In-vitro photo-translocation of antiretroviral drug delivery into TZMbl cells

Rudzani Malabi¹,², Sello Manoto ¹, Saturnin Ombinda-Lemboumba ¹, Malik Maaza² and Patience Mthunzi-Kufa ¹,²

¹Council for Scientific and Industrial Research (CSIR), National Laser Centre, P.O. Box 395 Pretoria, 0001, South Africa
²College Of Science, Engineering and Technology, Department of Physics, University Of South Africa, Science Campus Florida, South Africa

SPIE Photonics West 2017 Conference
Outline

- Introduction
- Problem statement
- Objectives
- Methodology
- Results
- Conclusion
- Acknowledgements
Introduction

• Globally, it is estimated that more than 35.3 million people are living with HIV infection or AIDS, ~70% HIV infection in Sub-Saharan Africa.

• Introduction of highly active antiretroviral therapy (HAART) led to the decline in HIV-1 mortality rate and decrease in the burden of disease.

• HIV remains a chronic and life-long infection because the virus remains hidden in certain physiological reservoirs.

(www.unaids.org.)
Problem statement

- **Poor bioavailability**
  - Oral route

- **Drug toxicity**
  - Side-effects
  - Drug combinations

- **Drug resistance**
  - Monotherapy
  - Genetic mutations

- **Viral reservoirs**
  - Cellular reservoirs (macrophages, microglia, astrocytes)
  - Anatomical reservoirs (Lymphoid organs, Genitourinary tract, central nervous system)

- **Shortcomings**

  - ◆ *Stumbling block for the complete eradication of HIV infection.*
Drug delivery systems

HIV researches done

• Pre-exposure prophylaxis
• Targeting efficacious drug concentrations

Laser aided drug delivery systems

• Highly efficient
• Non-invasive
• Sterile and non-toxic treatment to cells

Femtosecond lasers

• powerful laser photo translocation technique
• using ultrafast pulses with high peak powers
• to precisely disrupt the cell membrane in order to allow exogenous matter into live mammalian cells.

(Nelson et al., 2015)

(Mohanty 2012)
Objectives of the study

• To use femtosecond laser pulses in a photo-translocation system to deliver ARVs into HIV infected TZMbl cells.

• Investigate the influence of ARVs and laser on cellular processes using different molecular assays.
Methodology

Culturing of cells and preparing pseudoviruses

Sample preparation
Infected cells, Drugs (Nevirapine, Tenofovir, efavirenz)

Translocation of ARVs into TZMbL cells

Wavelength: 800 nm
Optimum power: 65 mW
Exposure time: 10 ms

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Cell viability (ATP assay)

Cell cytotoxicity (LDH assay)

HIV Inhibition (Luciferase Assay)
Results

Cell viability (ATP) assay
Cytotoxicity (LDH) assay

![Graph showing LDH absorbance at 490 nm for different conditions: cells only, Virus Control, PC 48 hours, DC 30 mins, and Experiment. The graph compares absorbance values for Nevirapine, Efavirenz, Tenofovir, cells only, and Virus control.]
HIV Inhibition (Luciferase) assay
Conclusion

- This study successfully demonstrated the use of femtosecond (fs) laser pulses in promoting targeted optical drug delivery of ARVs into TZMbl cells.

- Laser assisted drug delivery system was effective in reducing HIV viral infectivity

- Efavirenz showed more efficacy as compared to the other drugs.

- Future work will involve the use of coupling optical drug delivery systems with endoscope-like optical fibre for in-vivo applications.
Acknowledgements
Thank you