



HKU Discovers a Novel AIDS DNA Vaccine

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Updated Pandemic of HIV/AIDS by 2011

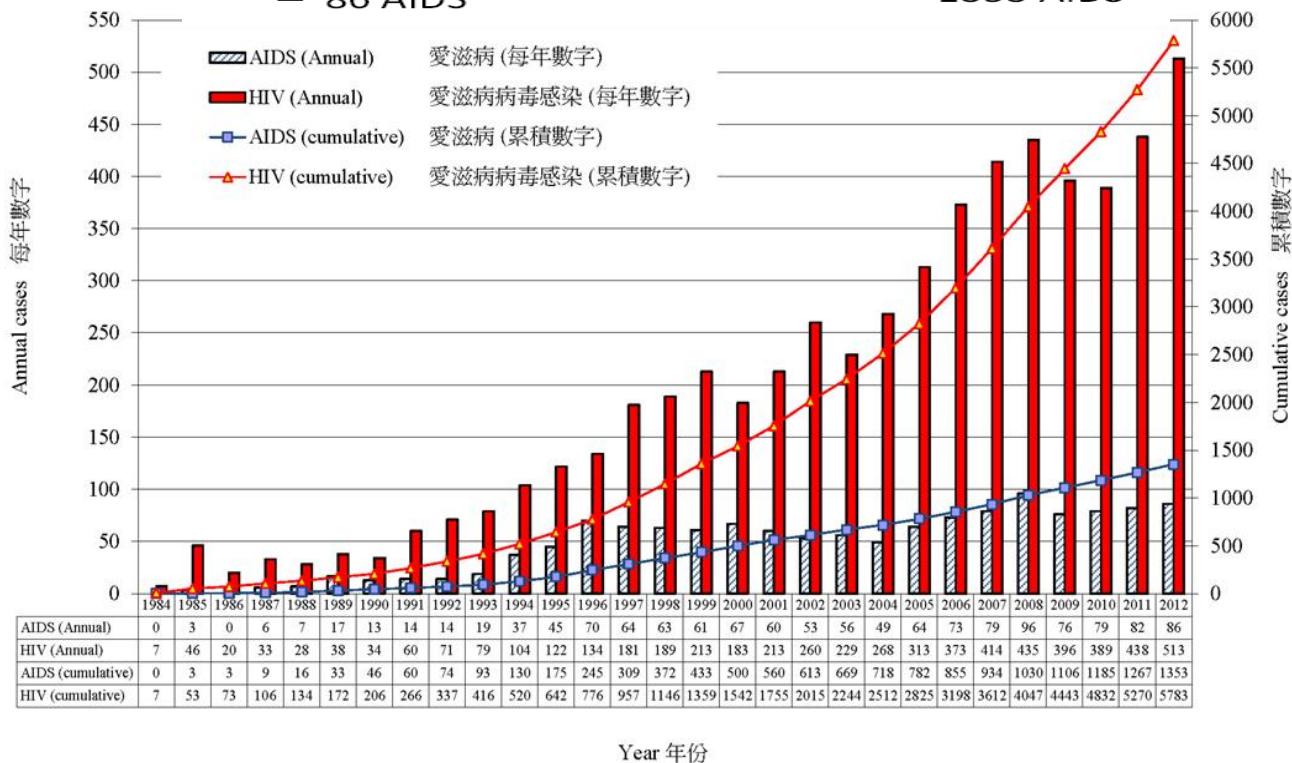
	2001	2011
Adults and children living with HIV	29.4 million [27.2 million – 32.1 million]	34 million [31.4 million – 35.9 million]
Adults and children newly infected with HIV	3.2 million [2.9 million – 3.4 million]	2.5 million [2.2 million – 2.8 million]
% Adult prevalence	0.8 [0.7 – 0.9]	0.8 [0.7 – 0.8]
Adult and child deaths due to AIDS	1.9 million [1.7 million – 2.2 million]	1.7 million [1.5 million – 1.9 million]
Young people (15-24) prevalence (%)	<i>Male</i>	0.4 [0.3 – 0.5]
	<i>Female</i>	0.7 [0.6 – 0.9]

- An estimated **5 million** people in **Asia** were living with HIV up till now.



HIV/AIDS epidemic in Hong Kong

- 2012
 - 513 HIV (record-high)
 - 86 AIDS
- Cumulatively
 - 5783 HIV
 - 1353 AIDS



- 97.7% of HIV / AIDS cases were due to sexual transmission
- 4% prevalent rate was found among MSM (Men who have sex with men) in 2012.
- With the increasing number of HIV / AIDS cases, an effective vaccine is necessary for AIDS prevention and immunotherapy.



Current challenges against HIV/AIDS

- ***Lack of a Therapeutic Cure:***
- **HAART** (Highly active antiretroviral therapy, or called **cocktail** therapy) suppresses patients' HIV load, extends patients' life and reduces secondary HIV spread.
- Yet, issues of **drug toxicity, drug resistance and failure of eliminating HIV** remain unsolved.



- ***Lack of an Effective Vaccine:***
- Current vaccines are rather weak and **poorly immunogenic**.

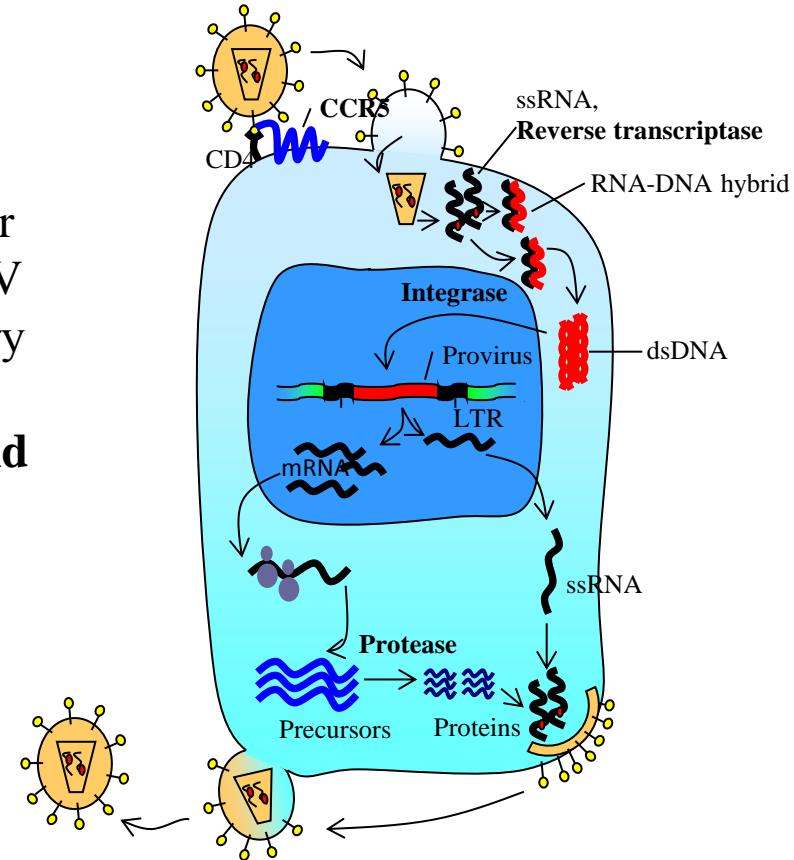


Illustration of HIV life cycle and drug target



Role of CD8⁺ T cells in controlling HIV infection

- CD8⁺ T cells belong to a group of white blood cells known as cytotoxic lymphocytes or killer T cells.
- They play a central role in cell-mediated immunity by killing HIV-infected cells and cancer cells.
- They are well-known for their critical role of suppressing HIV replication and eliminating latent reservoir in the body.



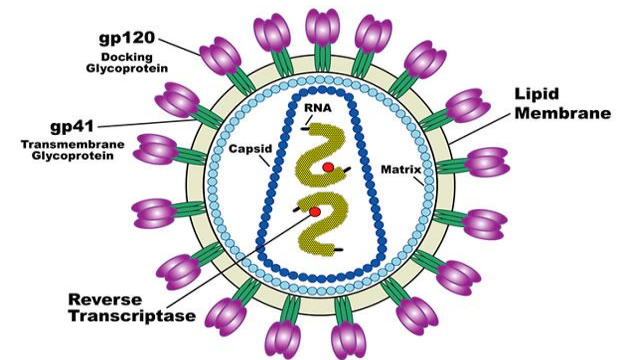
Unknown to Scientists

How to induce a **high frequency** of protective HIV-specific CD8⁺ T cells for both preventive vaccine and therapeutic cure?



HKU's Discovery

- 1) We have discovered a **novel AIDS DNA vaccine** that induces a high frequency of broadly reactive, poly-functional and protective CD8⁺ T cells against HIV.
- 2) This new vaccine works by **targeting HIV antigen to dendritic cells via the PD1/PDL binding**, which results in the distinct and robust CD8⁺ T cell immunity.



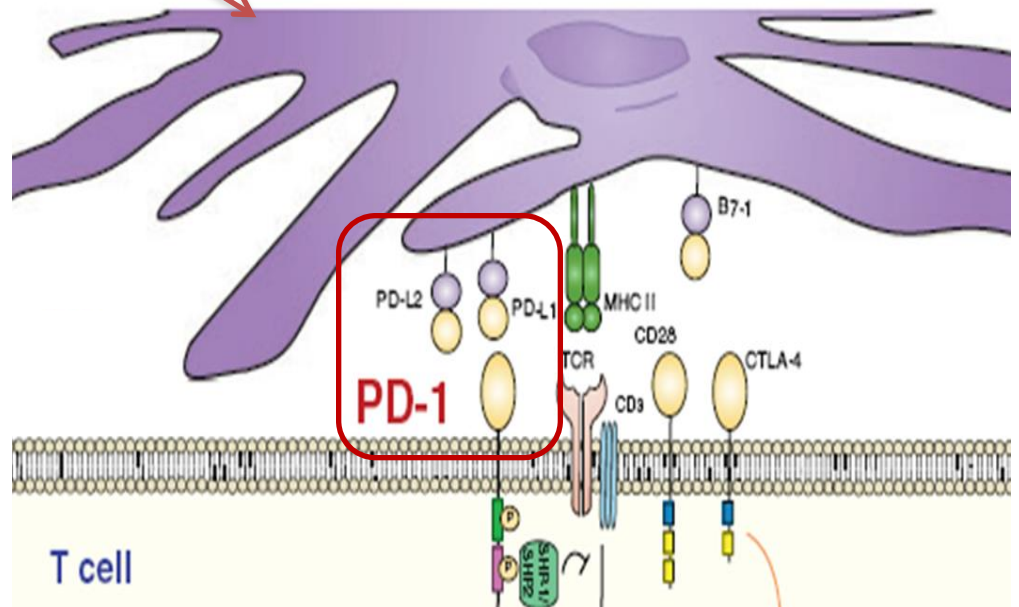
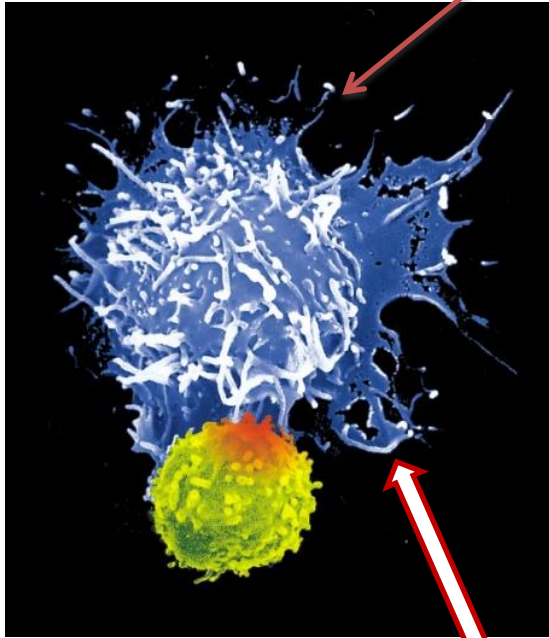
Structure of HIV



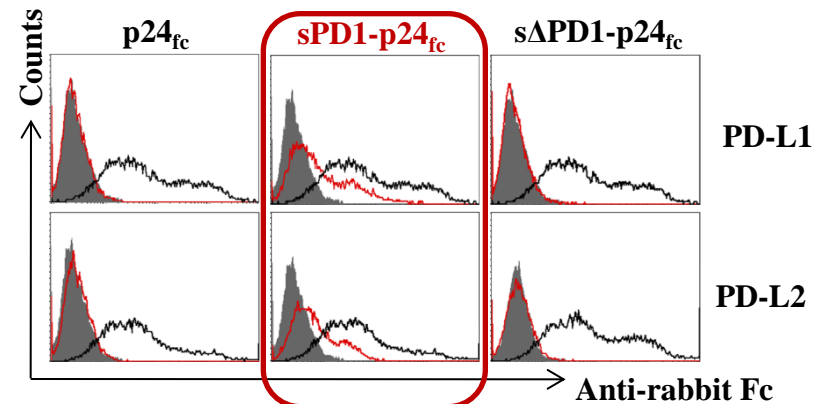
Novel AIDS DNA Vaccine Design

- PD1-guided delivery of p24 to dendritic cell

Dendritic Cell



More effective to induce robust CD8⁺ T cells.





Experimental Schedule

Immunization



0 (weeks)



3



6

Antibody & T-cell responses



8

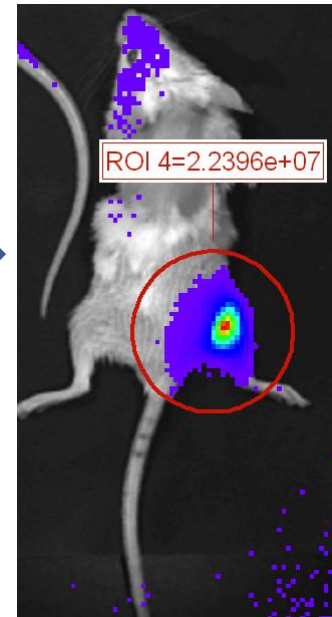
Memory Response



30



TERESA-Gene Delivery Device
for in vivo electroporation (EP)

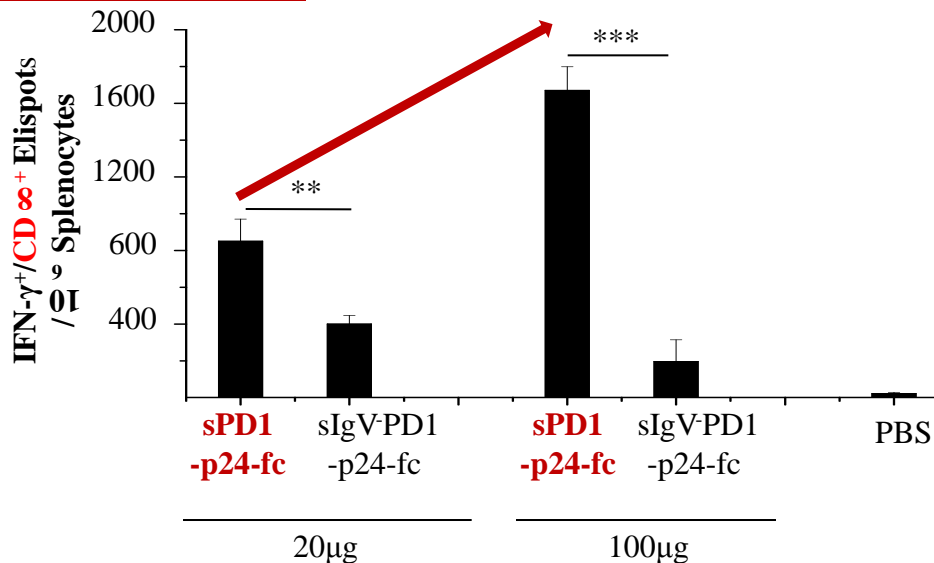


EP efficiently delivers DNA Vaccine

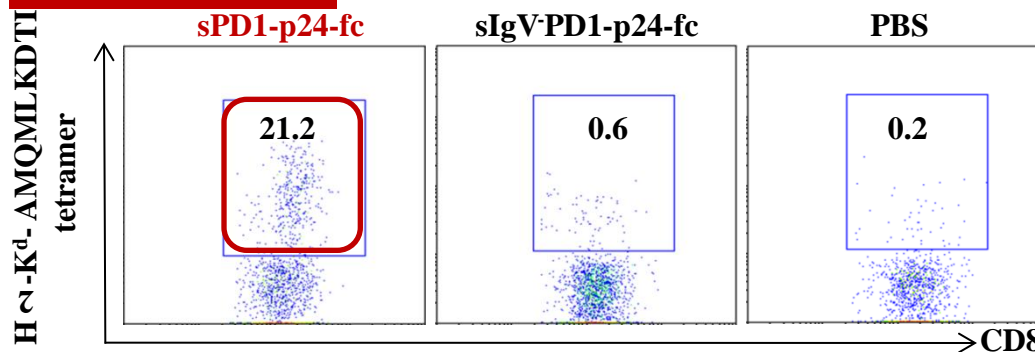


Novel AIDS DNA Vaccine Greatly Intensified CD8⁺ T cells in a Dose-Dependent Way

ELIspot Assay



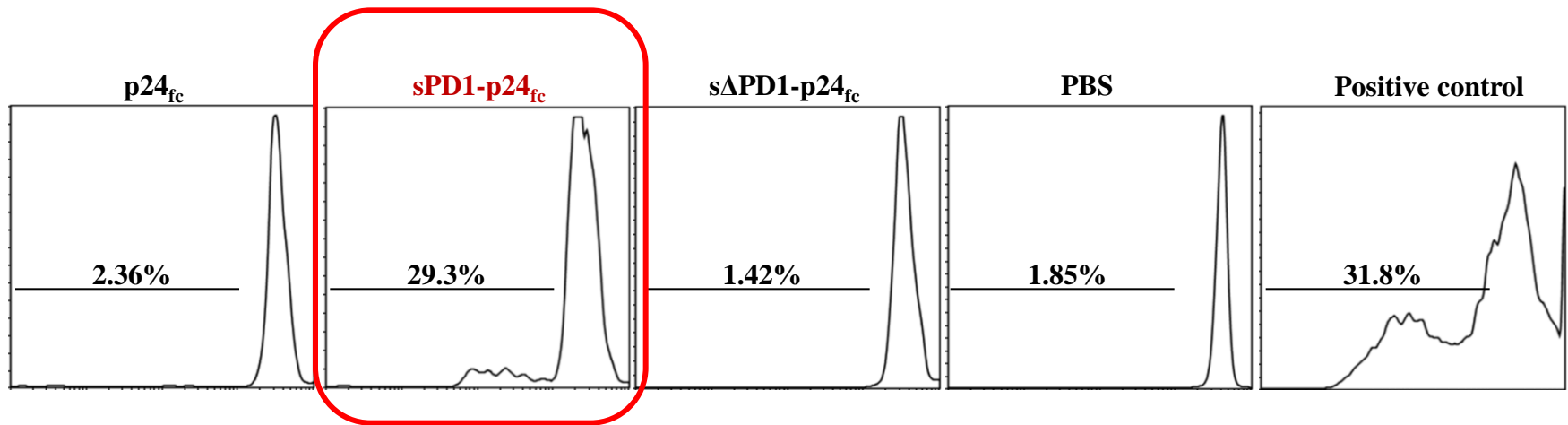
Tetramer Assay





Long Term Memory CD8⁺ T cells Response

30 weeks post-vaccination

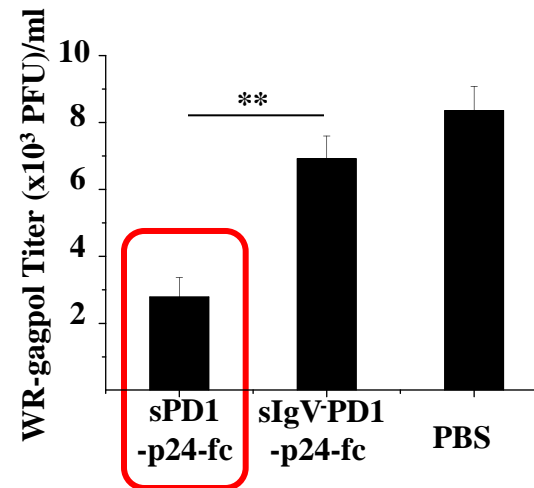
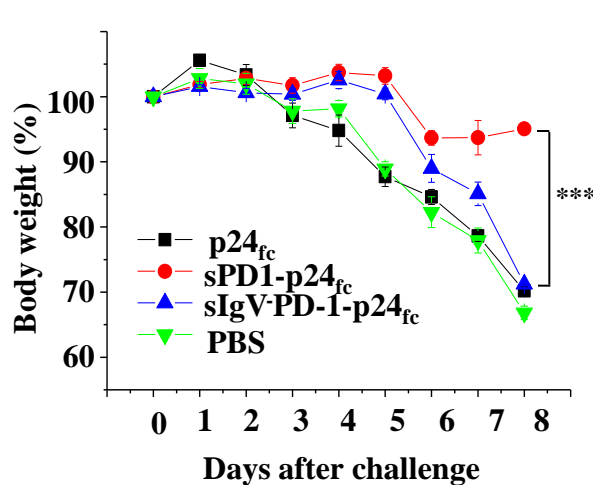


The novel AIDS DNA Vaccine induces long lasting anti-HIV memory CD8⁺ T cells as compared with control vaccines.



Significant Protection against Lethal Viral Challenges in Mice

Virulent vaccinia WR-gag Challenge

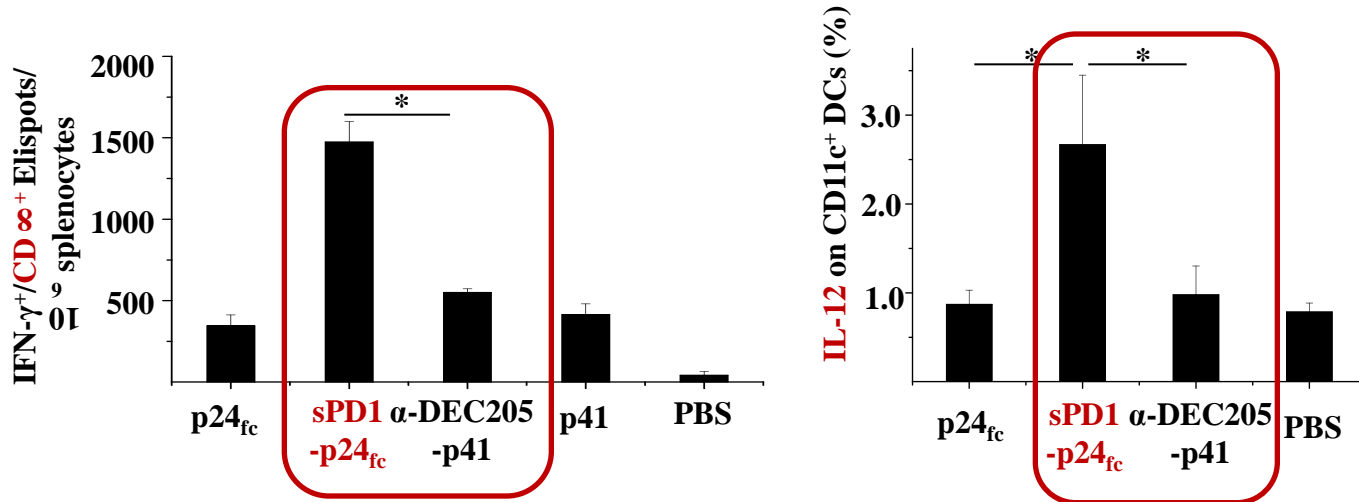


- (Left) The line with circle illustrates that the new vaccine significantly increases the body weight of mice as compared with control vaccines

- (Right) The number of lethal virus has remarkably decreased after vaccination.



Direct Comparison of Two Methods of Antigen-Targeting to DCs



Early DNA vaccine (α -DEC205-p41)

- a vaccine published in JCI 2008 by Prof R. Steinman (2011 Nobel Prize in Medicine).
- DC-targeting: through DEC205

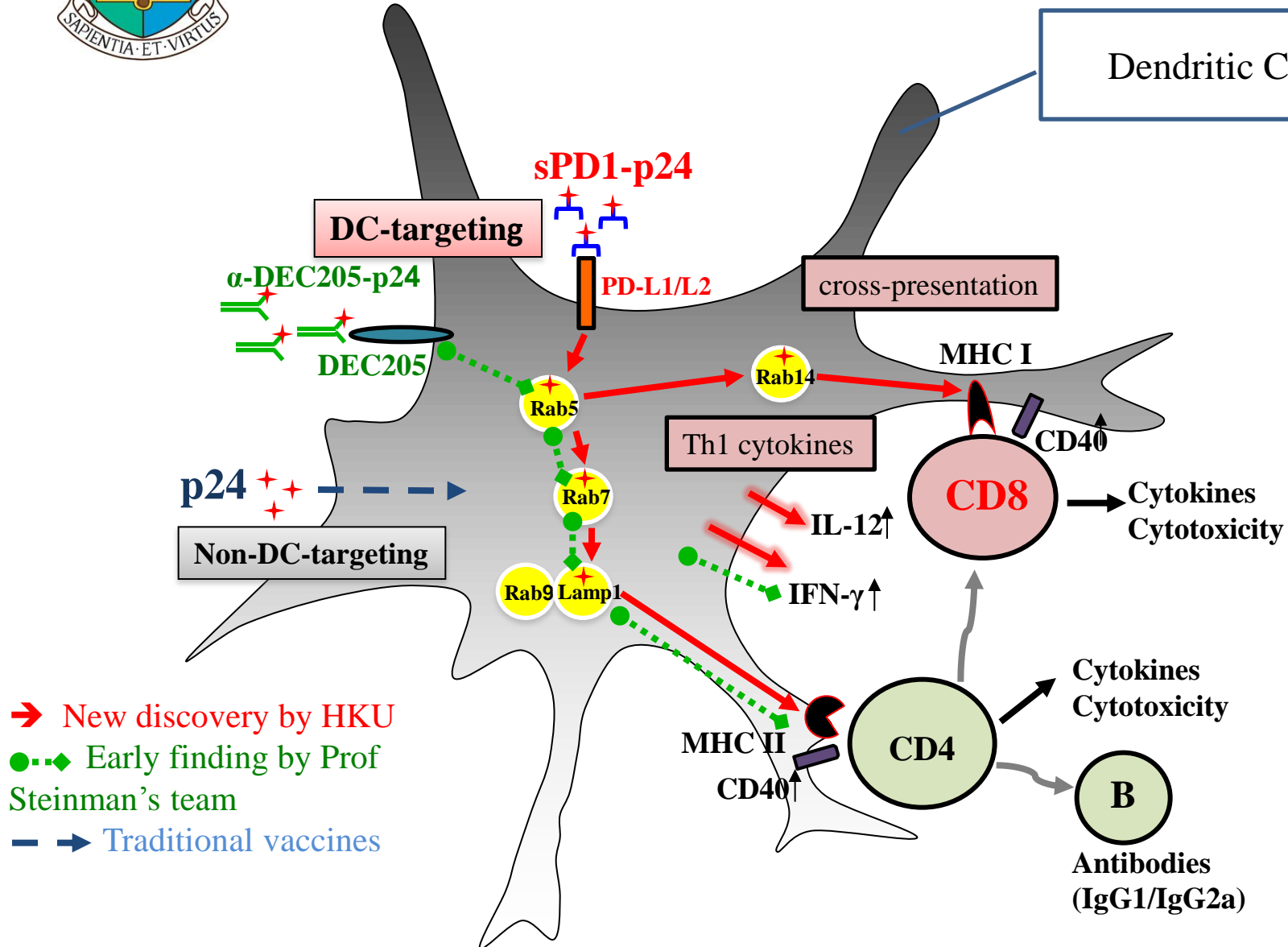
New AIDS DNA vaccine (sPD1-p24fc)

- New discovery by HKU
- DC-targeting: through PD1/PD-L interaction to induce a high frequency of CD8 $^+$ T cells (left) and IL-12 releasing DCs (right).

- New vaccine is more effective in inducing higher frequency of CD8 $^+$ T cells



Mechanism of Novel AIDS DNA vaccine





Importance of the findings

- Our findings shed light on how to induce a high frequency of protective HIV-specific CD8⁺ T cells - important for an effective vaccine to either prevent or cure AIDS.
- The study obtained the international patent, implying that Hong Kong researchers have capability to invent novel AIDS vaccine
- Our results provide new insights on how immune system works in regulating CD8⁺ T cell responses.
- Besides against HIV/AIDS, our new technique can be used for making vaccines for prevention and immunotherapy against other diseases (e.g. TB, Malaria and Cancer).

Questions and Answers

AIDS vaccine is
the ultimate
solution

