PER.C6

A Human Designer cell Line Providing a Pandemic Proof Platform for the Manufacturing of Safe Influenza Vaccines

FONS

MARCH 26,

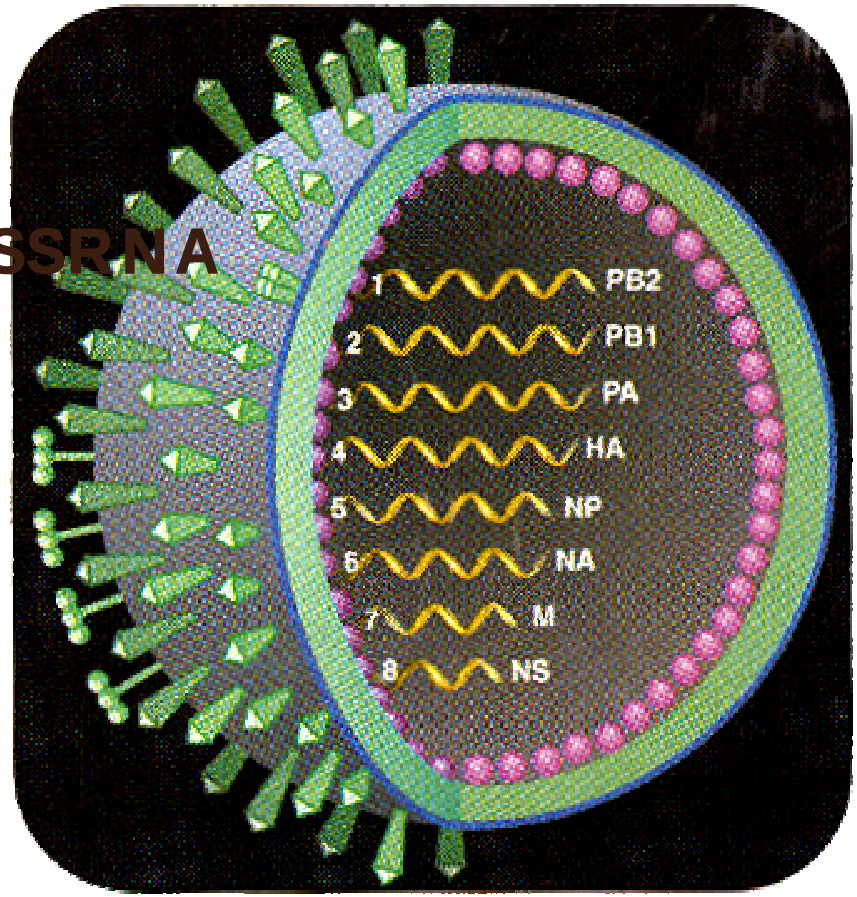
Crucell

1918-1919 FLU PANDEMIC

~30 MILLION DEATHS

THE DEVIL IN

- ✓ ENVELOPED VIRIONS
- ✓ LINEAR NEGATIVE-SENSE SSRNA
- ✓ SURFACE
  - HAEMAGGLUTINI
  - NEURAMINIDASE (NA)



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"... NO INDIVIDUAL VACCINE PRODUCING HAVE THE CAPACITY TO PRODUCE ONE PANDEMIC VACCINE FOR EACH OF ITS

ESWI, Ferney Voltaire-June 10-11, 2001

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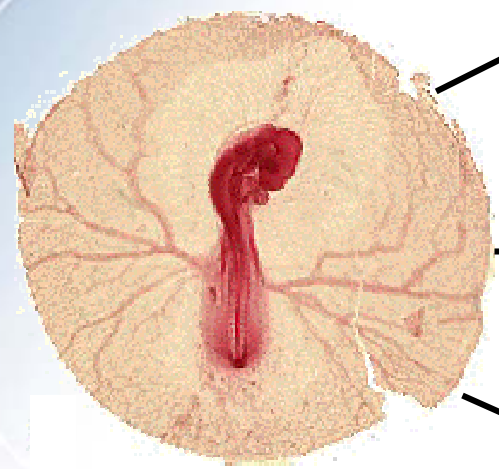
PRODUCTION ON CHICKEN EMBRYONATED EGGS



- REASSORTANTS REQUIRED
  FAILURE TO GROW
- CUMBERSOME
- LIMITED
  LACKS FLEXIBILITY

NOT PANDEMIC

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WHO

AN IMPROVED INFLUENZA VACCINE

"... URGENT NEED FOR THE CELL CULTURE SYSTEMS WHICH WOULD UP OF PRODUCTION IN THE EVENT OF A

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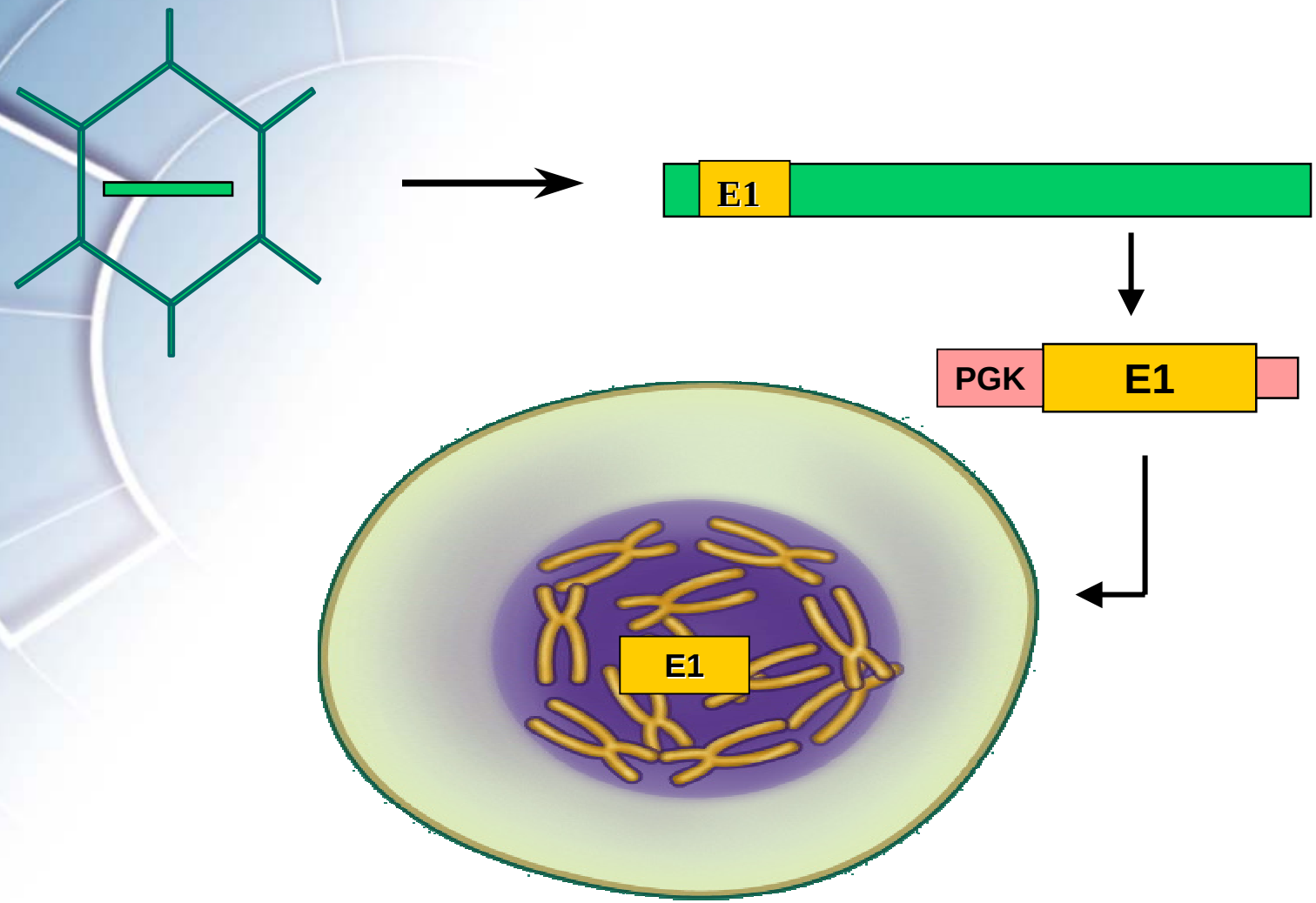
PER.C6 :A HUMAN DESIGNER



PER.C6

CHARACTERISTICS OF PER.C6

- IMMORTALIZED CELLS (NON TUMOR) ADENOVIRUS E1
- HUMAN CELLS – RETINA DERIVED- DOCUMENTED HISTORY
- MASTER & WORKING CELL BANKS QUALIFIED

PER.C6™ = PGK-E1 RETINA.CLONE 6

PER.C6
VACCINE MANUFACTURING

- SAFE TECHNOLOGY
- SCALABLE TECHNOLOGY
- HIGH YIELD FOR ALL INFLUENZA STRAINS

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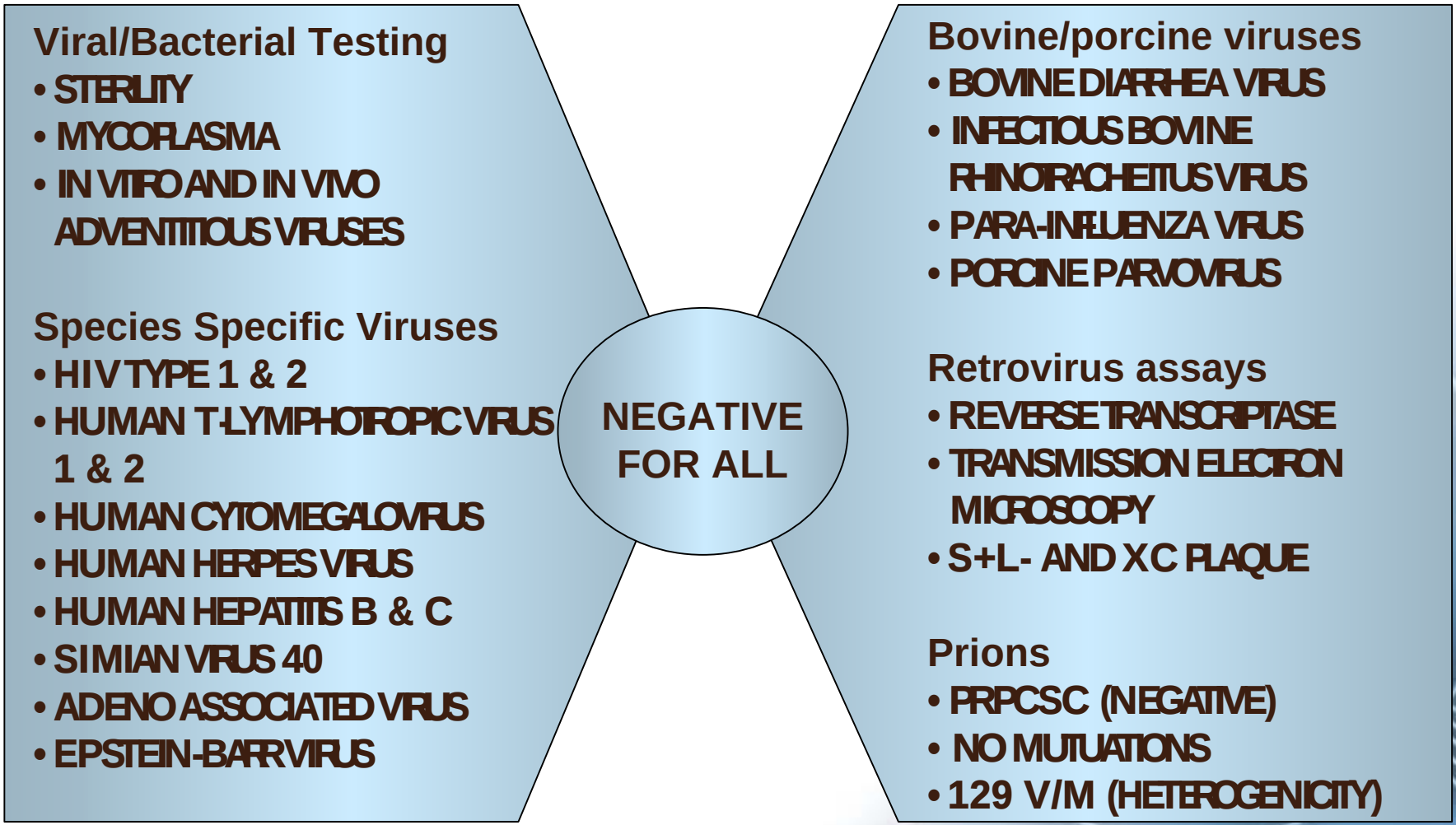
SAFE DESIGNER CELL

PER.C6 DETAILED SAFETY HISTORY



SAFE DESIGNER CELL

PER.C6
Detailed safety history

- **BEST DOCUMENTED CELLLINE TO DATE**
- **FULL SAFETY PROFILE**
- Animal component free culture medium
- **BMF AT FDA, UPDATED BY MERCK &CO.**

PER.C6
Products in clinical trials

- **VACCINES : PHASE I/II MERCK HIV VACCINE, WITH HEALTHY VOLUNTEERS & PATIENTS**
- **GENETHERAPY : MULTIPLE PHASE I-II TRIALS**

PER.C6
VACCINE MANUFACTURING

- SAFE TECHNOLOGY
- **SCALABLE TECHNOLOGY**
- HIGH YIELD FOR ALL INFLUENZA STRAINS

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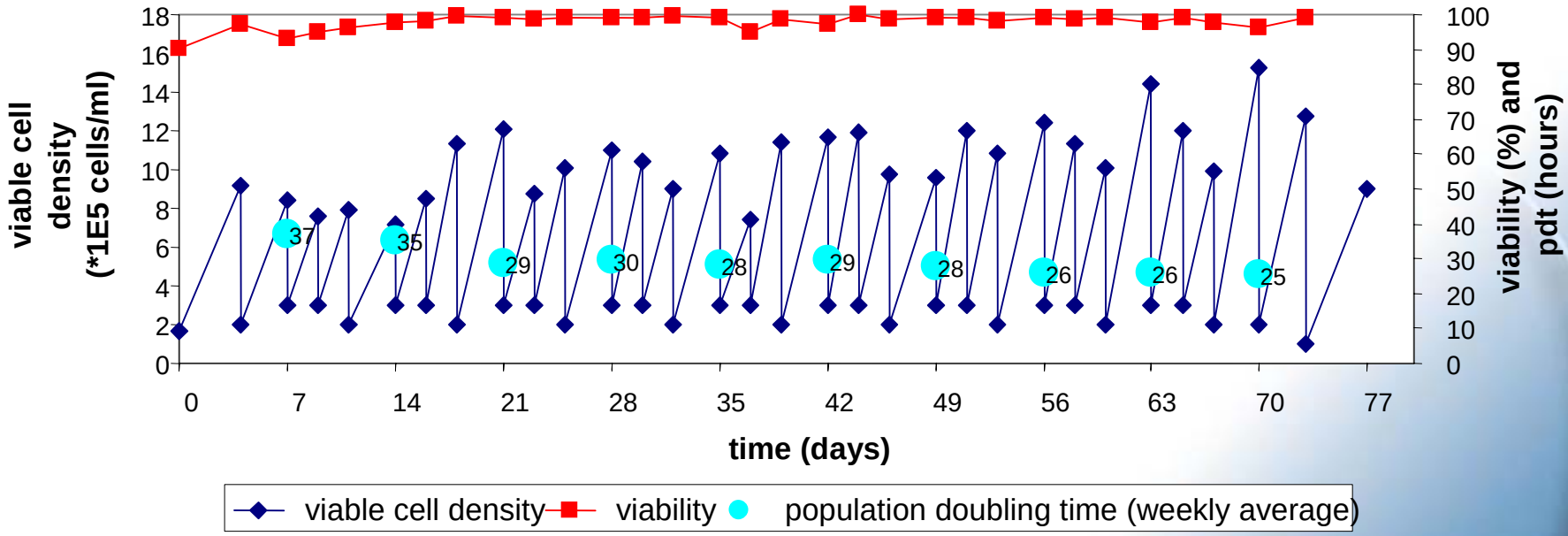
SCALABLE DESIGNER CELL

STABILITY OF PER.C6 SUSPENSION CULTURE



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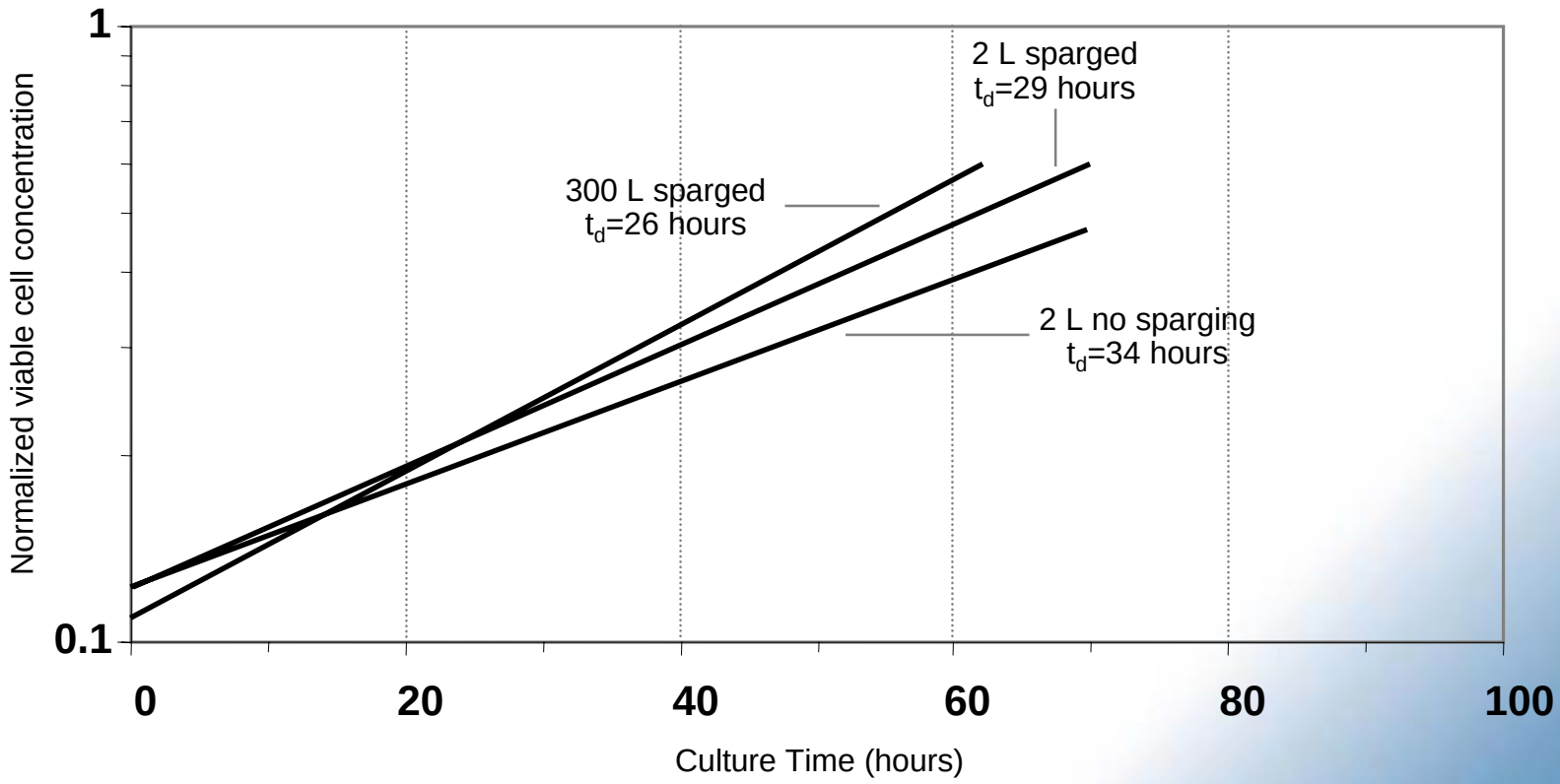
SCALABLE DESIGNER CELL

SUCCESSFUL SCALING FROM 2L TO 300L BIOREACTORS



Weichang Zhou, 2001 Merck & Co at Williamsburg Viral Vaccines Meeting

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VACCINE MANUFACTURING

- SAFE TECHNOLOGY
- SCALABLE TECHNOLOGY
- **HIGH YIELD FOR ALL INFLUENZA STRAINS**

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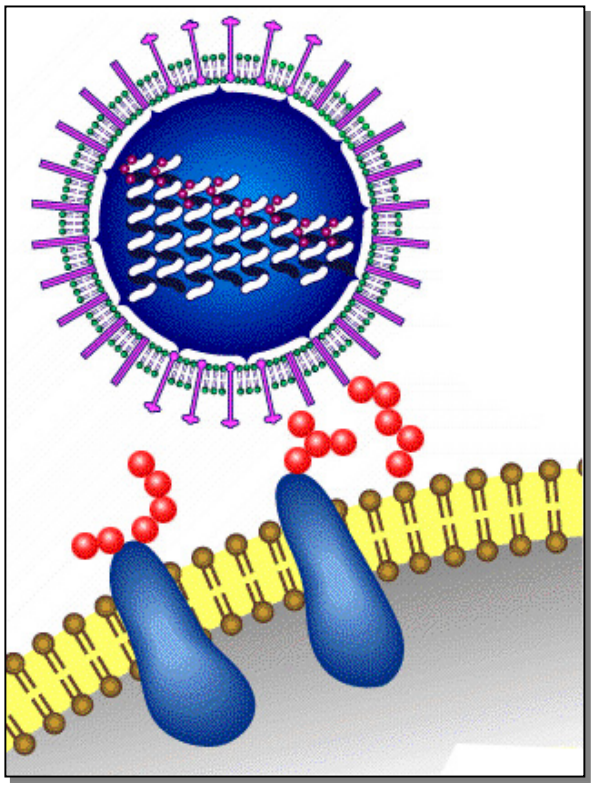
HOST CELL SPECIFICITY



- Hemagglutinin (HA) binds to sialic acid (SA) on glycoproteins and proteoglycans on the cell surface
- Human influenza HA: SAalpha2,6Gal (human respiratory tract)
- Avian influenza HA: SAalpha2,3Gal (avian intestine and egg chorioallantoic sac)

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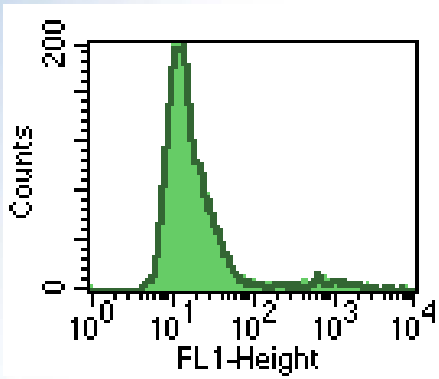
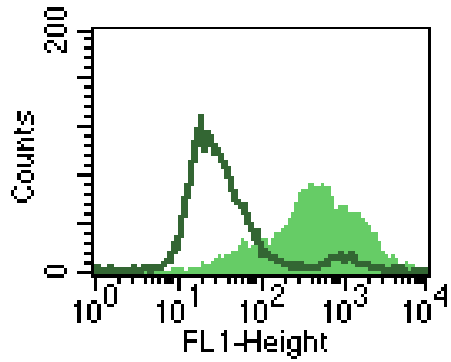
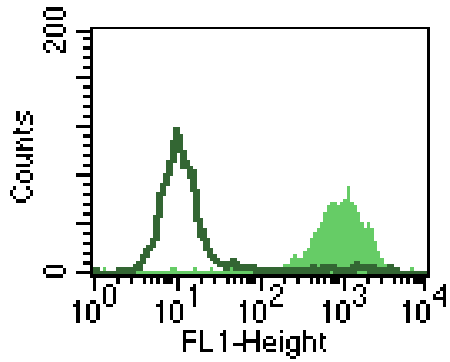
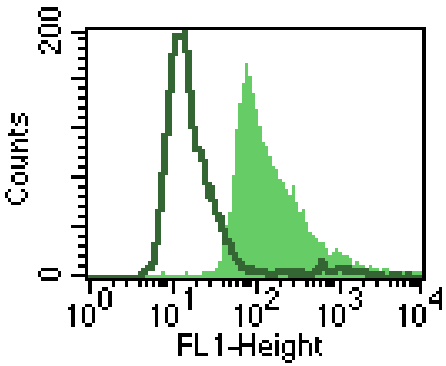
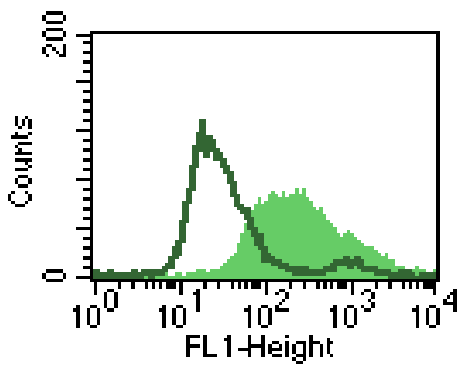
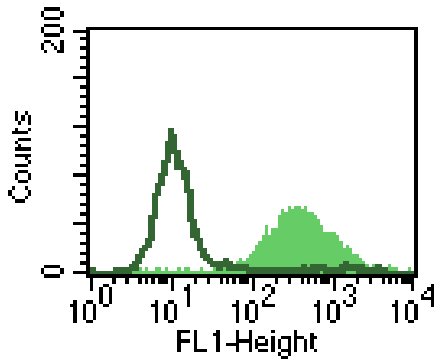
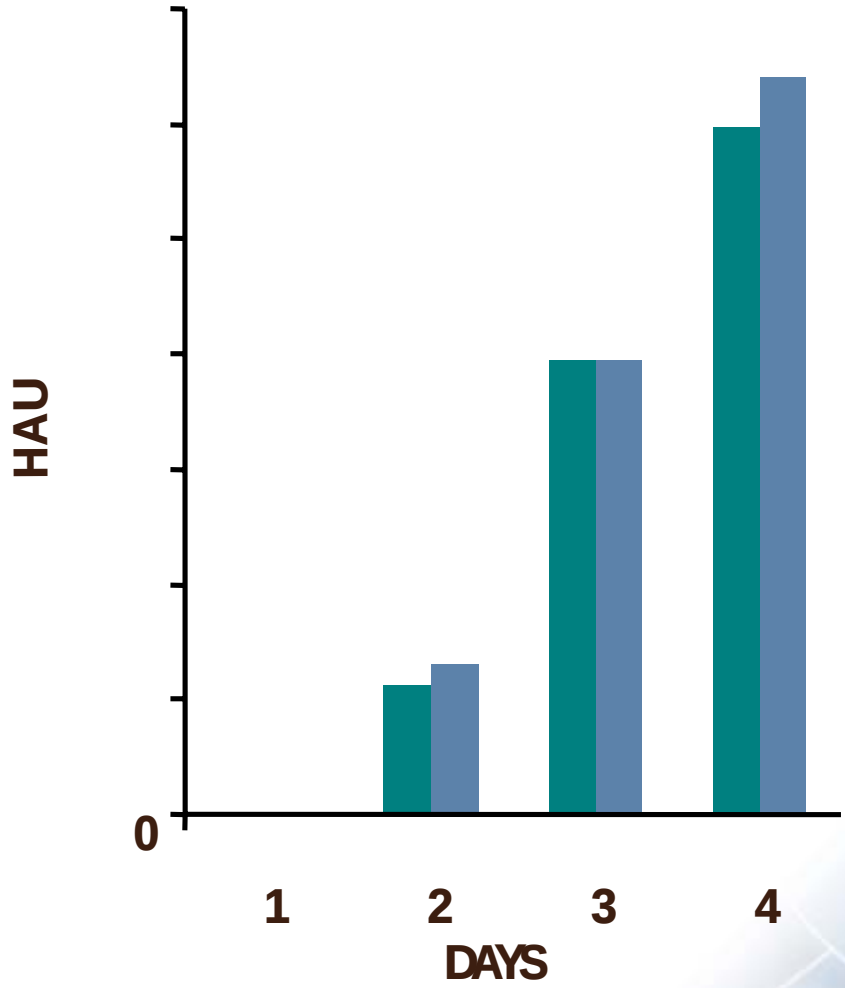
INFLUENZA HA CELL SURFACE

	CHO	PER.C6	MDCK
Sia 2-6 Gal			
Sia 2-3 Gal			

INFLUENZA VACCINE
REPLICATING STRAINS

- H3N2 strains
  - A/Sydney/5/97
  - A/Johannesburg/33/94
  - A/Nanchang/933/95
  - A/Wuhan/359/95
  - A/Moscow/10/99
  - A/Panama/2007/99
  - Resvir 17 A/Panama reass.
- H1N1 strains
  - A/Beijing/262/95
  - X-127 A/Beijing reassortant
  - A/New Caledonia/20/99
  - IVR-116 A/New Caledonia reass.
  - A/Johannesburg/282/96
  - A/Texas/36/91
- B strains
  - B/Harbin/7/94
  - B/Yamanashi/166/98
  - B/Beijing/184/93
  - B/Shandong/7/97
  - B/Victoria/504/2000
  - B/Johannesburg/5/99
  - B/Sichuan/379/99
  - B/Guandong/120/2000
  - B/Canada/16188/2000
- Avian strains
  - A/Duck/Singapore
  - Q/F119-3/97

INFLUENZA VACCINE
FAST KINETICS



A/SYDNEY/5/

1μG/ML

35°C

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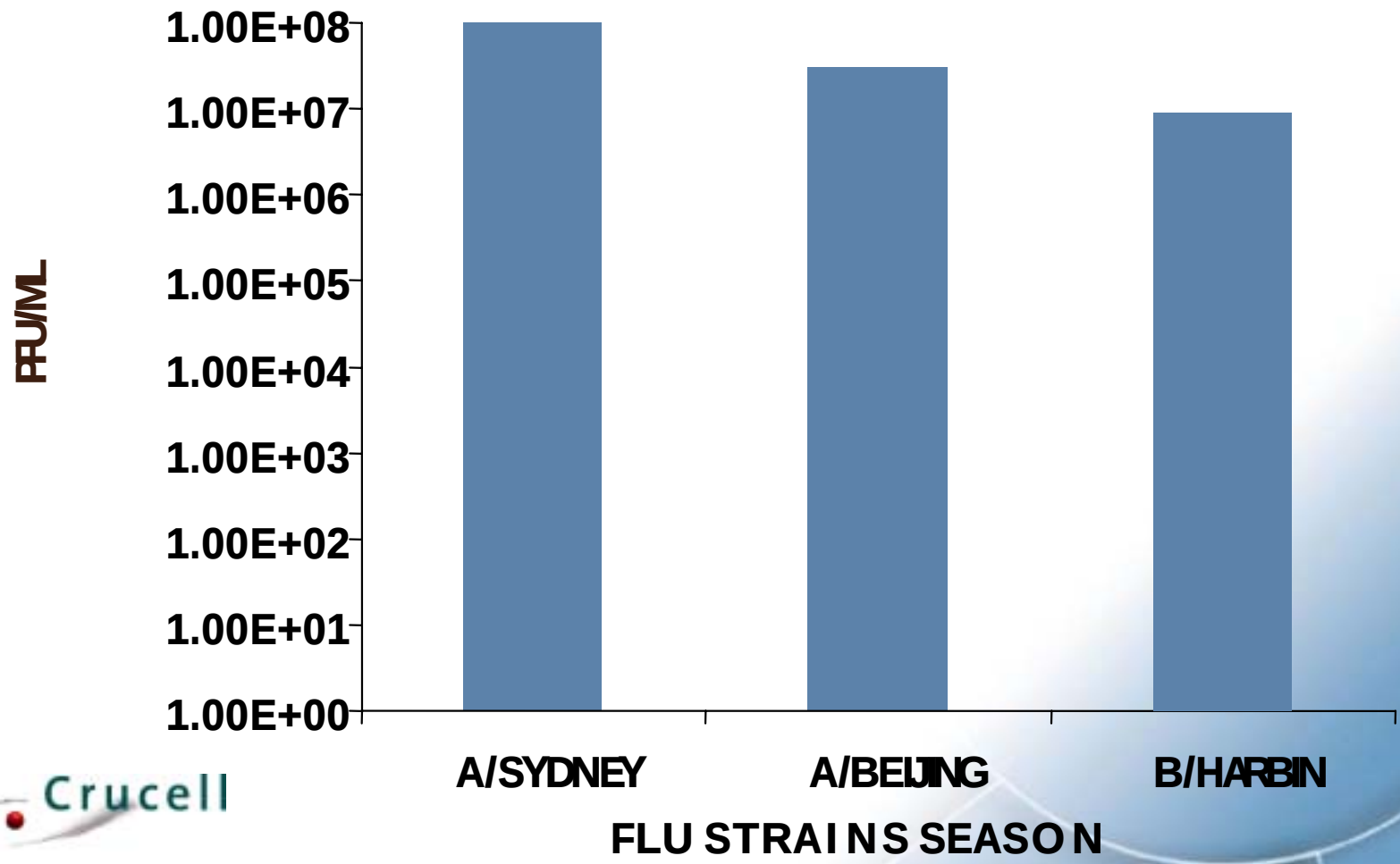
INFLUENZA VACCINE
HIGH TITERS



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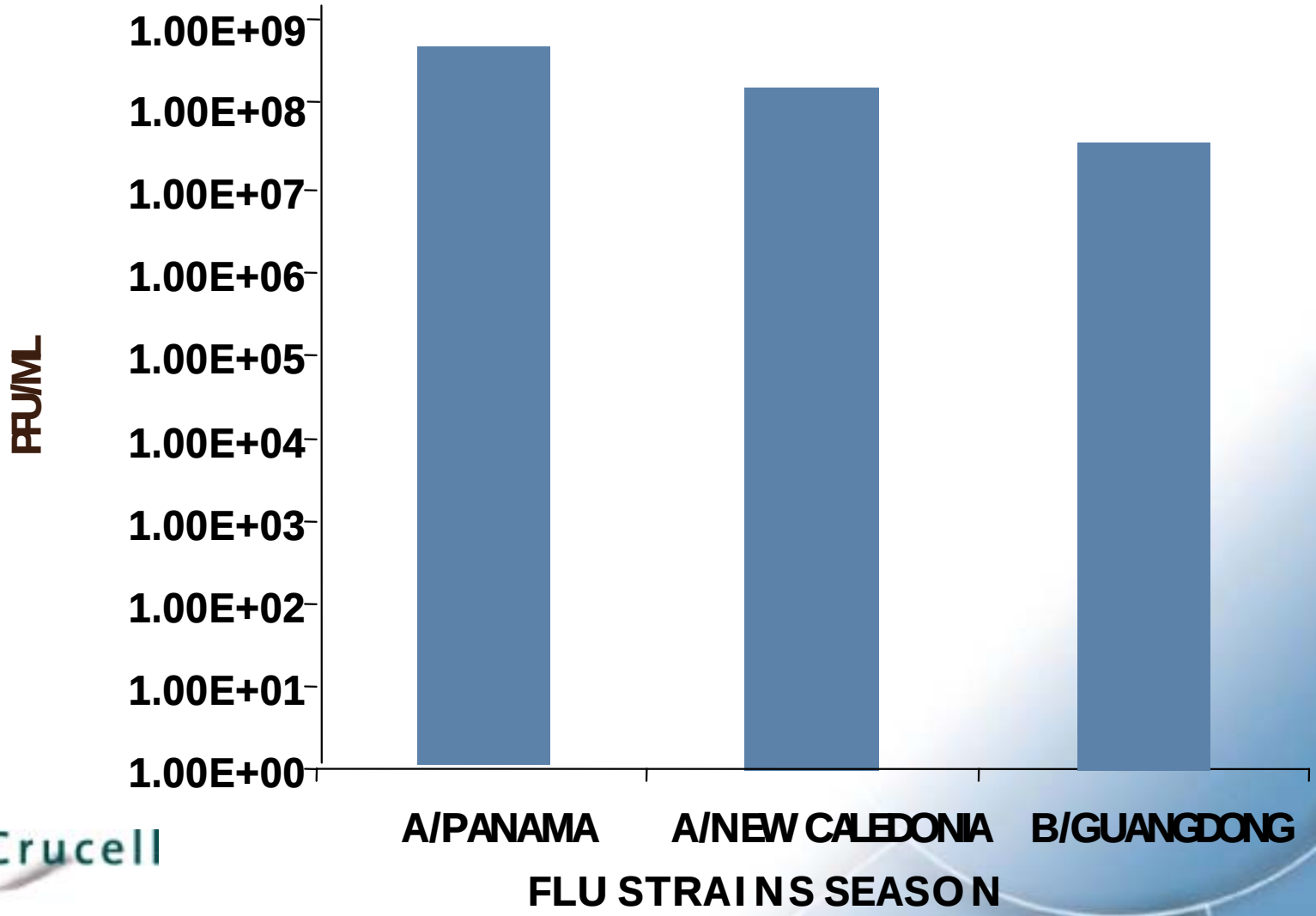
INFLUENZA VACCINE

HIGH TITERS



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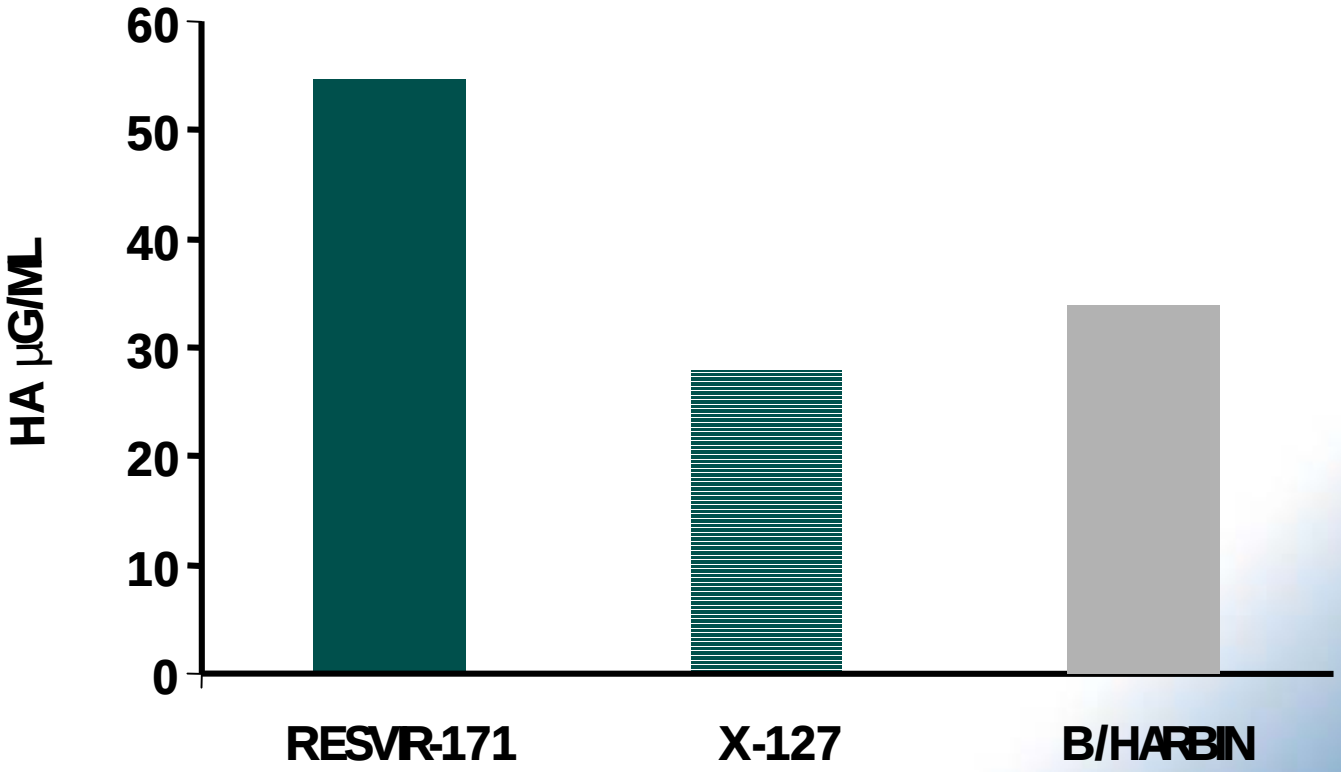
INFLUENZA VACCINE
HIGH HA YIELDS



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PER 6 Flu

Responding to the Challenge of Pandemic Influenza

1997 THE HONG-KONG

- **GROWTH OF WITH HIGH HA**
- **100 M MONOVALENT DOSES (15 UG HA/ML)**
- **TIME TO 3 MONTHS**

CREDEN

MARIA GRAZIA
GUISEPPE
JUTTA PASMAN
MARCO
RICHARD
ANDRE VOOYS
CARLA OPHORST
JAAP GOUDSMIT