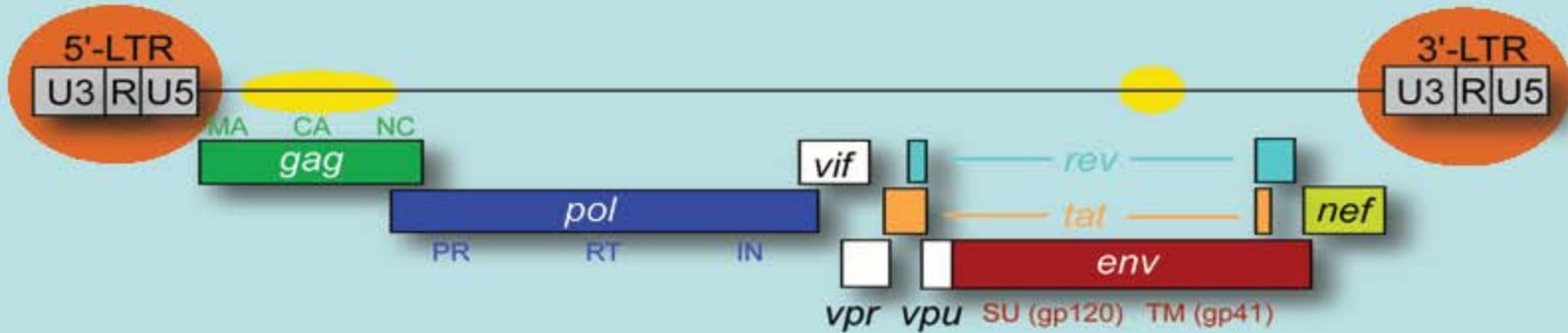
The EASY-HIT system: reporter gene

EASY-HIT: Exploratory Assay System for the discovery of HIV-inhibiTors



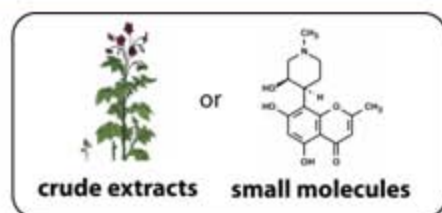
The LC5-RIC system: reporter gene

HIV DNA genome



HIV-reporter gene

EASY-HIT technology: overview

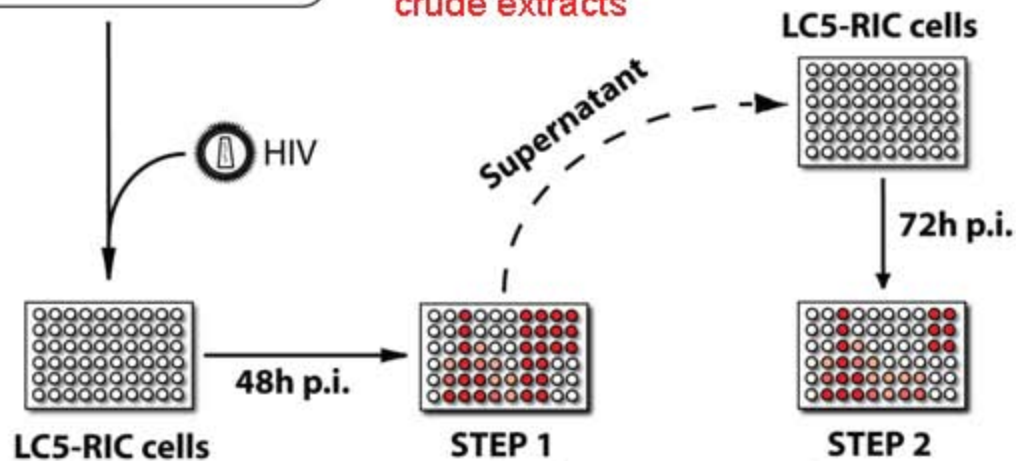


OPEN SOURCE

Small mol, proteins,
expression of proteins,
crude extracts

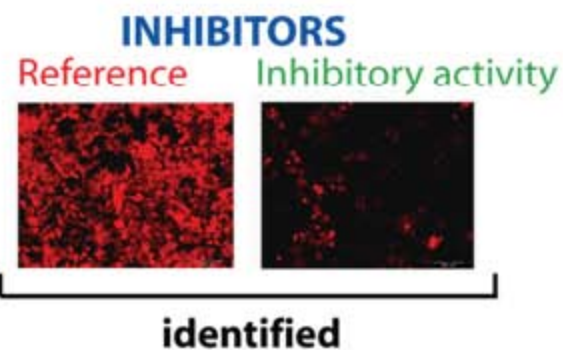
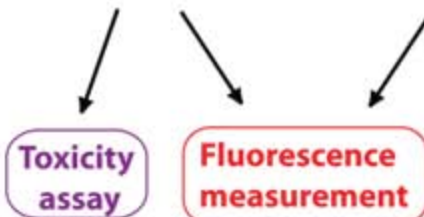
OPEN TARGET

Full replication assay
includes all steps of HIV
replication including cellular
targets

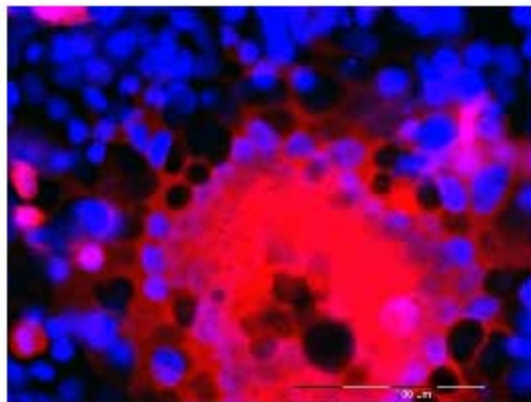
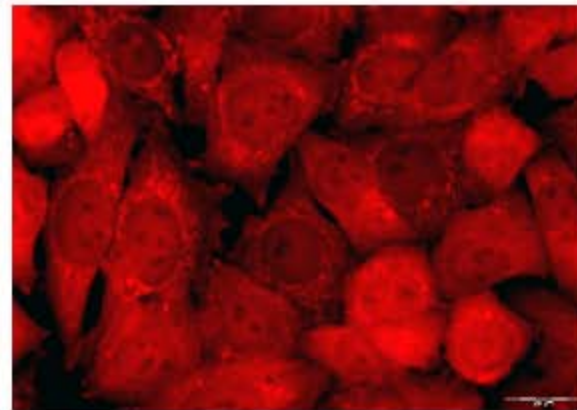
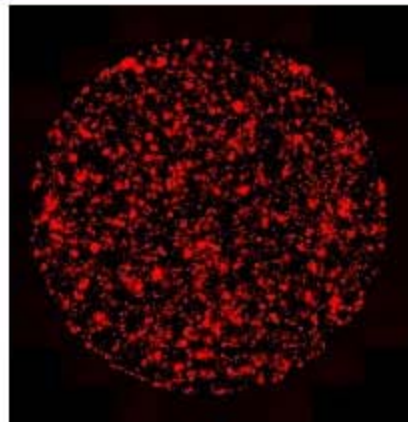


ADHERENT CELLS

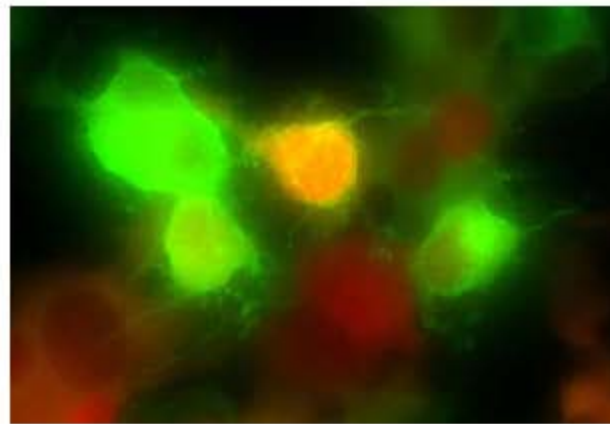
Easy and convenient
handling; important for
coloured or autofluorescent
compounds



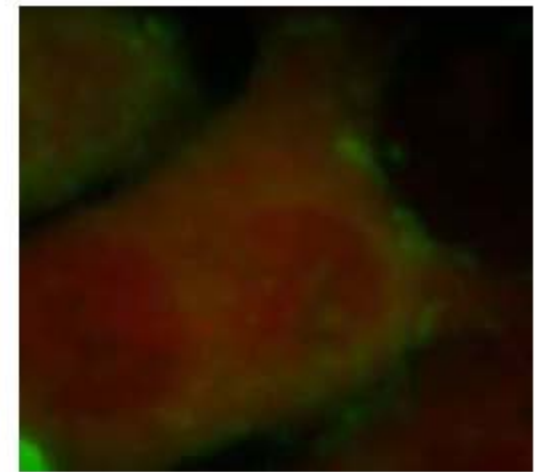
Exposure of indicator cells (LC5-RIC) to HIV triggers red fluorescence



Formation of syncytia

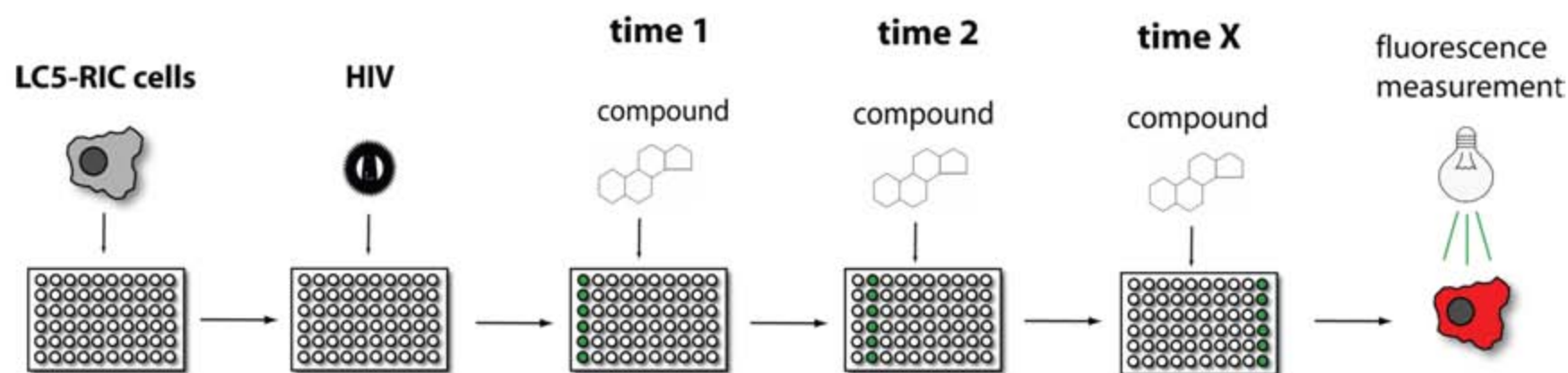


Colocalization studies with labelled viruses



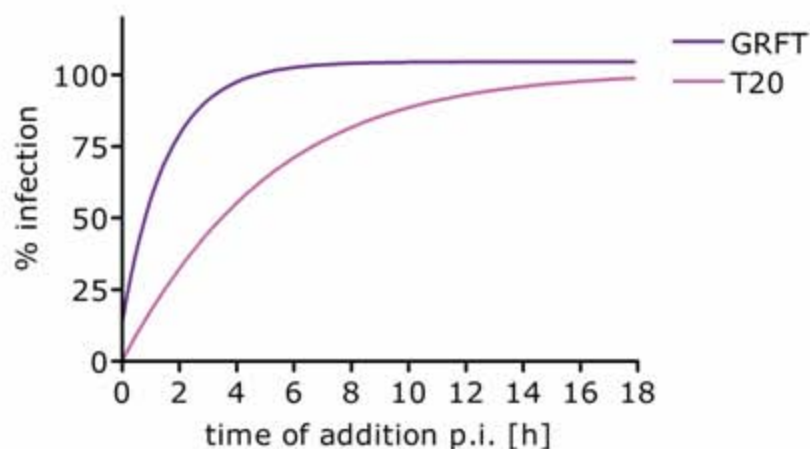
Further characterization of active compounds

Determining the window-of-efficacy of a compound by varying its time-of-addition relative to HIV exposure

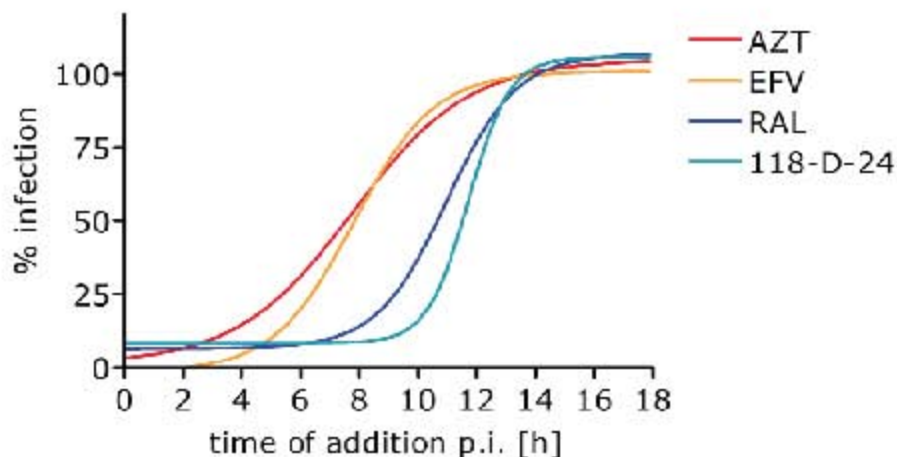


Further characterization: early replication events

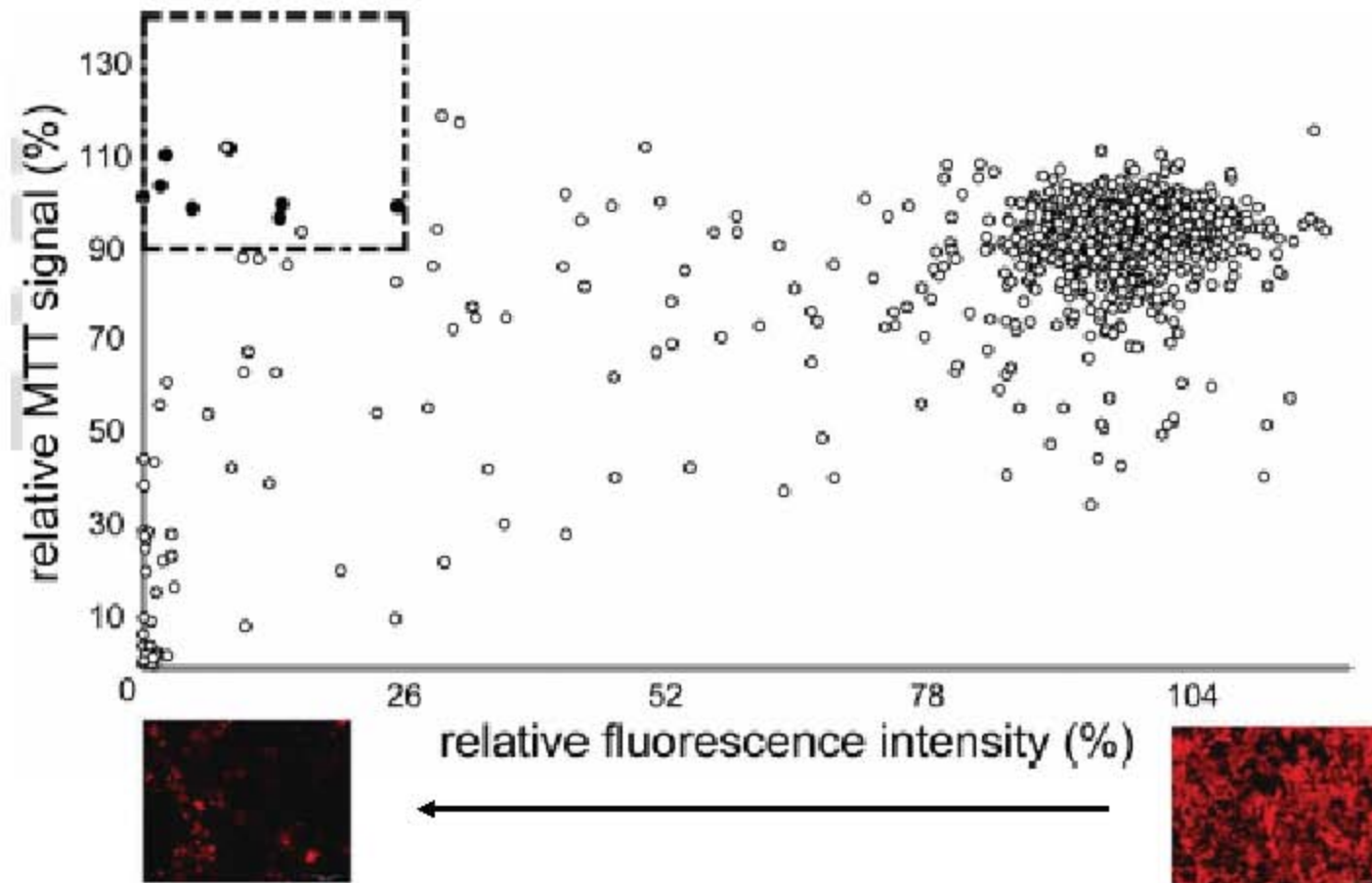
Attachment and Fusion



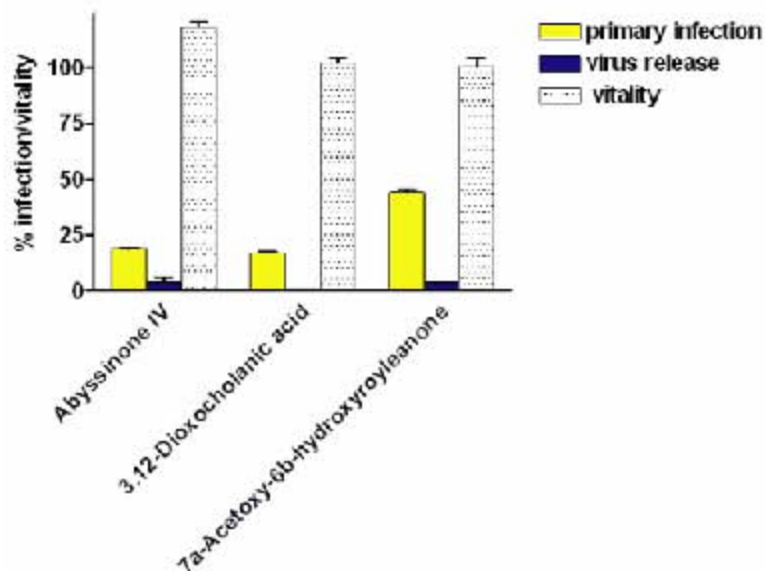
Reverse transcription and provirus integration

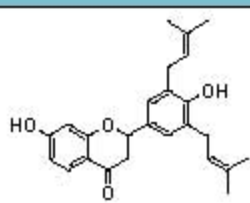
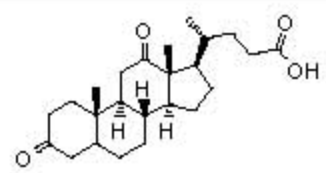
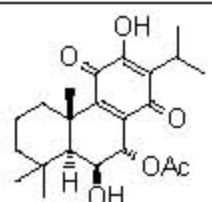


Screening of compound libraries

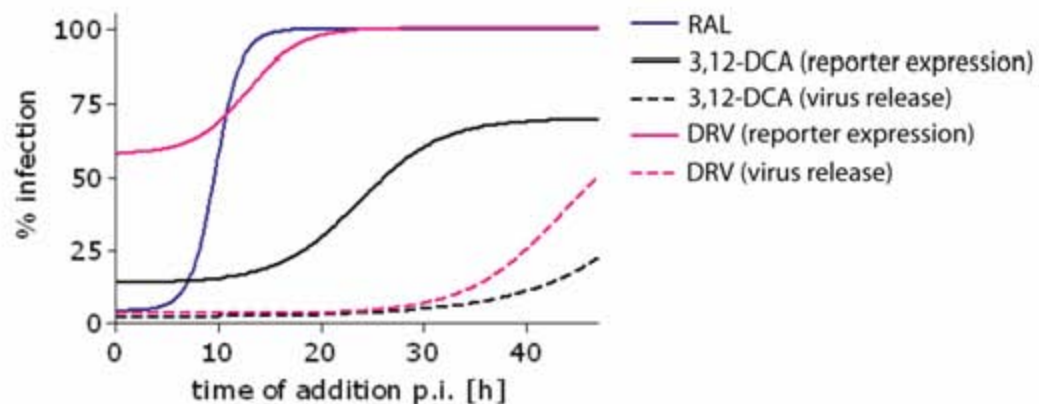
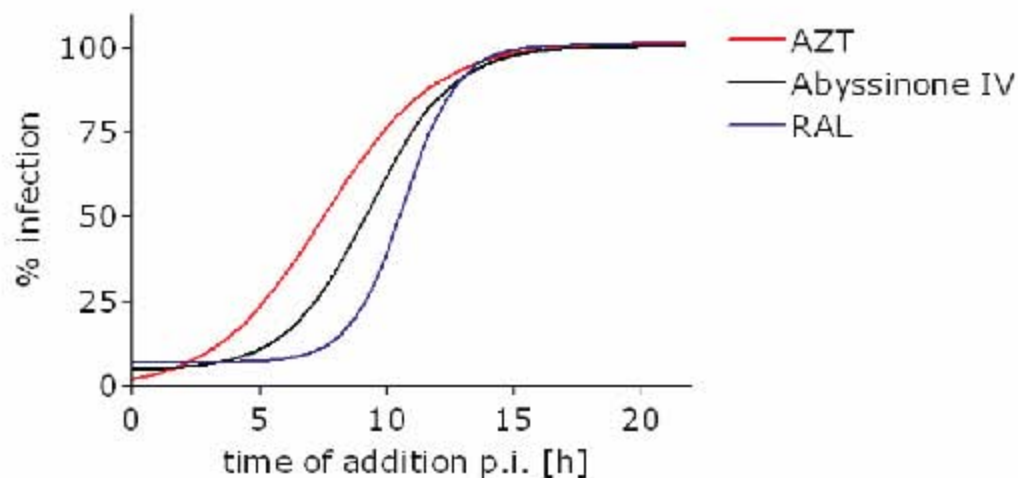


Screening of compound libraries

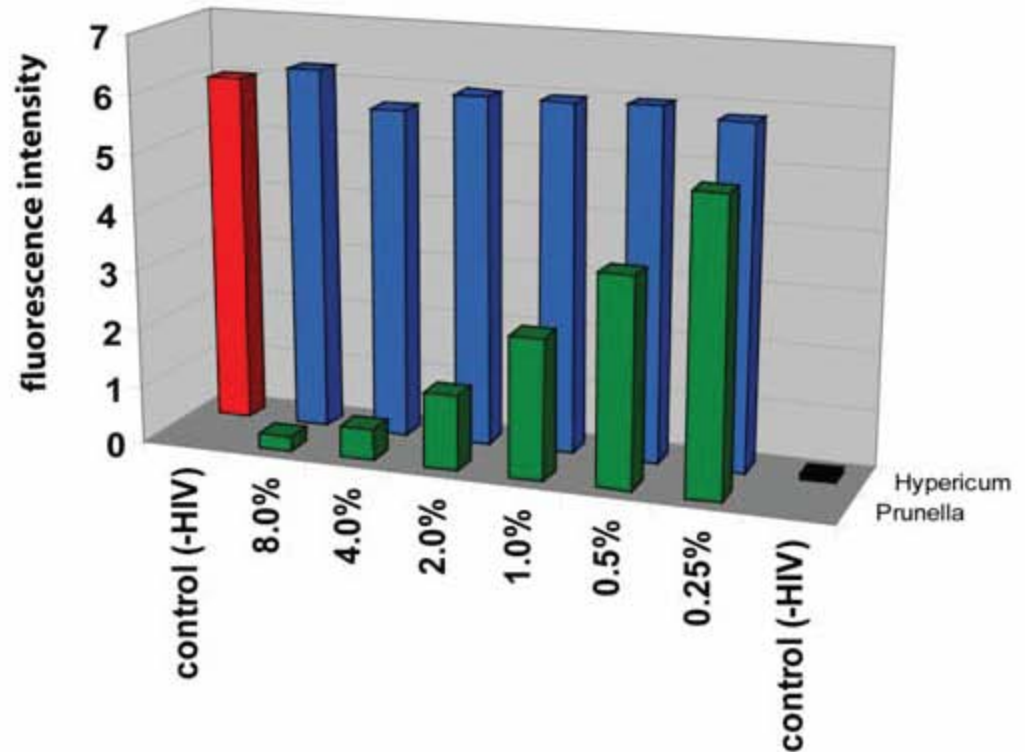


<u>NAME</u>	<u>IC50</u> (μM)	<u>IN HIV</u> <u>DATA-</u> <u>BASE?</u>	<u>STRUCTURE</u>
Abyssinone IV	2.3	No	
3,12-Dioxocholanic acid	2	No	
7a-acetoxy-6b-hydroxyroyleanone	1.8	No	

Characterization of active compounds



Detection of anti-HIV activities in crude plant extracts



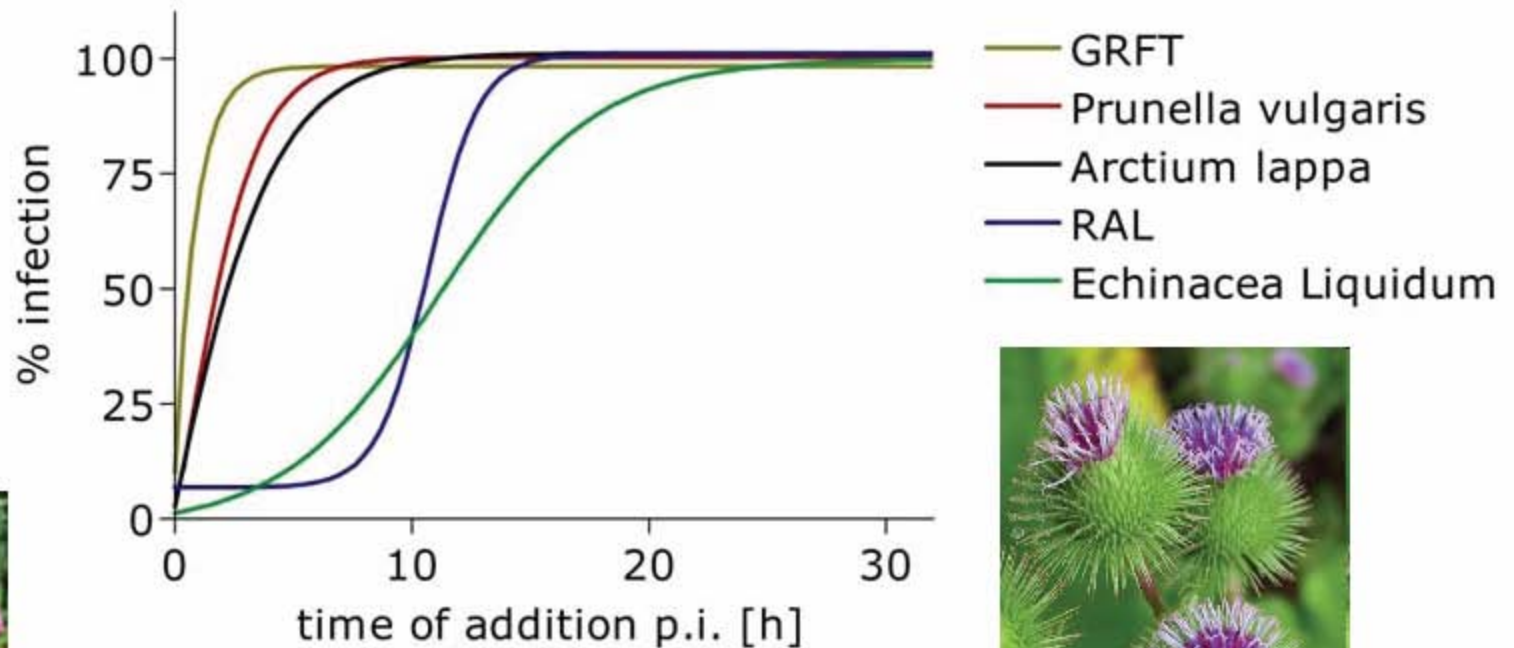
Characterization of anti-HIV activities in crude plant extracts



(Prunella vulgaris)



(Echinacea sp.)



(Arctium lappa)

Antiviral activity of marine macroalgae



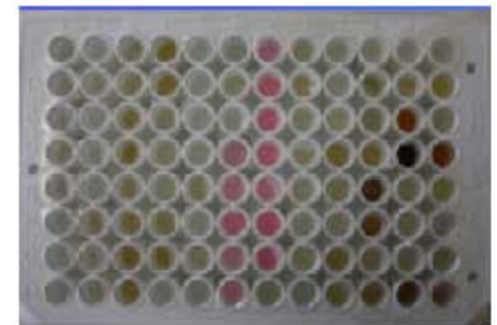
Collection of more than 50 different algal samples on a field trip to coral reefs off Belize (Caribbean Sea) in 2009



Marine habitats

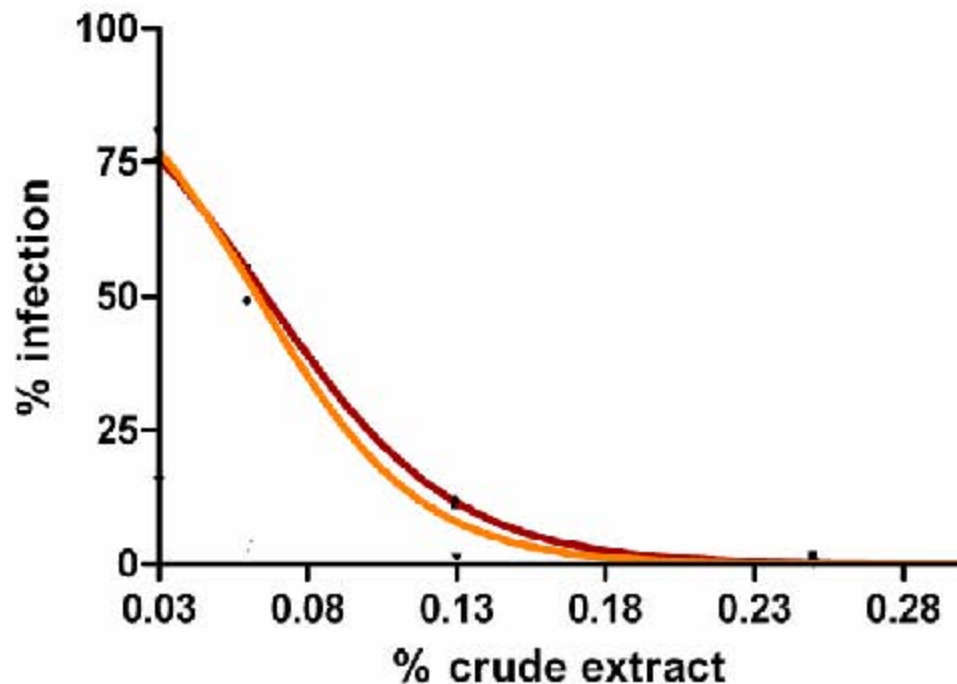


Algal samples

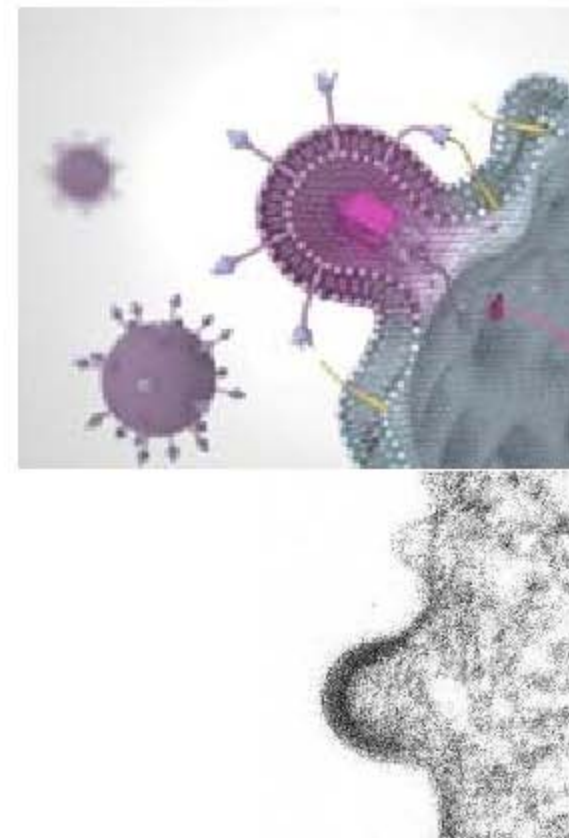
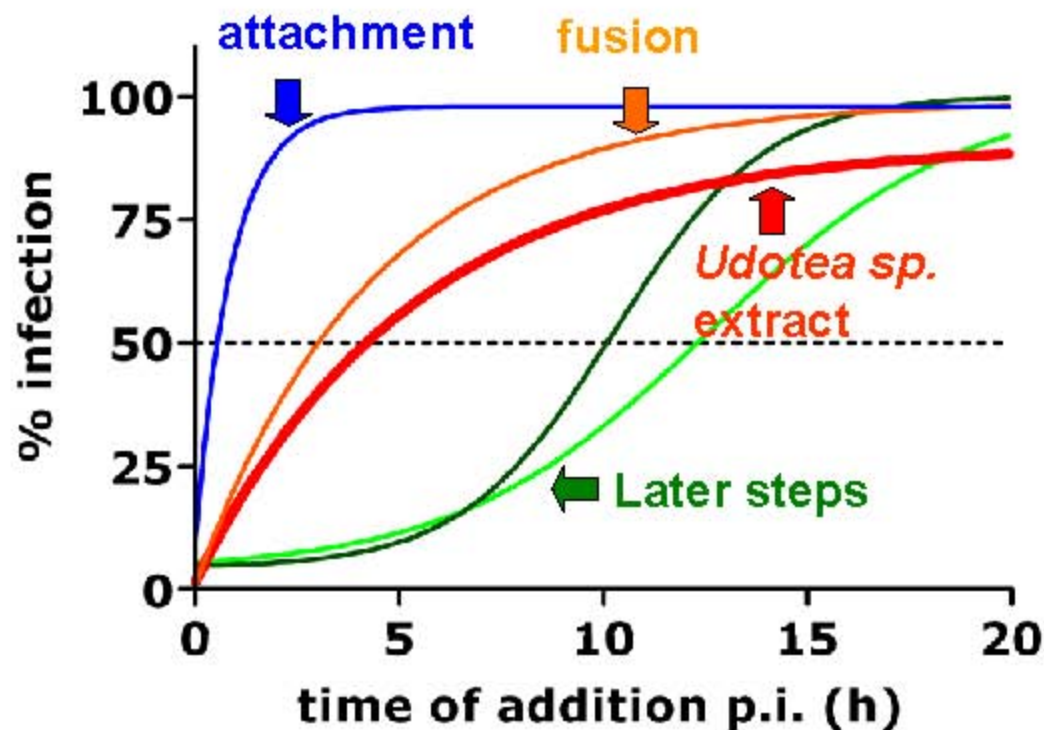


Crude Extracts

Antiviral activity of marine macroalgae

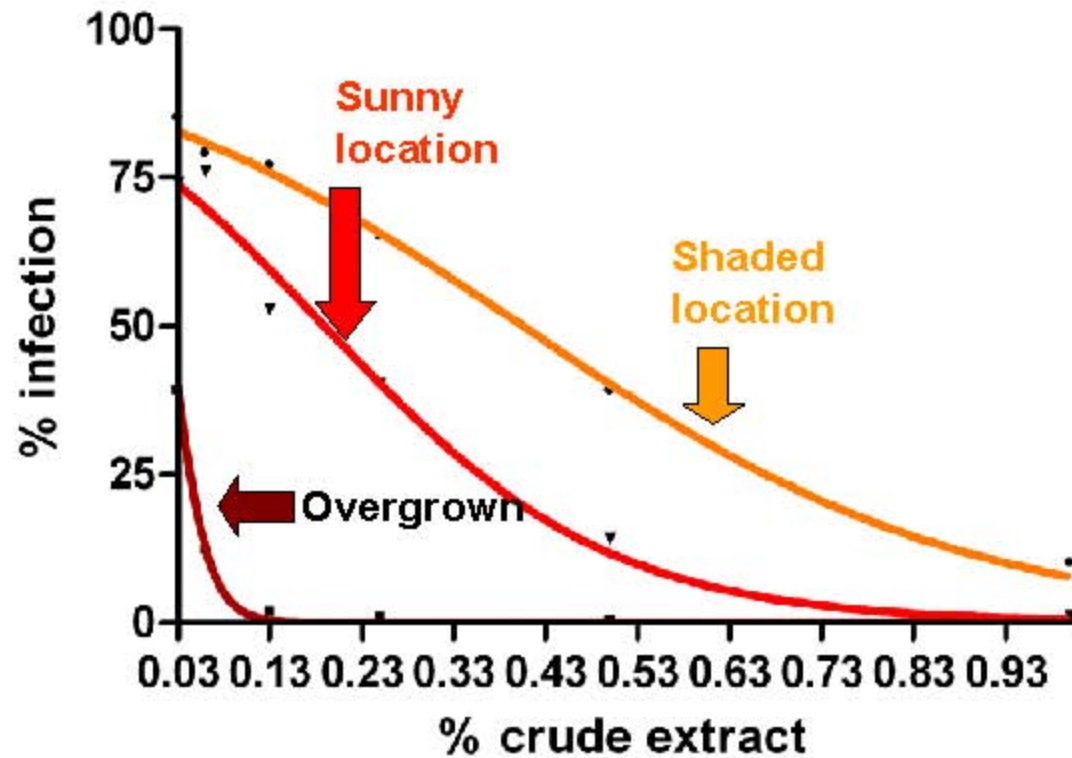


Antiviral activity of marine macroalgae

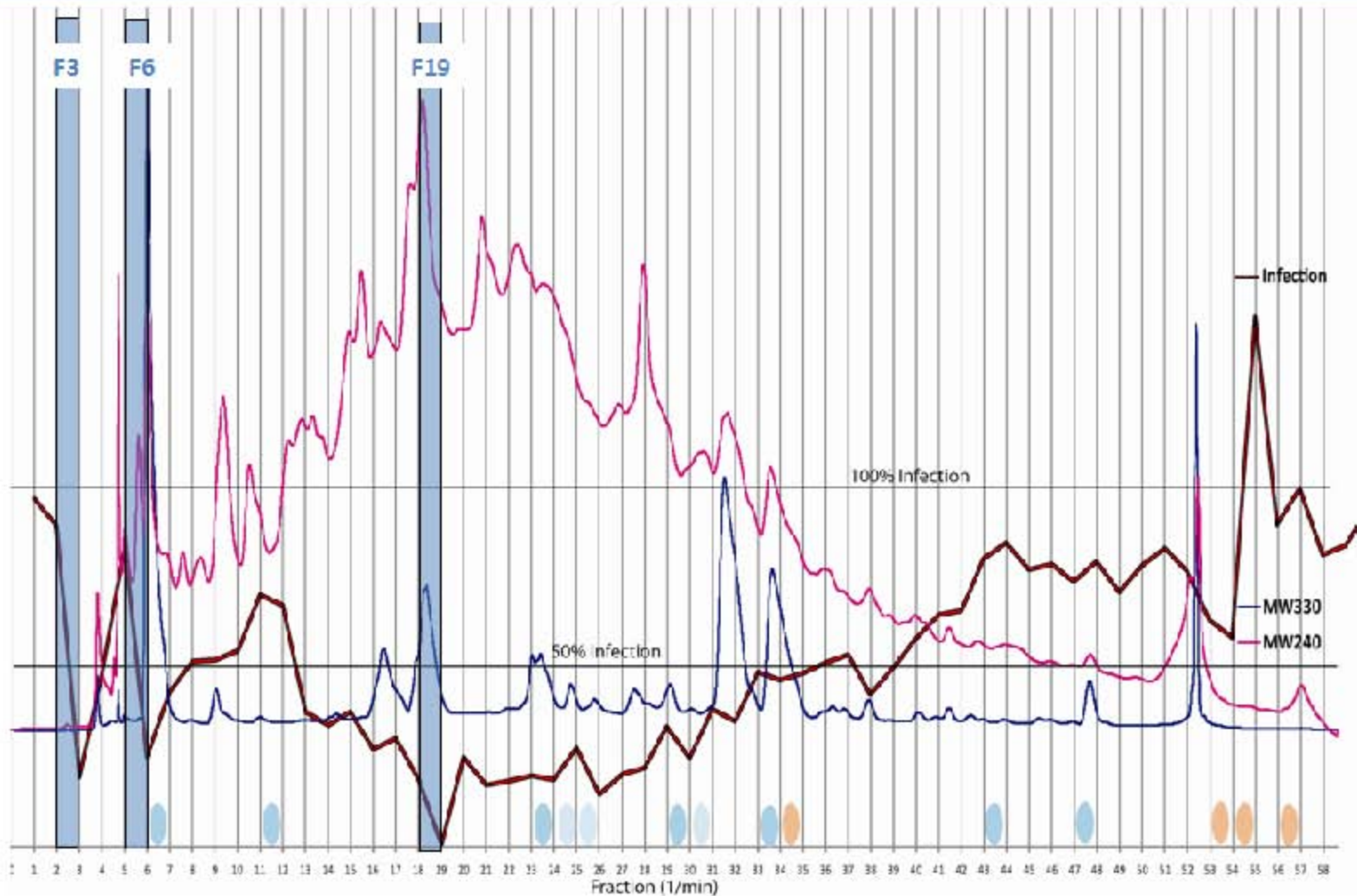


The green algal extracts probably inhibit HIV-1 fusion

Antiviral activity of marine macroalgae



Bioassay-guided fractionation of biological extracts



Acknowledgement

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Thank you for your attention

