

2013



Emerging Researchers Symposium

Optical delivery of ARV drugs into HIV-1 permissive cells

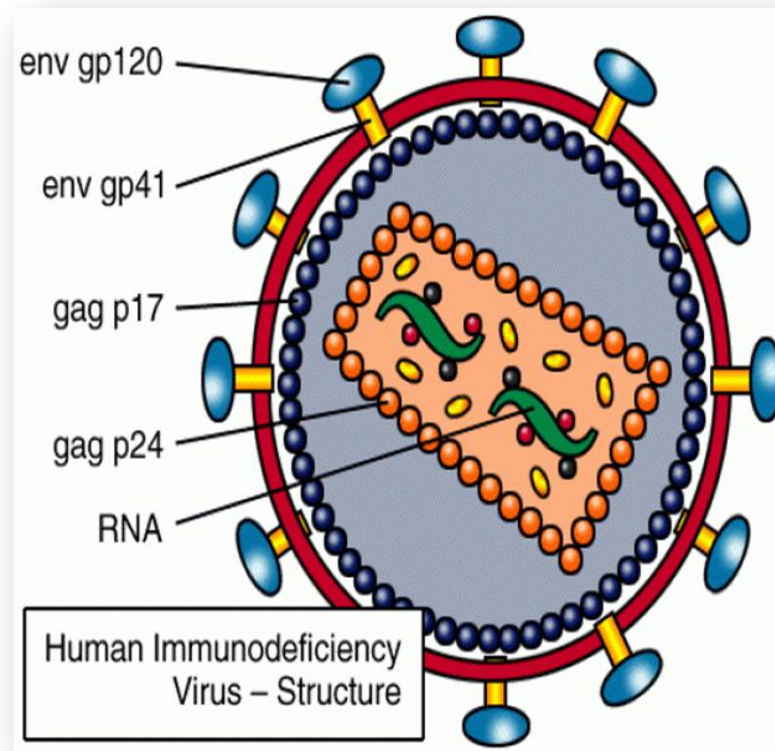
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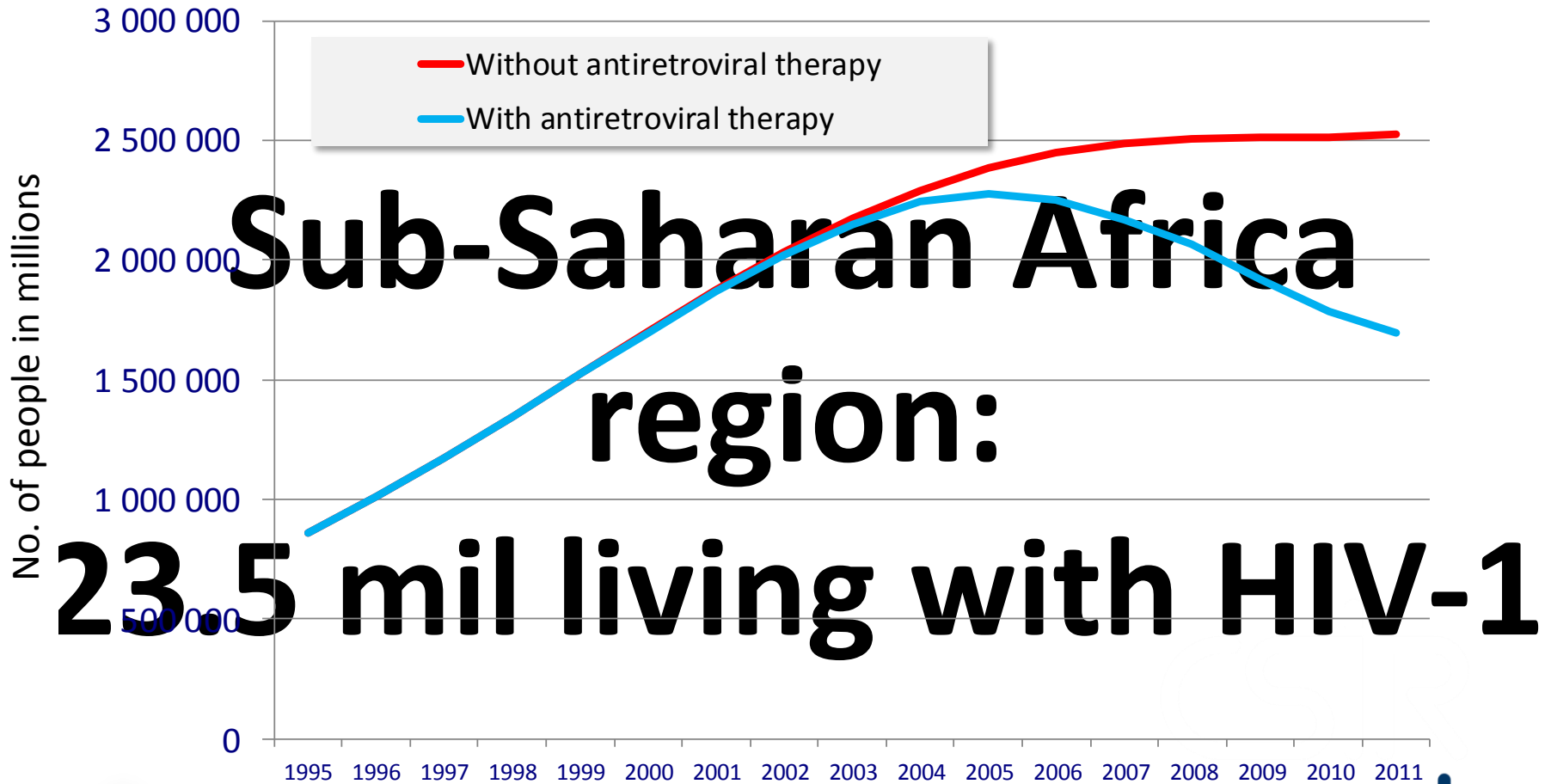
What is HIV-1?



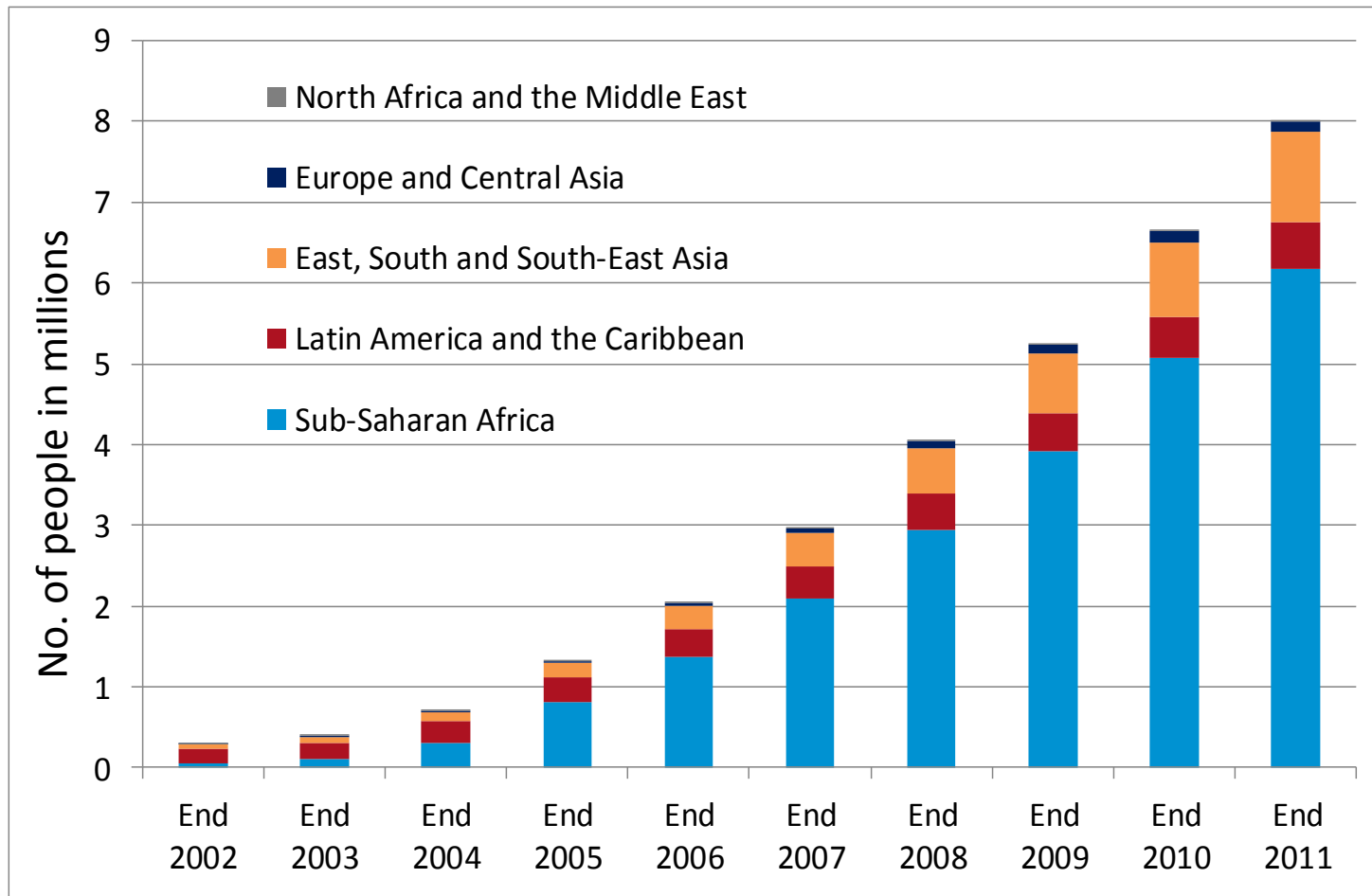
1996 - “Ongoing declines in AIDS incidence and deaths in developed nations, primarily due to widespread use of HAART”

(Roger J Pomerantz and David L Horn)

AIDS-related deaths, 1995–2011



People receiving HAART, 2002–2011



Downfalls of HAART

Treatment is lifelong

- Long-term toxicities and side effects

Emergence of drug resistance

Poor targeting ability to latent sites

- Lymphatic system, macrophages, CNS and lungs

Solution=Drug delivery system: Photo-translocation

Deliver anti-HIV-1 drugs using femtosecond (fs) laser pulses

- Optical delivery of therapeutic drugs has not yet been demonstrated in literature

Previous studies where method was used

- DNA plasmids – pGFP (Tirlapur & Konig, 2002)
- Viability dyes – Trypan blue (Stevenson, D *et al*, 2006)
- Transcription factors
- Applicability to stem cell differentiation (Mthunzi, P *et al*, 2010)

Objectives

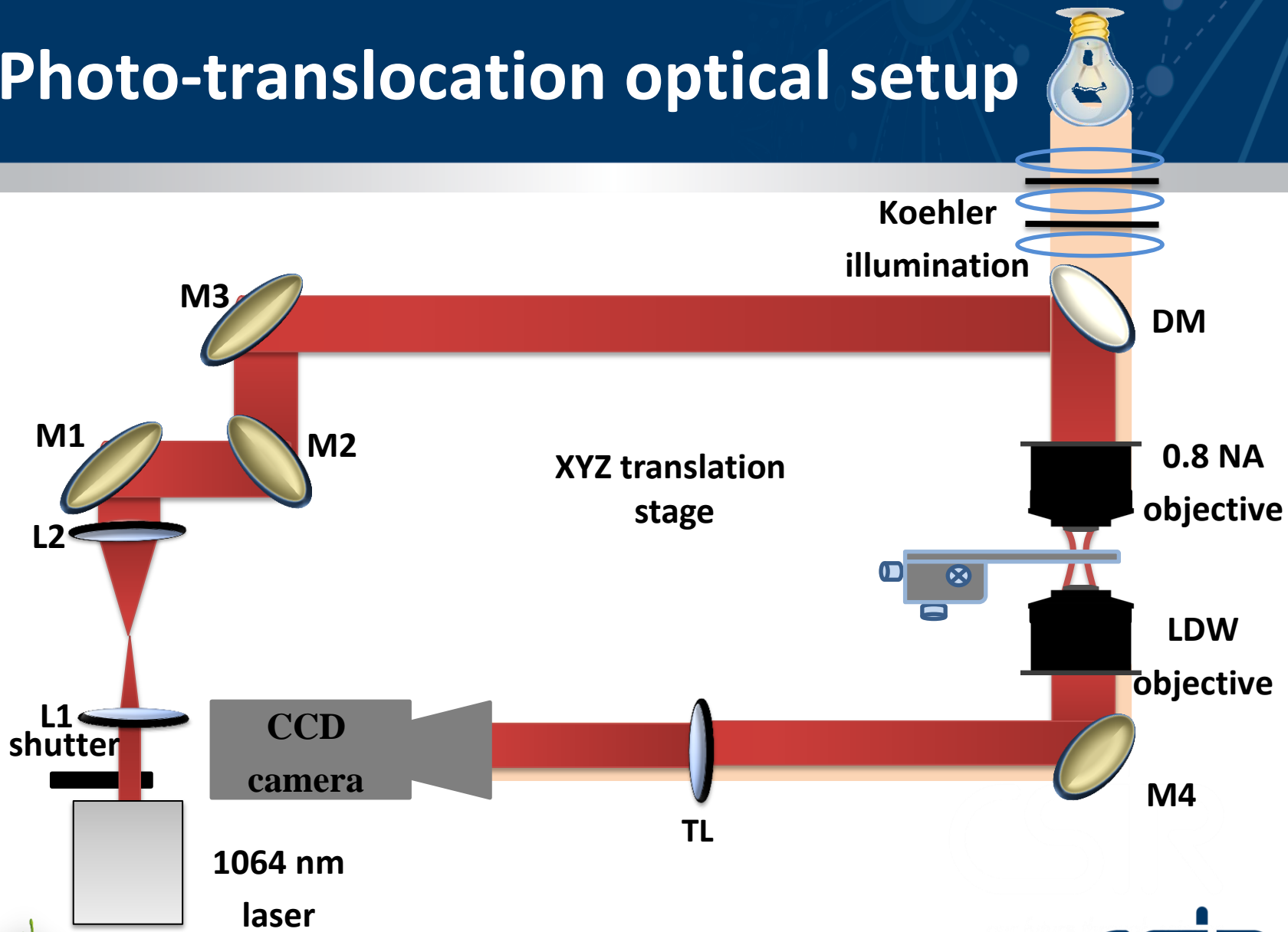
Assemble and characterise an optical translocation setup

Optically deliver tenofovir via fs laser pulses into TZM-bl cells

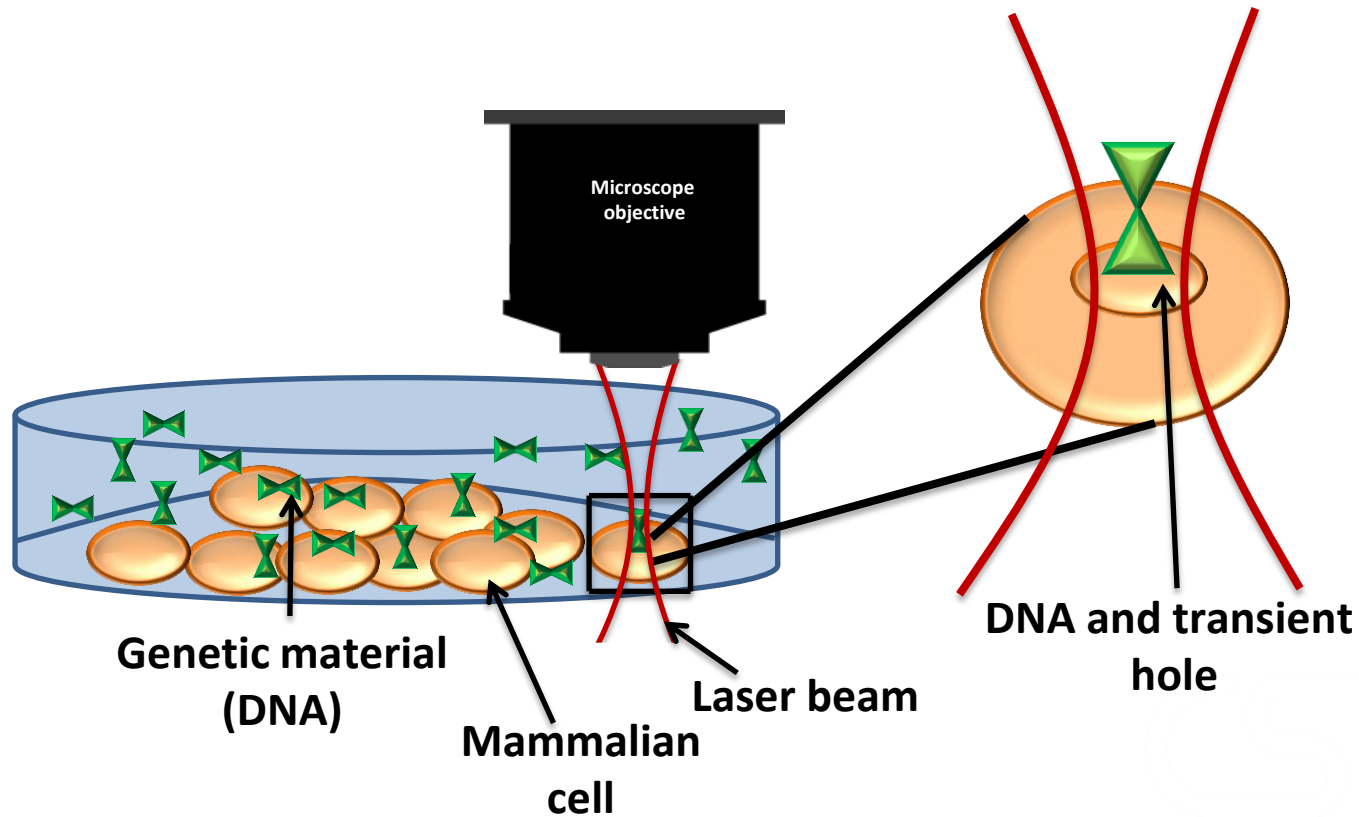
Miniaturise current drug inhibition assay protocol *in vitro*:

- Drug – cell exposure time
- Cell concentration
- Reagents used

Photo-translocation optical setup



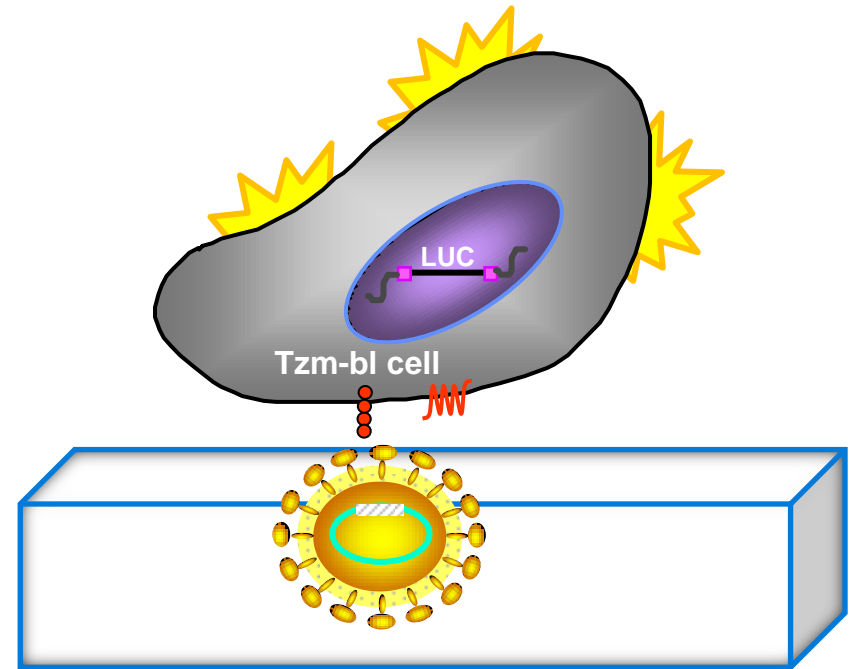
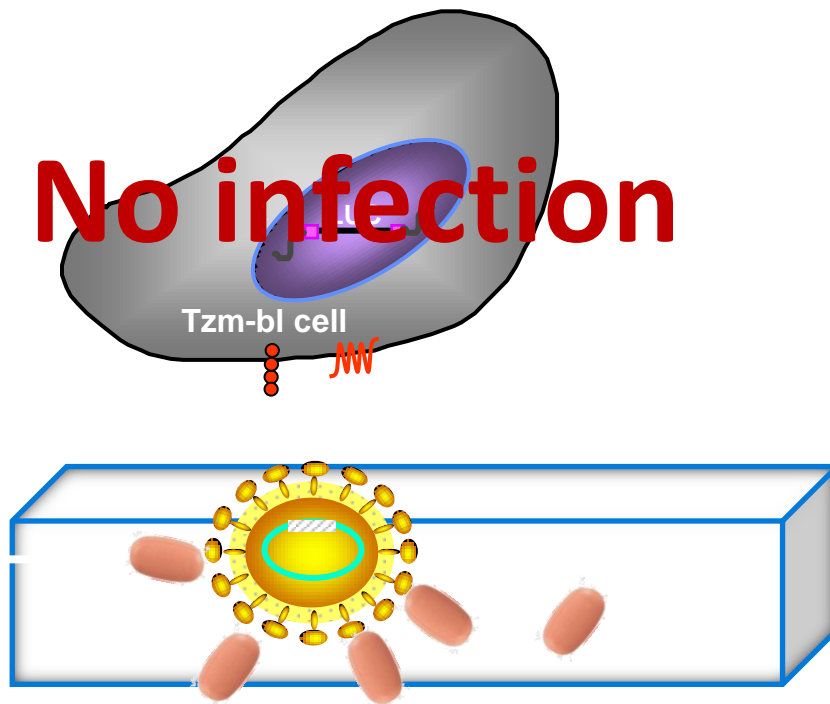
Selective and non-invasive nature of photo-translocation



HIV-1 inhibition assay



No infection



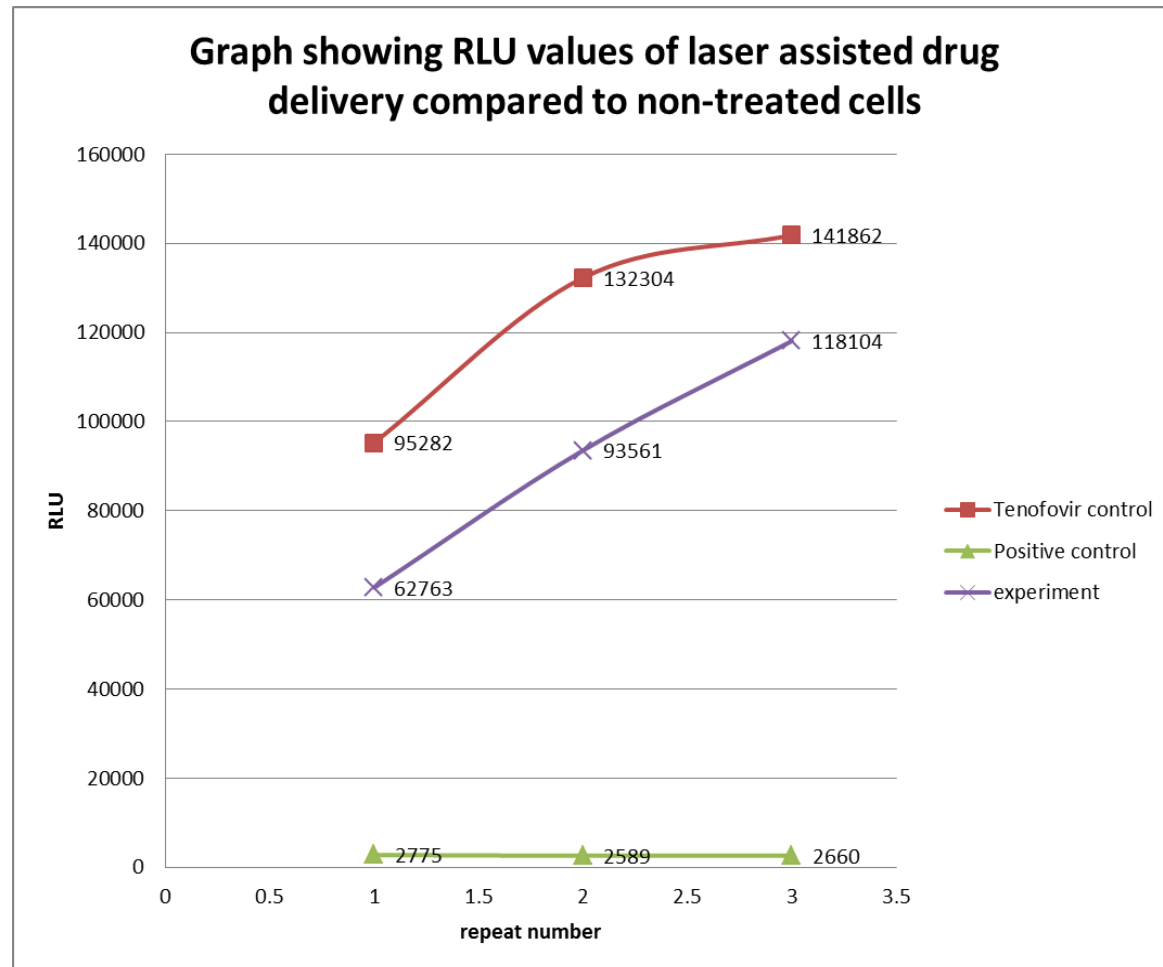
Laser-assisted drug delivery enhances HIV-1 inhibition

Table showing obtained RLU values

TC	PC	Experimen
95282	2775	62763
132304	2589	93561
141862	2660	118104

- TC – tenofovir control
- PC – positive control
- Experiment: Laser-treated cells

Graph showing RLU values of laser assisted drug delivery compared to non-treated cells

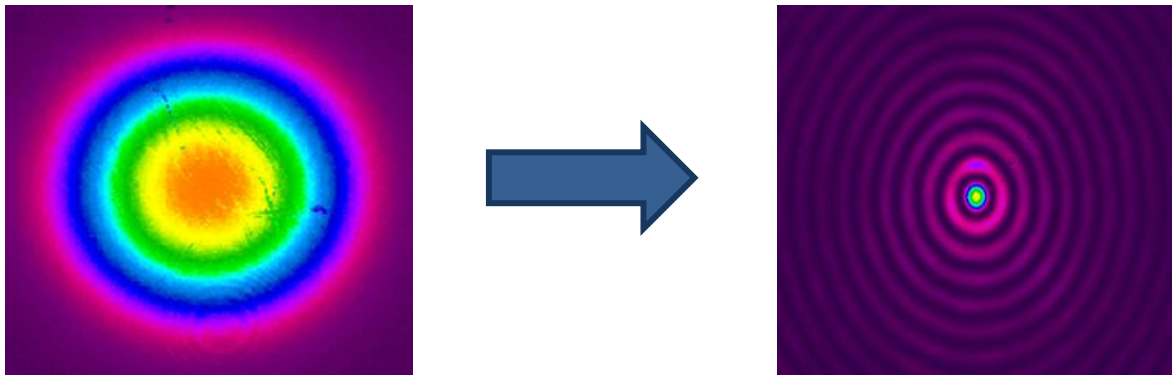


Conclusions

- Successful assembly of photo-translocation setup
- Successful photo-translocation of tenofovir into TZM-bl cells
 - Increased drug uptake
 - Reduction of drug – cell exposure time
 - 48 hours to 30 minutes
- Decreased cell concentration
 - 1×10^4 to 5×10^3
- Decreased ELISA plate well usage
 - 96 wells to 12 wells
 - Decreased reagents

Future perspectives

- Decrease diameter of sample chamber
- Further decrease in cell numbers
- Change laser beam shape



- Compare photo-translocation efficiency
- Drug delivery into multiple number of cells by incorporating SLM
- Cytotoxicity and cell viability testing

Acknowledgements

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Thank you

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