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# Quantification and a Molecular Dynamics Study of Viral Membrane Lipids through Plasmon Coupling Microscopy

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# Quantification and a Molecular Dynamics Study of Viral Membrane Lipids through Plasmon Coupling Microscopy

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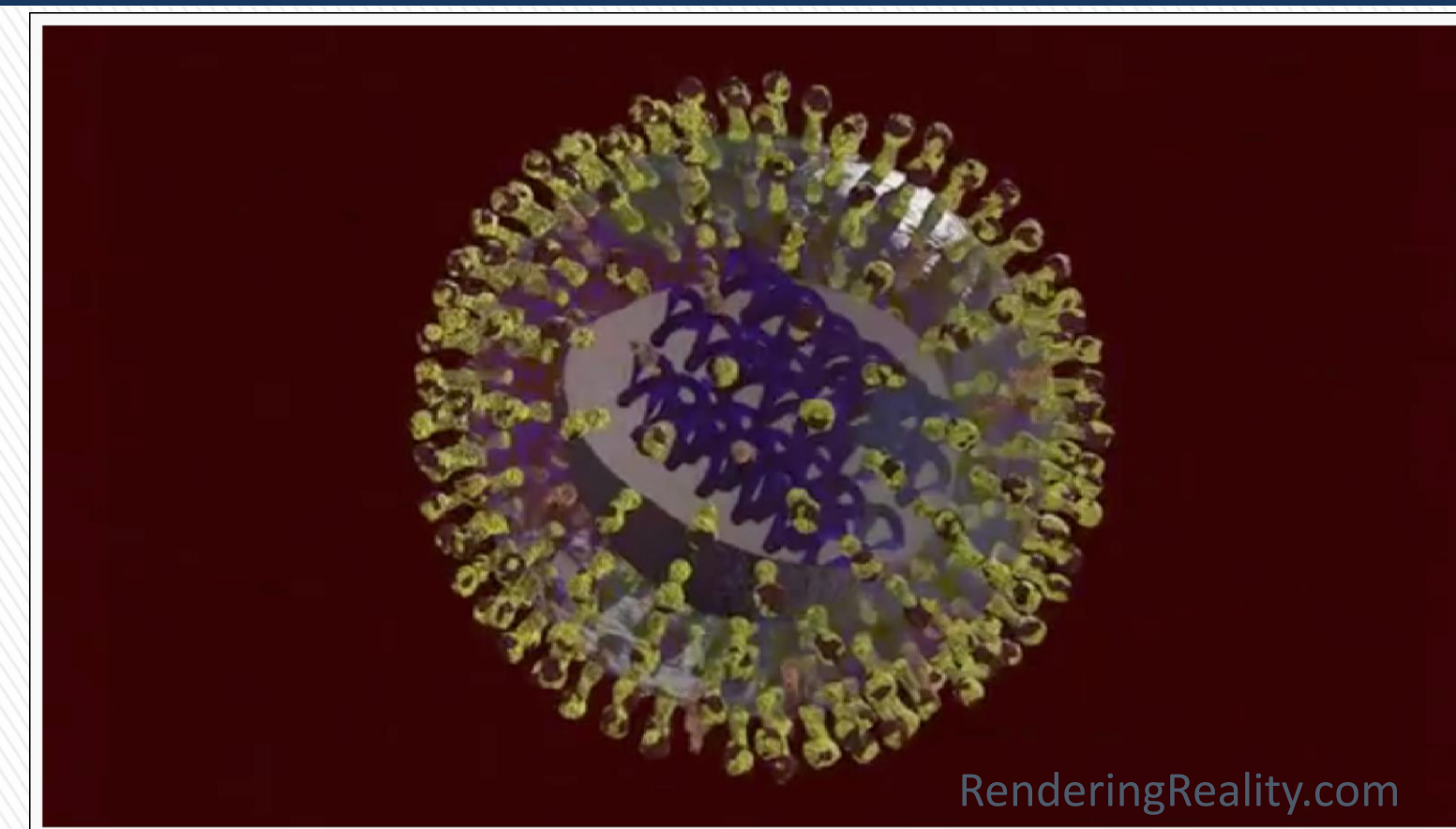


## ABSTRACT

Phosphatidylserine (PS) and monosialotetrahexosylganglioside ( $G_{M1}$ ) are examples of two host-derived lipids in the membrane of enveloped virus particles that are known to contribute to virus attachment, uptake, and ultimately dissemination. A quantitative characterization of their contribution to the functionality of the virus requires information about their relative concentrations in the viral membrane. Here, a gold nanoparticle (NP) binding assay for probing relative PS and  $G_{M1}$  lipid concentrations in the outer leaflet of different HIV-1 and Ebola virus-like particles (VLPs) using sample sizes of less than  $3 \times 10^6$  particles is introduced. The assay evaluates both scattering intensity and resonance wavelength and determines relative NP densities through plasmon coupling as a measure for the target lipid concentrations in the NP-labeled VLP membrane. In addition, the mechanical properties of the viral membrane have been found to be contributing to the efficient reproduction cycle of the virus. Membrane fluidity which is a function of temperature and membrane composition is one of the crucial factors in viral activity. We have used temporally-resolved microscopy on silver NPs to track these molecular dynamics.

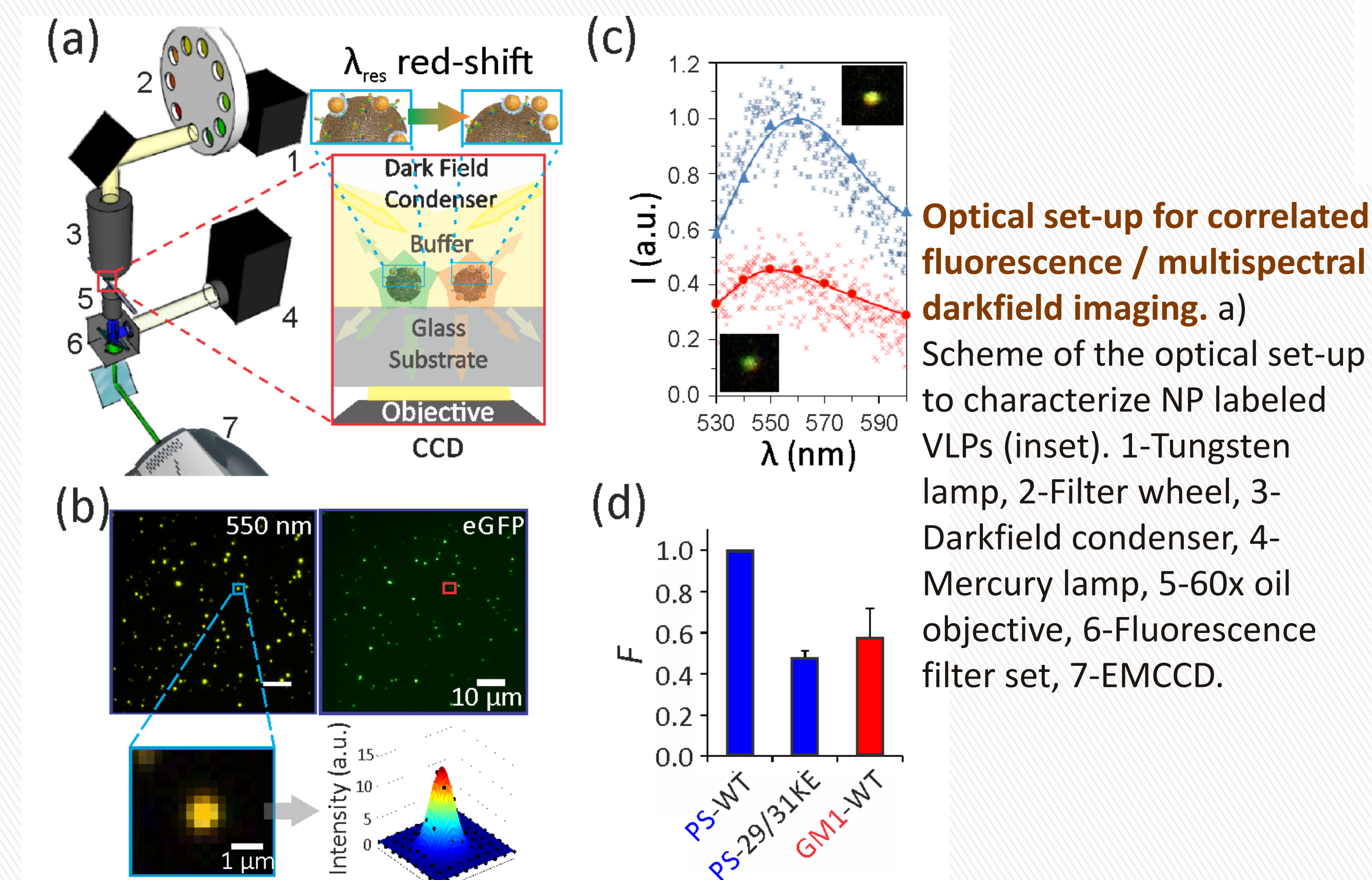
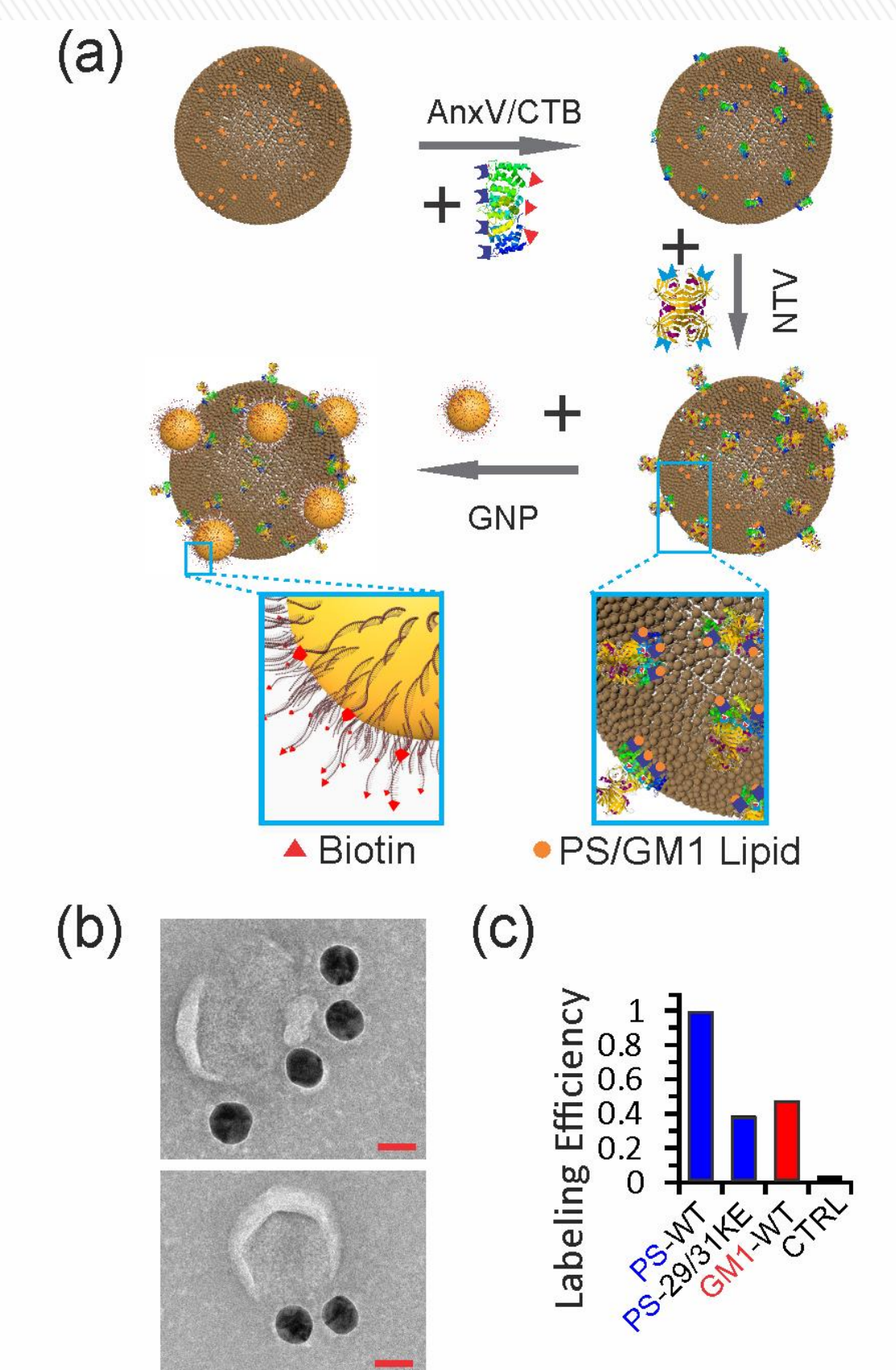
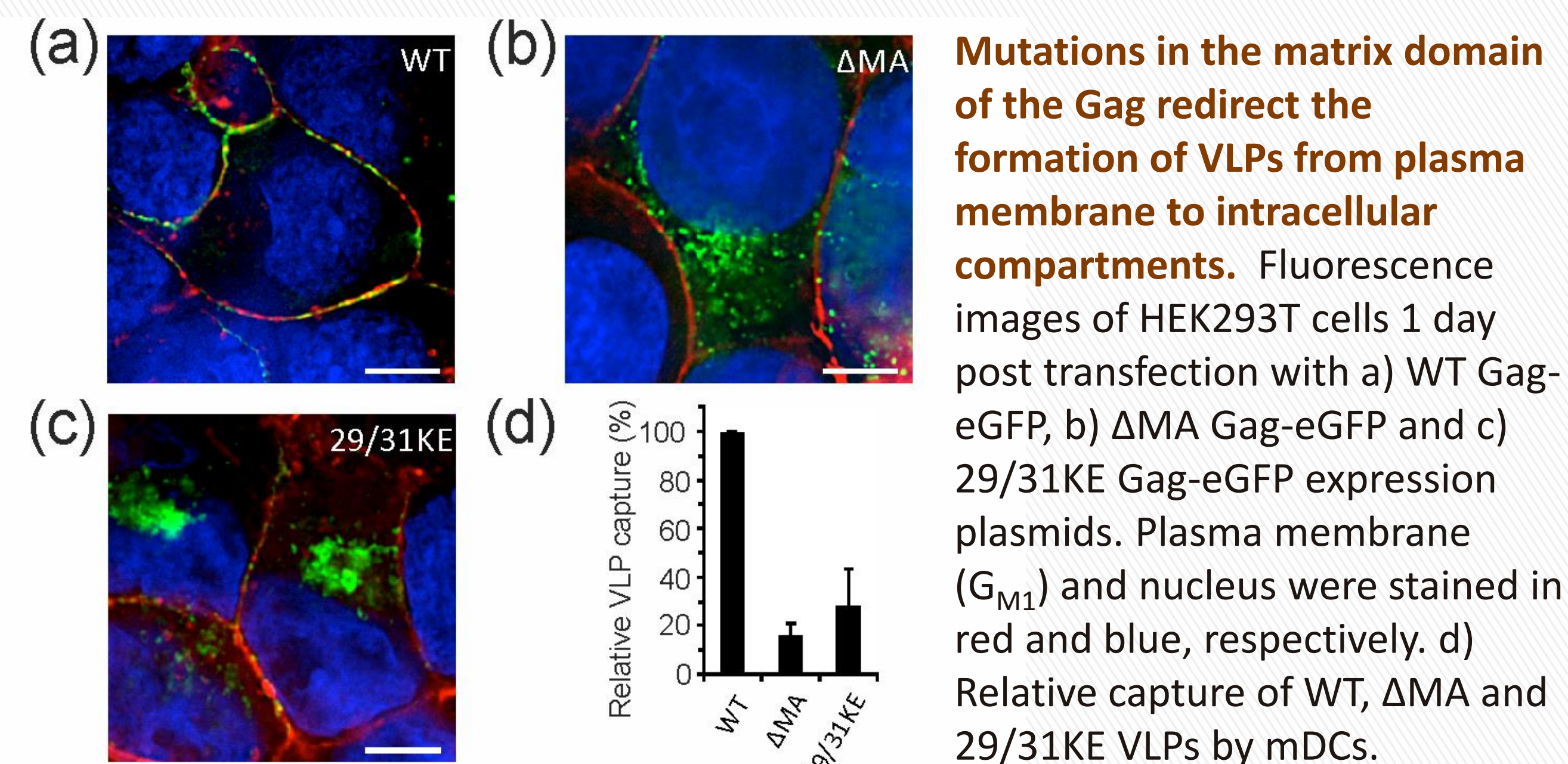
## INTRODUCTION

- Enveloped viruses are a class of viruses that are enveloped in a lipid bilayer.
- It is becoming increasingly clear that the host-derived membrane of an enveloped virus contributes more to the infection mechanism than simply forming a molecular scaffold for the presentation of virus encoded membrane glycoproteins.
- Phosphatidylserine (PS), for instance, has been shown to facilitate apoptotic mimicry and enhance glycoprotein-independent uptake of Vaccinia, Ebola and Dengue viruses.
- Glycosphingolipids (GSLs) are another important class of lipids that mediate interactions between virus particles and host cells.
- Lipids contribute significantly to mediating virus – host-cell interactions, and this realization has motivated great interest in a quantitative analysis of viral lipidome to identify potential diagnostic and therapeutic targets.



The structure of an enveloped virus particle

## METHODS and RESULTS



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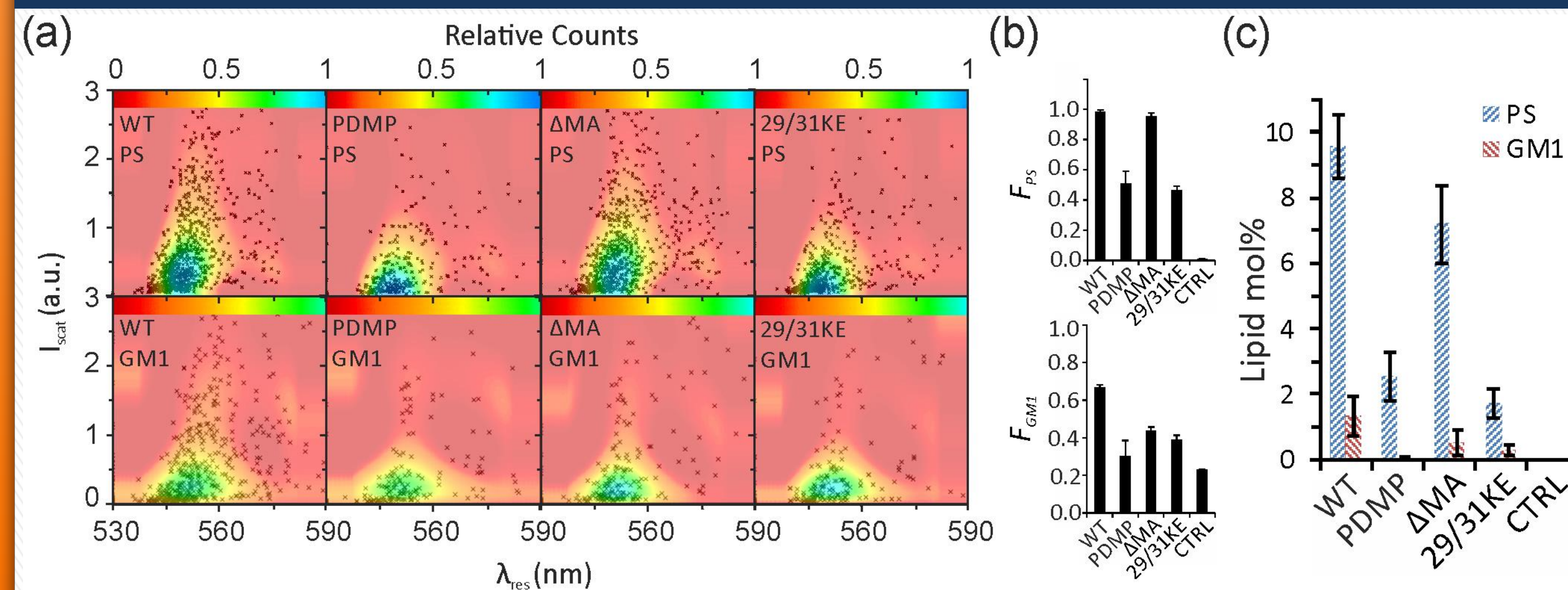
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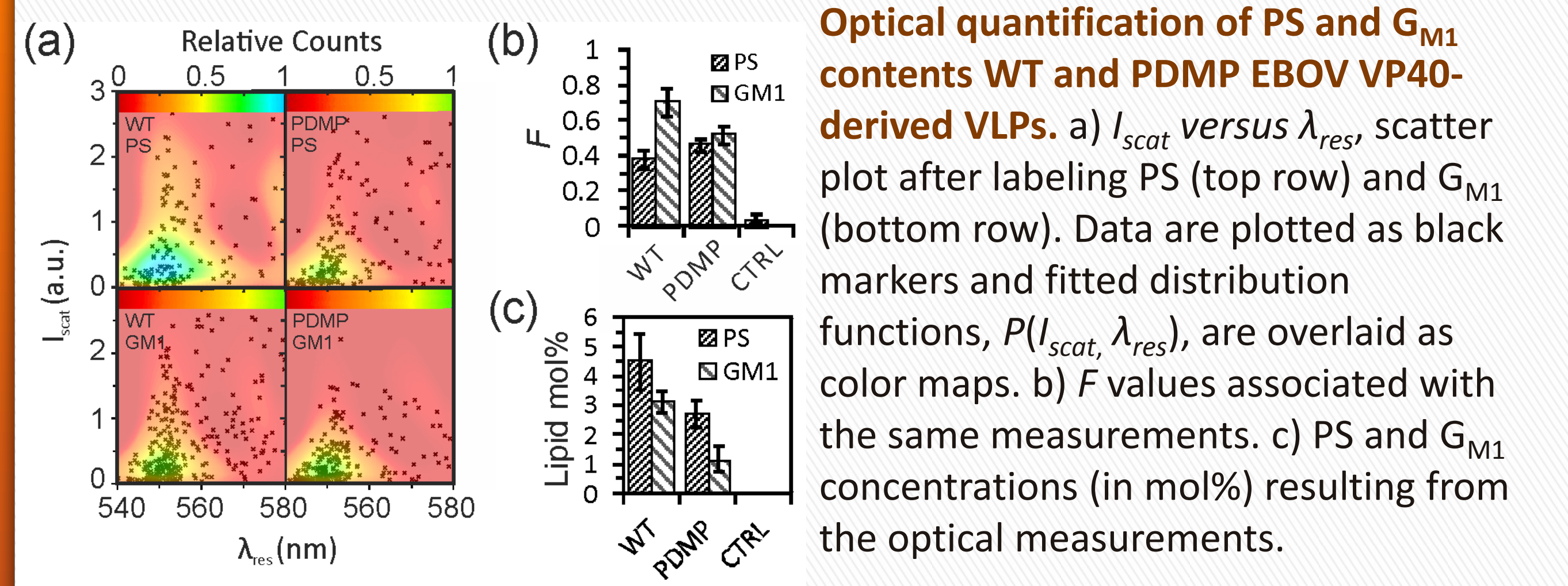


## RESULTS CONTINUED



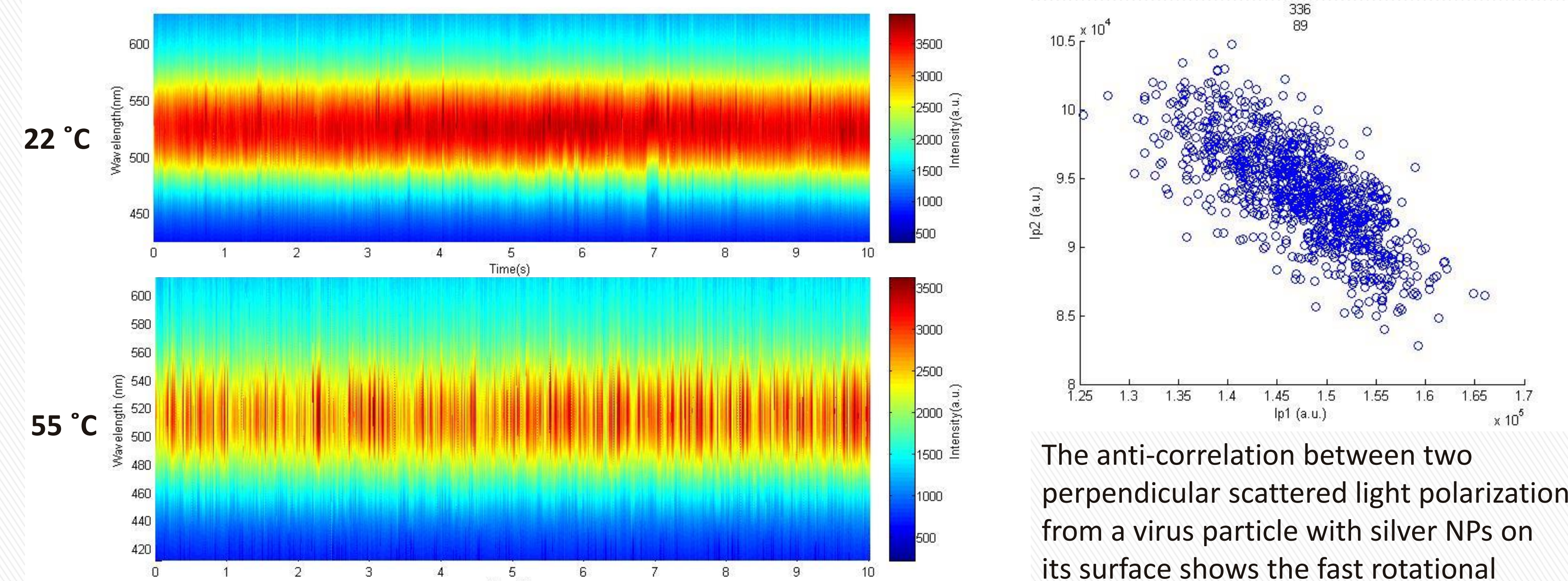
### Optical quantification of PS and $G_{M1}$ contents in 4 different HIV-1 VLPs.

a)  $I_{scat}$  versus  $\lambda_{res}$  scatter plot after labeling PS (top row) and  $G_{M1}$  (bottom row) in (from left to right) WT, PDMP,  $\Delta MA$  and 29/31KE VLPs. Each plot contains the data of 500-1500 VLPs obtained in 3 or more independent experiments with one batch of VLPs. Data are plotted as black markers and fitted distribution functions,  $P(I_{scat}, \lambda_{res})$ , are overlaid as color maps. b)  $F$  values for lipid-VLP combinations shown in (a) and a WT VLP negative control that lacked any AnxV or CTB treatment. c) PS and  $G_{M1}$  content determined with Eq. 1 and 2 from the data in (a) and (b).



### Optical quantification of PS and $G_{M1}$ contents WT and PDMP EBOV VP40-derived VLPs.

a)  $I_{scat}$  versus  $\lambda_{res}$  scatter plot after labeling PS (top row) and  $G_{M1}$  (bottom row). Data are plotted as black markers and fitted distribution functions,  $P(I_{scat}, \lambda_{res})$ , are overlaid as color maps. b)  $F$  values associated with the same measurements. c) PS and  $G_{M1}$  concentrations (in mol%) resulting from the optical measurements.



The translational motions of the silver NPs on the surface of a virus particle and therefore plasmon coupling fluctuations is temperature dependent. The anti-correlation between two perpendicular scattered light polarization from a virus particle with silver NPs on its surface shows the fast rotational motions of the NPs on the virus surface.

## CONCLUSIONS

In conclusion, we have introduced a new optical assay for measuring the lipid contents in VLP and viral envelope membranes based on the spectral analysis of gold nano-label binding and plasmon coupling. In addition, based on the same lipid targeting strategy, we are able to track translational and rotational lipid motions in the membrane of virus particles through time-resolved scattering spectroscopy and scattering polarization fluctuation microscopy of silver NP labels. We believe these techniques can contribute significantly to understanding the underlying mechanisms of virus-cell interactions.

## REFERENCES

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