



香港大學

THE UNIVERSITY OF HONG KONG



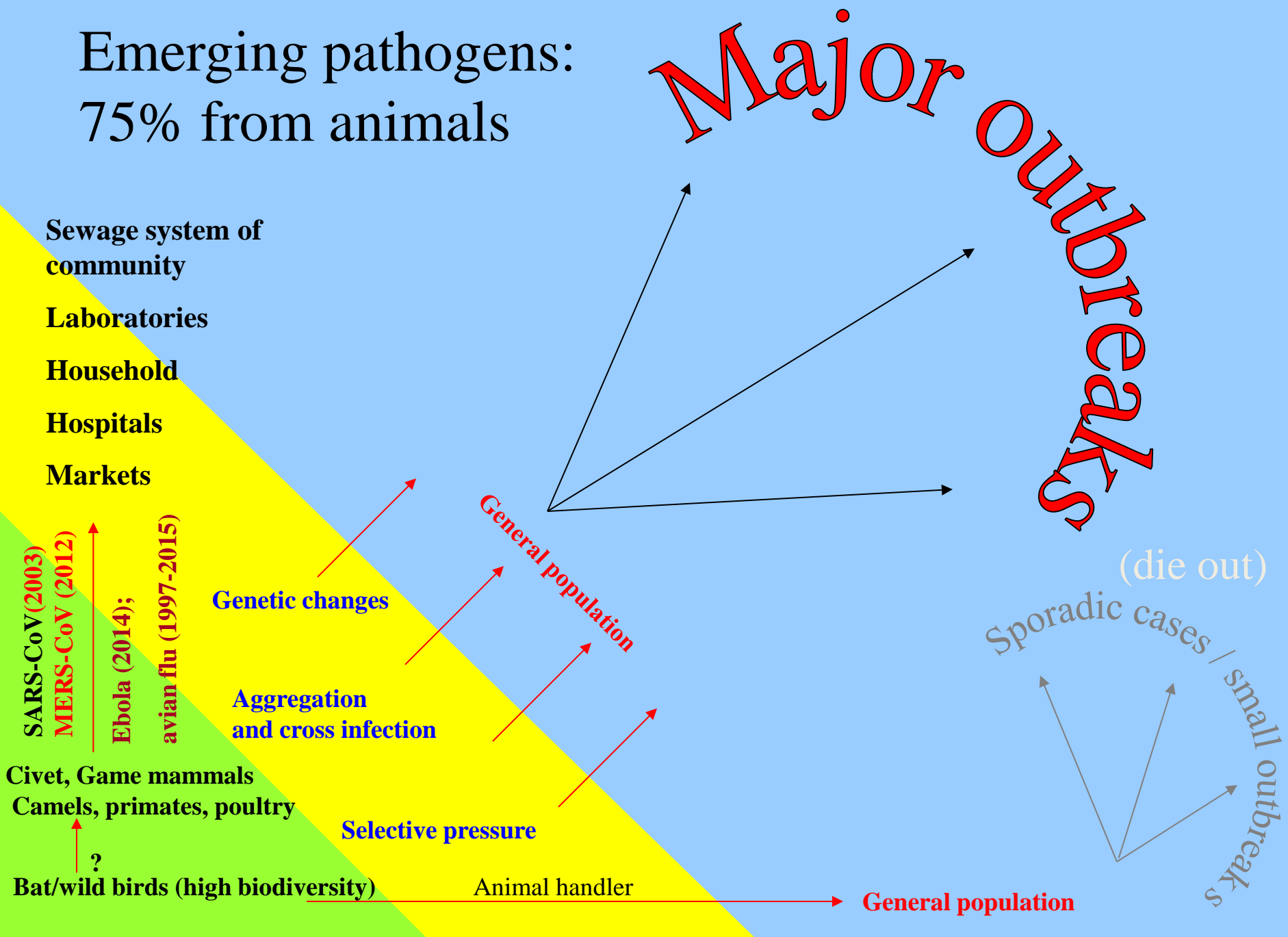
THE HONG KONG
POLYTECHNIC UNIVERSITY
香港理工大學

**HKU and Poly U
announce the establishment of
Respiratory Virus Research Foundation**

(supporting HKU research published in
Lancet infectious diseases)

November 12, 2015

Emerging pathogens: 75% from animals



Control of emerging infectious diseases depend on the availability of

1. Rapid, broad and accurate diagnostic test kits
2. Effective & safe antimicrobial agents
3. Rapidly effective & safe vaccines
4. Personal & environmental protective equipment;

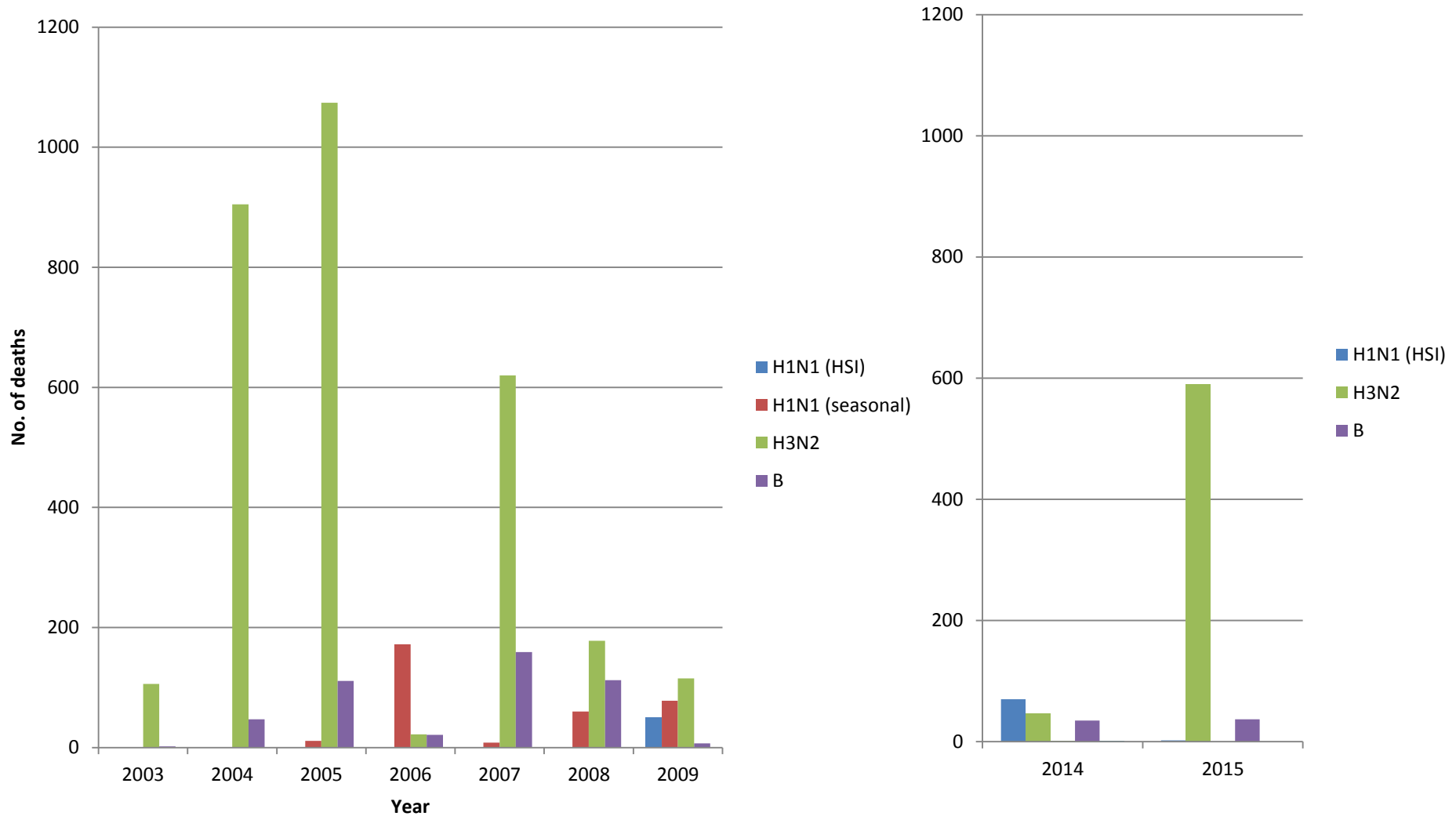
Good **basic research** output (**HKU**) BUT lacks support & coordination from (**donors, Innovation & Technology Bureau & DH/CHP/HA**) so as to develop our research findings into **industrial manufacturing (PolyU)!!!**

Establishment of the Respiratory Virus Research Foundation

A total of HK\$ 24 million donated by:

- **D. H. Chen Foundation (Nan Fung Group)**
- **Madam Yat-Wah Fong & Shaw Foundation**
- **Mr Pony Ma**
- **The University of Hong Kong**
- **The Hong Kong Polytechnic University**
- **Macau Henry Fok Foundation**
- **Stanley Ho Medical Foundation**
- **Moonchu Foundation**

No. of deaths from influenza in Hong Kong



**Wrong prediction of influenza vaccine strain due to antigenic drift!
What HKU can do?**

Topical Imiquimod

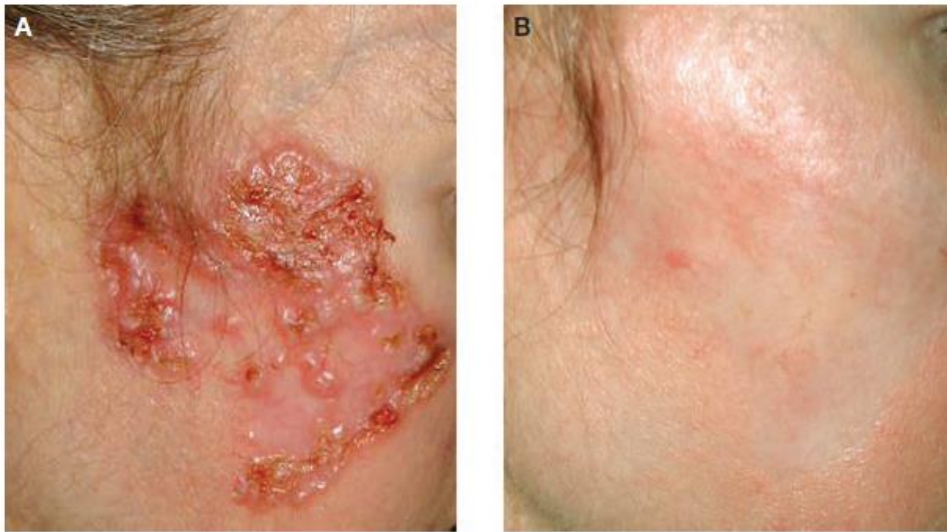
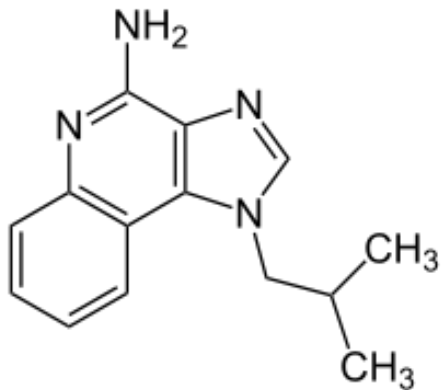


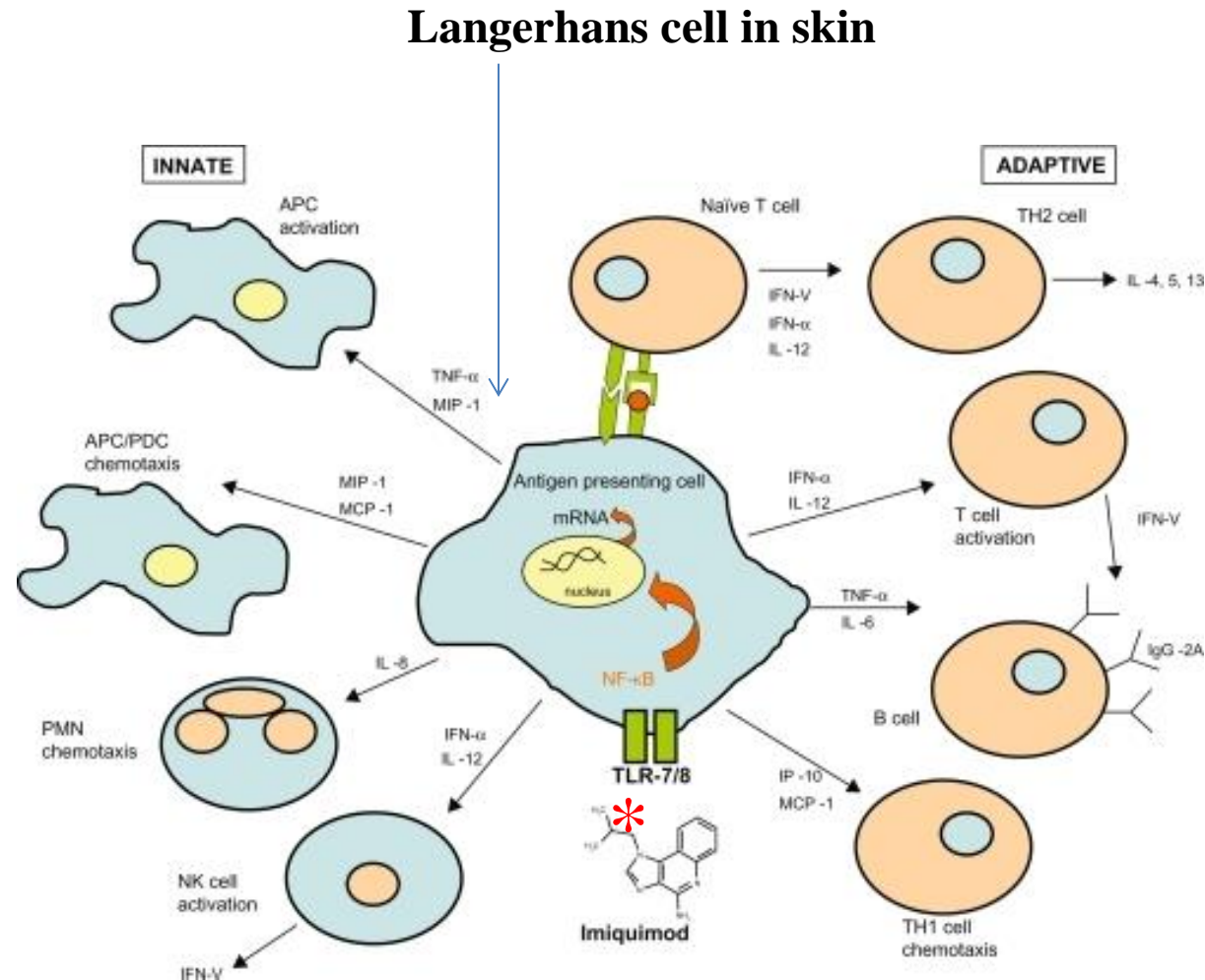
Figure 6 Treatment of a basal-cell carcinoma with imiquimod. (A) A young woman being treated with imiquimod for a superficial basal-cell carcinoma



Anogenital wart before & after topical imiquimod Rx

Imiquimod like receptor 7 of antigen stimulate innate & adaptive immune response

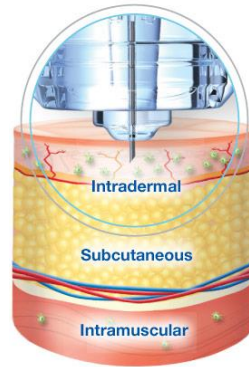
- Genital wart
- Skin cancer
- Little side effect



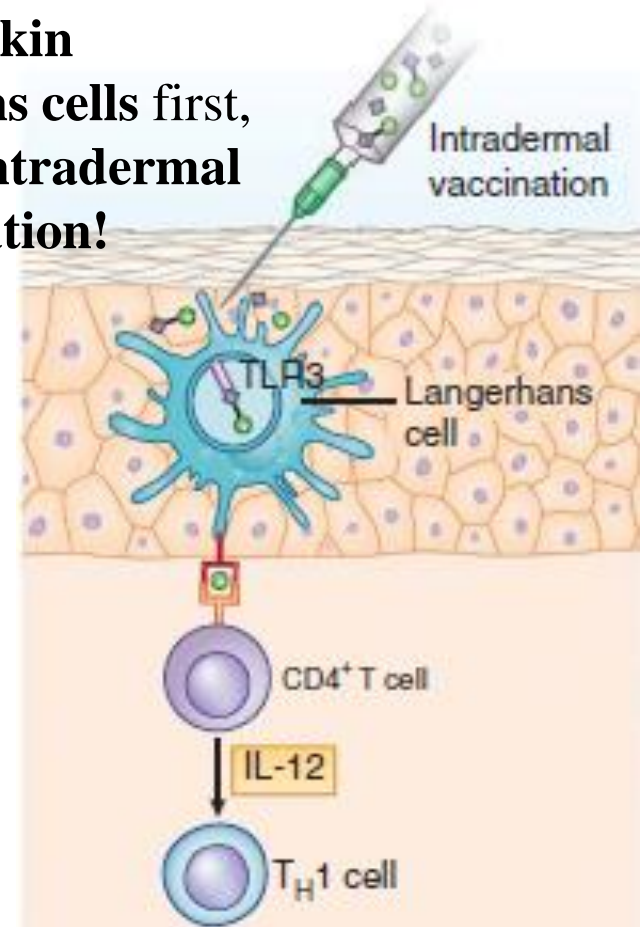
Intramuscular vaccine injection
needle: 38mm



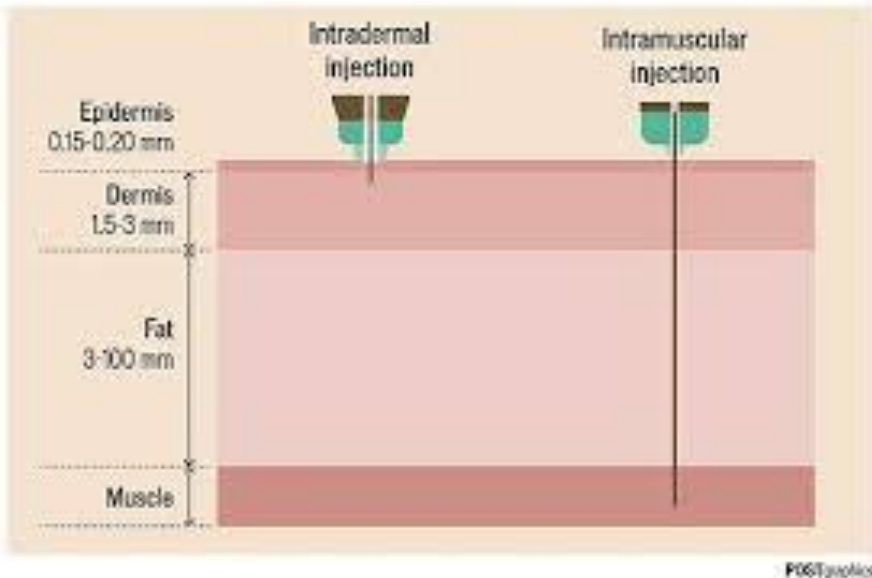
Intradermal needle 1.5mm



We apply **topical imiquimod** to stimulate skin Langerhans cells first, then give **intradermal flu vaccination!**



Langerhan cells (highly efficient **antigen presenting cells**) abundantly present in dermis;



Toll-Like Receptor 7 Agonist Imiquimod in Combination with Influenza Vaccine Expedites and Augments Humoral Immune Responses against Influenza A(H1N1)pdm09 Virus Infection in BALB/c Mice

Anna J. X. Zhang,^{a,b,c} Can Li,^a Kelvin K. W. To,^{a,b,c} Hou-Shun Zhu,^b Andrew C. Y. Lee,^b Chuan-Gen Li,^b Jasper F. W. Chan,^{a,b,c} Ivan F. N. Hung,^{a,c,d} Kwok-Yung Yuen^{a,b,c}

State Key Laboratory of Emerging Infectious Diseases,^a Department of Microbiology,^b Research Centre of Infection and Immunology,^c and Department of Medicine,^d The University of Hong Kong, Hong Kong, China

MAJOR ARTICLE

Clinical Infectious Diseases® 2014;59(9):1246–55

Immunogenicity of Intradermal Trivalent Influenza Vaccine With Topical Imiquimod: A Double Blind Randomized Controlled Trial

Ivan F. N. Hung,^{1,2} Anna J. Zhang,¹ Kelvin K. W. To,¹ Jasper F. W. Chan,¹ Can Li,¹ Hou-Shun Zhu,² Patrick Li,¹ Clara Li,¹ Tuen-Ching Chan,² Vincent C. C. Cheng,¹ Kwok-Hung Chan,¹ and Kwok-Yung Yuen¹

¹State Key Laboratory for Emerging Infectious Diseases, Carol Yu's Centre for Infection and Division of Infectious Diseases, and ²Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong Special Administrative Region, China

Topical imiquimod before intradermal trivalent influenza vaccine for protection against heterologous non-vaccine and antigenically drifted viruses: a single-centre double-blind, randomised, controlled phase 2b/3 trial



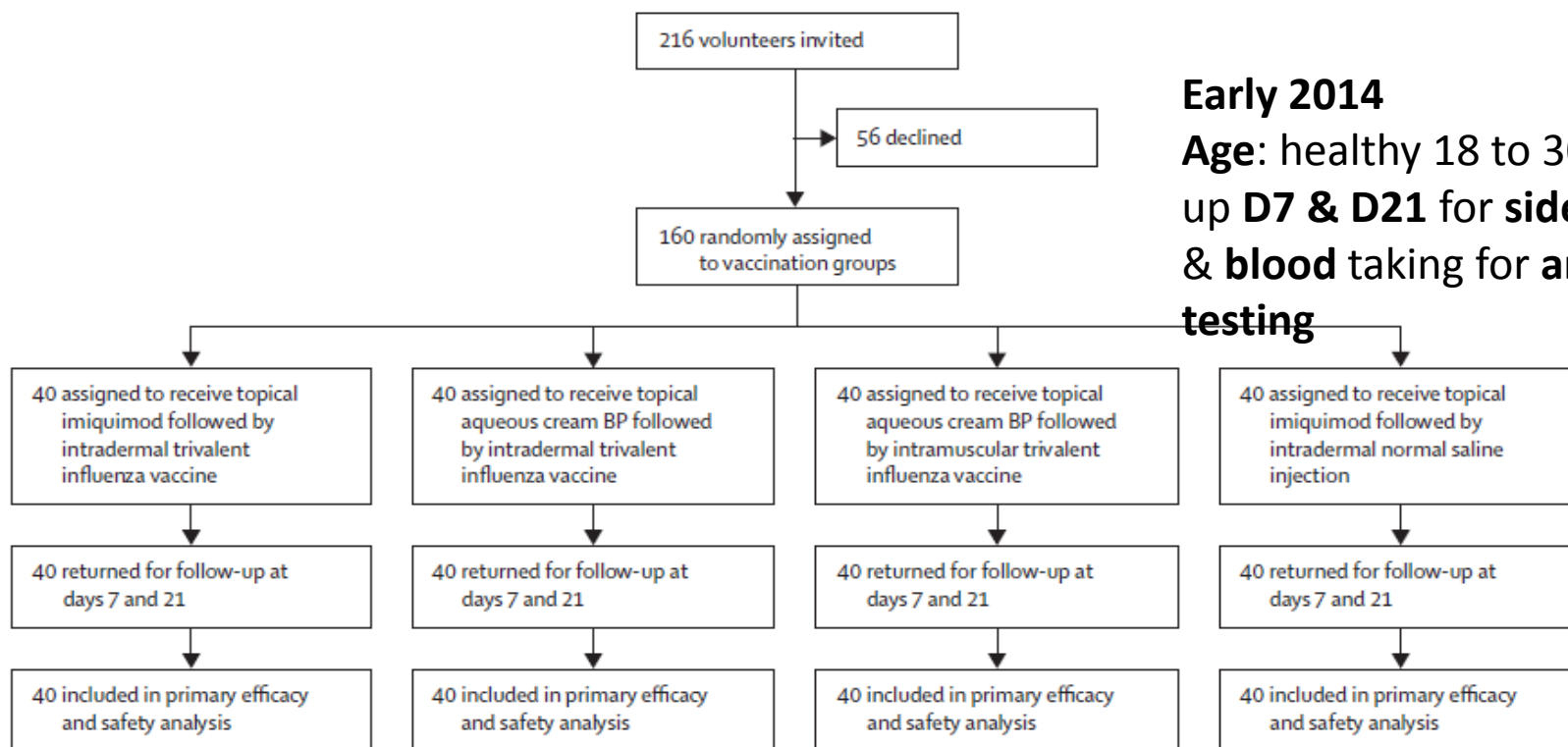
Ivan Fan-Ngai Hung, Anna Jinxia Zhang, Kelvin Kai-Wang To, Jasper Fuk-Woo Chan, Patrick Li, Tin-Lun Wong, Ricky Zhang, Tuen-Ching Chan, Brian Chun-Yuan Chan, Harrison Ho Wai, Lok-Wun Chan, Hugo Pak-Yiu Fong, Raymond Kar-Ching Hui, Ka-Lun Kong, Arthur Chun-Fung Leung, Abe Ho-Ting Ngan, Louise Wing-Ki Tsang, Alex Pat-Chung Yeung, Geo Chi-Ngo Yiu, Wing Yung, Johnson Y-N Lau, Honglin Chen, Kwok-Hung Chan, Kwok-Yung Yuen

Summary

Background Pretreatment with topical imiquimod, a synthetic agonist of toll-like receptor 7 significantly improved the immunogenicity of influenza vaccination in elderly people. We aimed to clarify its effect in a younger age group.

Lancet Infect Dis 2015

Carol Yu's Centre for Infection



Seroconversion rate (4X increase in antibody titre) against **Vaccine strains**

	Imiquimod + ID vaccine	IM vaccine
Day 7		
H1N1/A/California	98%	45%
H3N2/A/Victoria	75%	10%
B/Massachusetts(Yamagata lineage)	90%	43%
Day 21		
H1N1	98%	55%
H3N2	78%	18%
B	90%	50%

Side effects minimal & similar to intramuscular vaccine:
mainly redness (13%), swelling(18%), pain (10%)and low grade fever (3%)

Seroconversion rate against **Non-Vaccine strains**

	Imiquimod + ID vaccine	IM vaccine
Day 7		
H1N1 (1933 WSN)	75%	3%
H1N1 (pre-pandemic seasonal)	63%	5%
H3N2 (2014 antigenic drifted, Switzerland-like lineage)	70%	8%
B (Victoria lineage)	63%	10%
Day 21		
H1N1 (1933 WSN)	75%	3%
H1N1 (prepandemic)	65%	15%
H3N2 (2014 antigenic drifted)	70%	10%
B	63%	10%

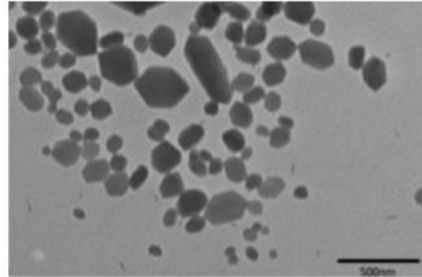
Topical imiquimod just before intradermal influenza vaccination

- **Rapid onset** of effective antibody response
- Highly active against **vaccine virus** strains
- **ALSO** Highly active against **non-vaccine related virus** strains
- Likely to confer **protection even** when WHO **wrongly predicts** the epidemic strains;
- Should be tested for vaccines other than influenza

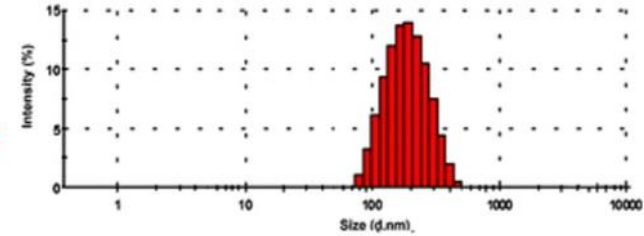
Product Development

(continuing support from the Respiratory Viral Research Foundation and collaboration with Nanotechnology and Advanced Materials Institute, Hong Kong)

Step 1



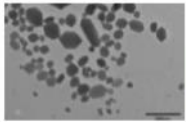
Nano crystal in hydrogel



Monitor particle size and formulation stability

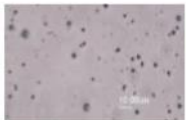
Step 2

Approach 1: Nano crystal



hydrogel

Vs.

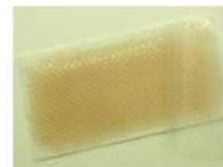
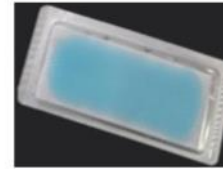


hydrogel

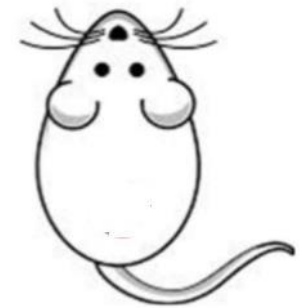
Approach 2: Nano emulsion



Franz cell diffusion tests



Nanomized imiquimod in hydrogel matrix patch



In vivo skin irritation test

Final evaluation



Measure hemagglutination (HI) and antibody titers in vaccine injected mouse

Thank you