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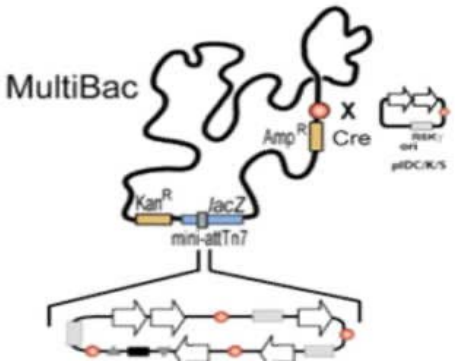

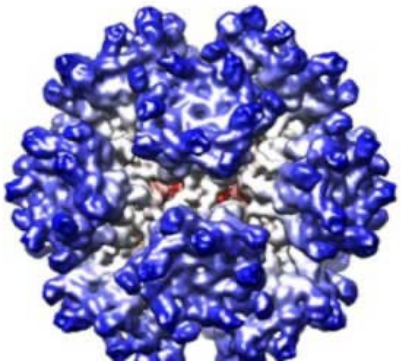

Baculovirus Expression System for Vaccine Development

Baculovirus Expression System (BEVS) for Vaccine Development - Advantages

- Can be grown in serum-free suspension culture and are more robust than animal cell lines
- Availability of effective baculovirus vector construction techniques
- S2 stably modified insect cells can be grown in continuous mode in perfusion cultures
- Proven industrial scale applicability for recombinant protein
- Do not represent a risk for human health as they are non-infectious and non-replicative, thus safe

BEVS for Commercial Vaccine Products

Human papilloma virus Vaccine (Cervarix®, Glaxo Smith Kline)

(L1 proteins from human papillomavirus type 16 and 18)

Influenza Vaccine (Flublok®, Protein Sciences Corporation, part of Sanofi Pasteur, Inc)

(Influenza virus hemagglutinin (HA))

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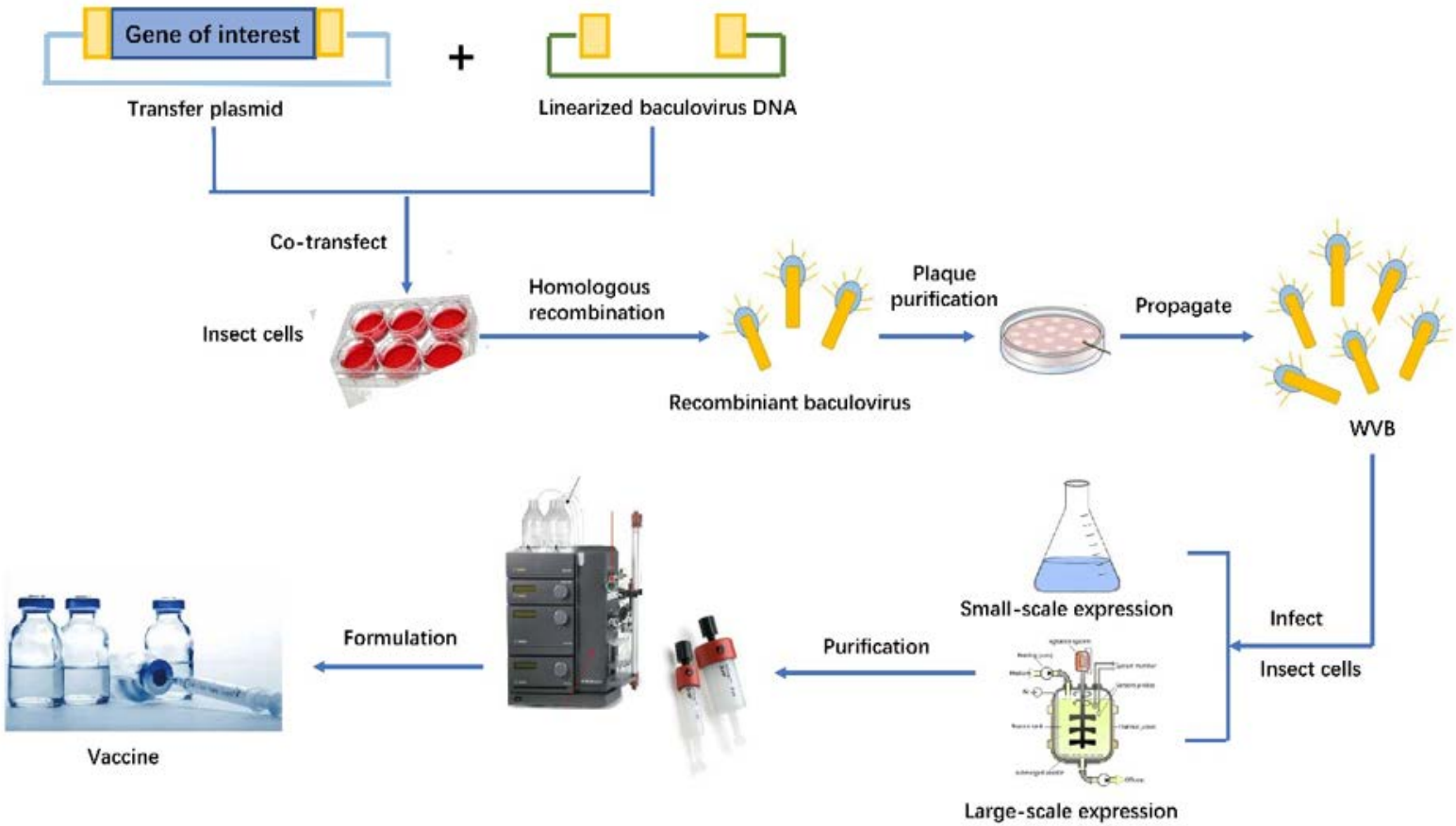

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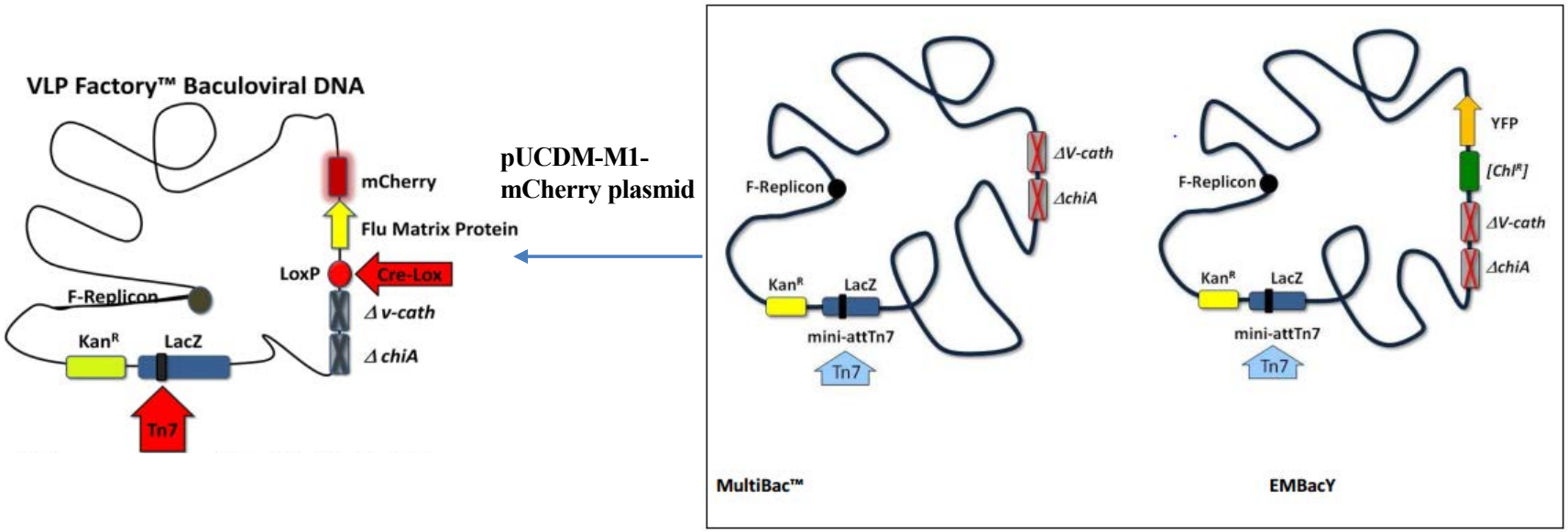
VLP of influenza HA protein in BEVS (Insect cell -SF21)



VLP - Factory competent cells

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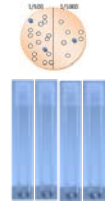
1. VLP-Factory competent cells
2. EmBacY competent cell

HA-pACEBac1

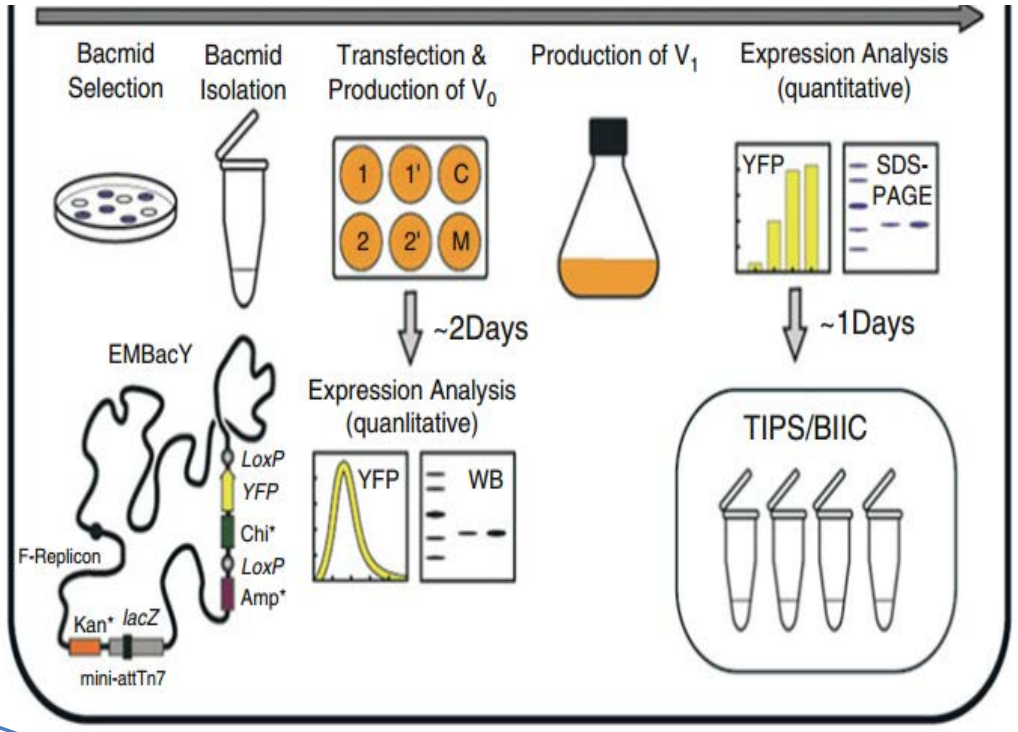


Blue/white screening clone

Blue/white screening clone

Tranfection Bacmid -insect cell

Harvest Vo- Amplication V1



Freezing Baculovirus-infected insect cells (BIIC) stocks

Test BIIC

(SSE) small scale expression

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SF21 cell culture

Infect SF21 with VLP-HA

Centrifuge Harvest Supernatal

Remove host cell DNA with Benzonase

Chromatography with Heparin column

Chromatography with Capto Q column

Ultracentrifuge

Harvest pellet- Resuspend with PBS buffer

Ultracentrifuge in Sucrose 20% and 60% Harvest while layer

Ultracentrifuge in Sucrose gradient 20%-60% Harvest While layer Keep -80°C

1. Test all fraction with SDS gel
2. Test VLP viral with Electron Microscope (EM).

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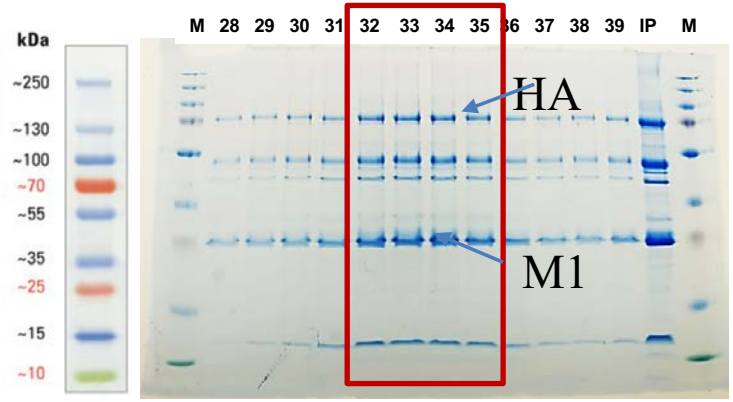
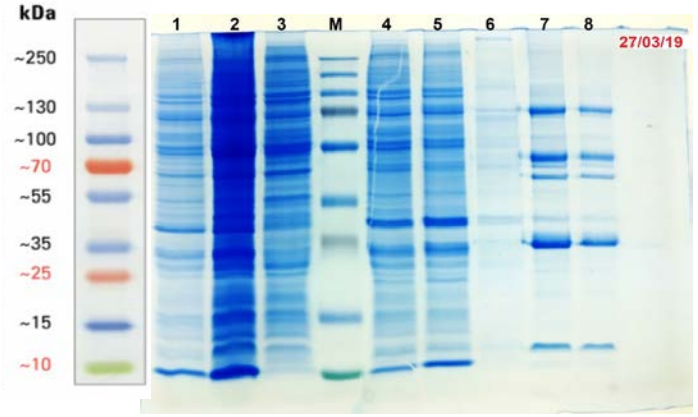
M Ladder
IP input
Fraction after ultracentrifuge
28 to 39 sucrose gradient



BV4-HA (10^6 cell)	1: BV4-HA DPA24
	2: BV4-HA DPA72
	3: BV2-HA DPA72
VLP-HA (10^6 cell)	4: VLP-HA #1 DPA72
	5: VLP HA#5 DPA72
VLP-HA purify	6: Supenatal havest VLP-DPA 72
	7: Ultracentrifuge Sucrose 1
	8: Ultracentrifuge Sucrose gradient
	Ladder



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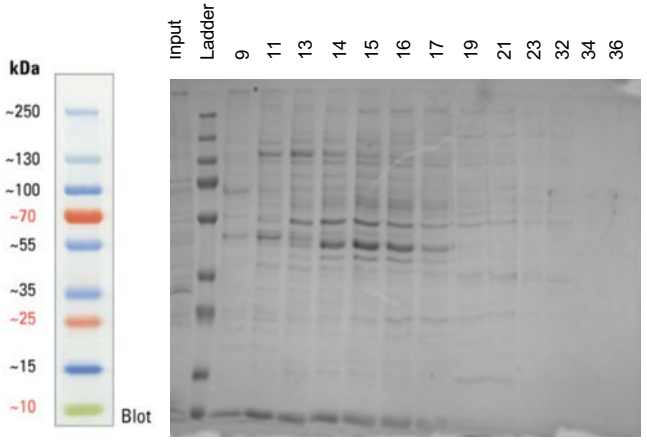
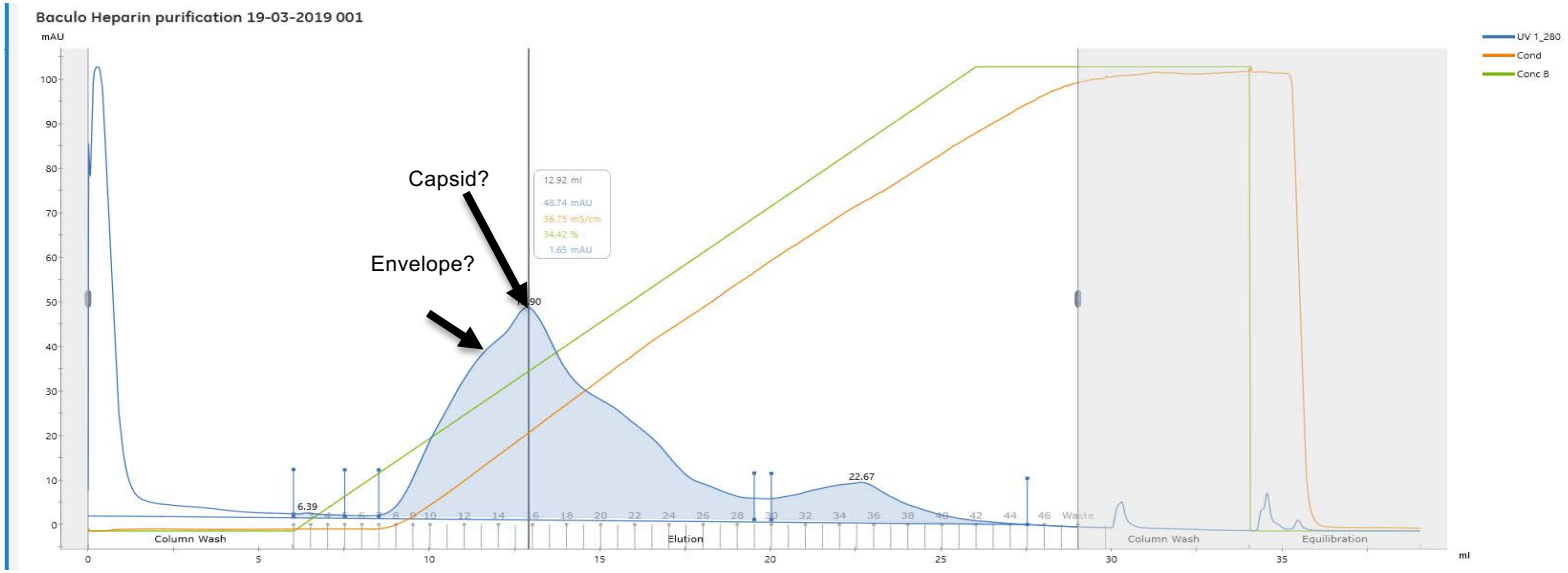
Purification by Heparin column





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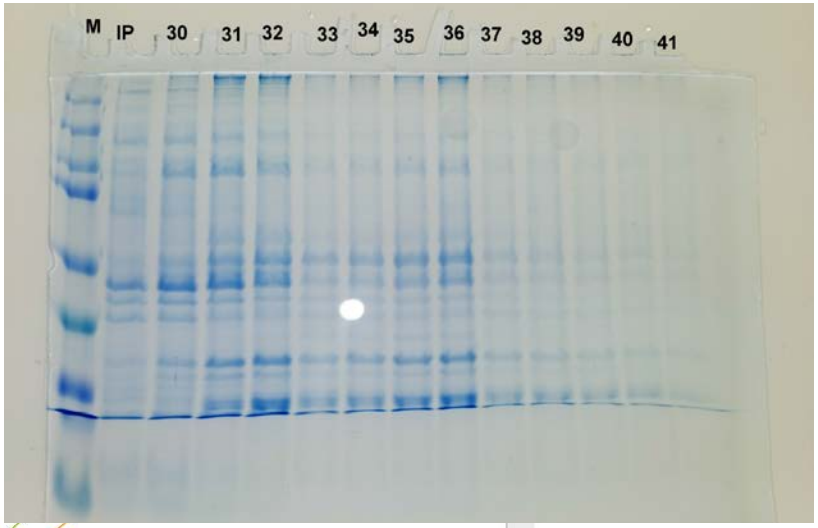
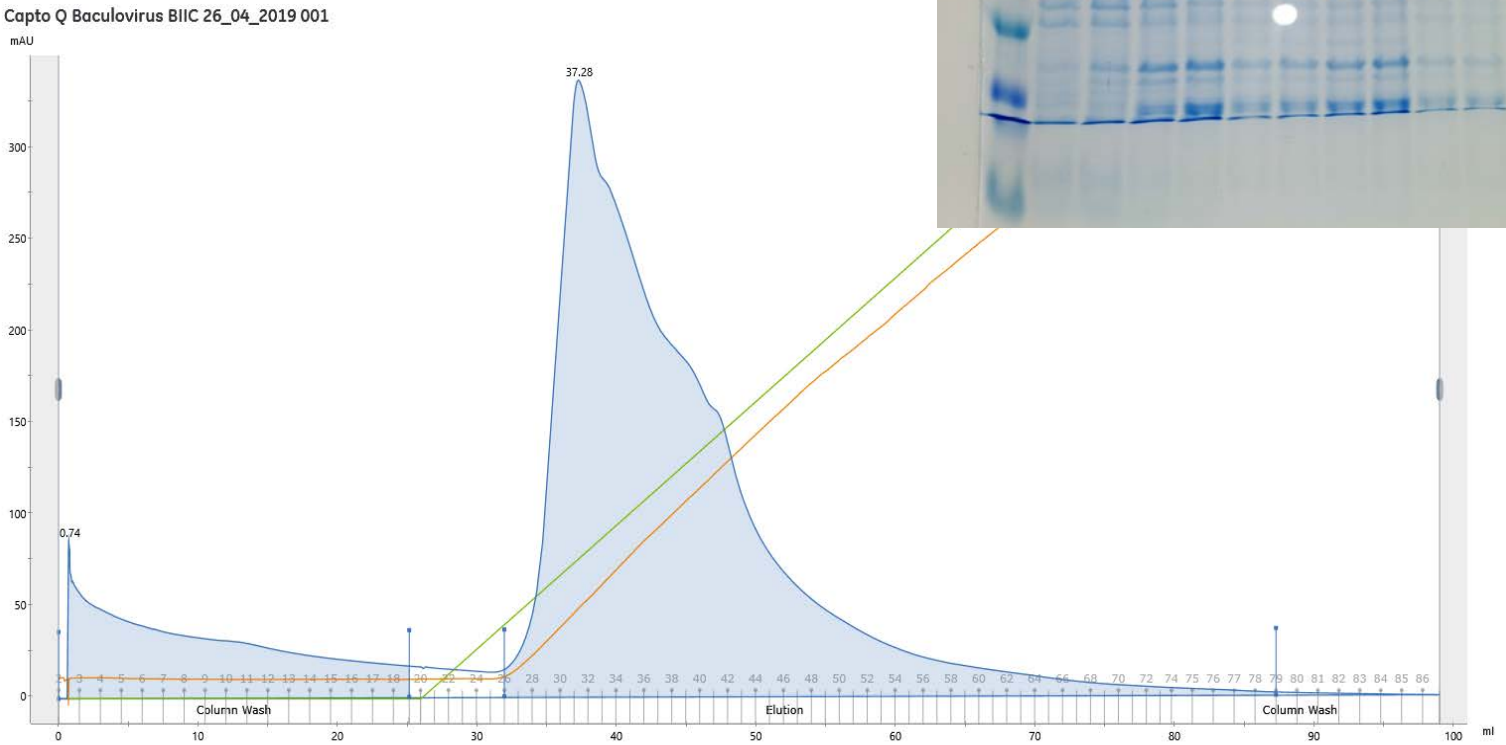
Purification by Capto Q 5ml column





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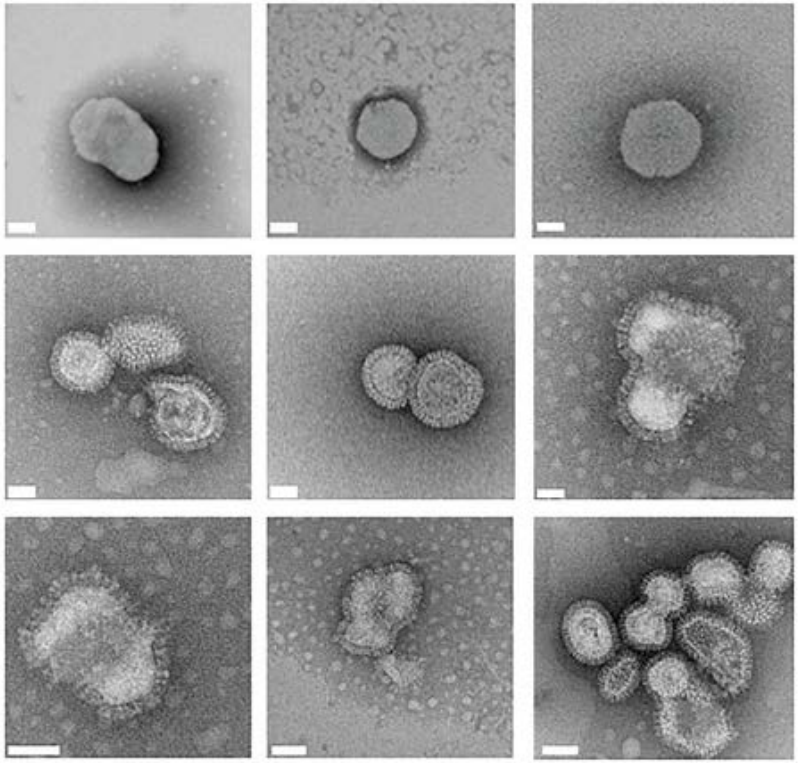
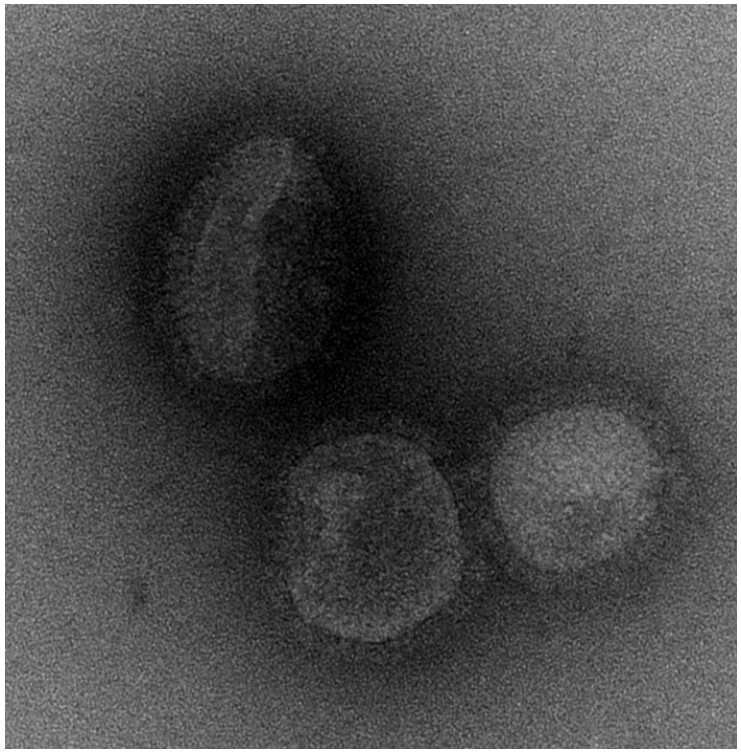




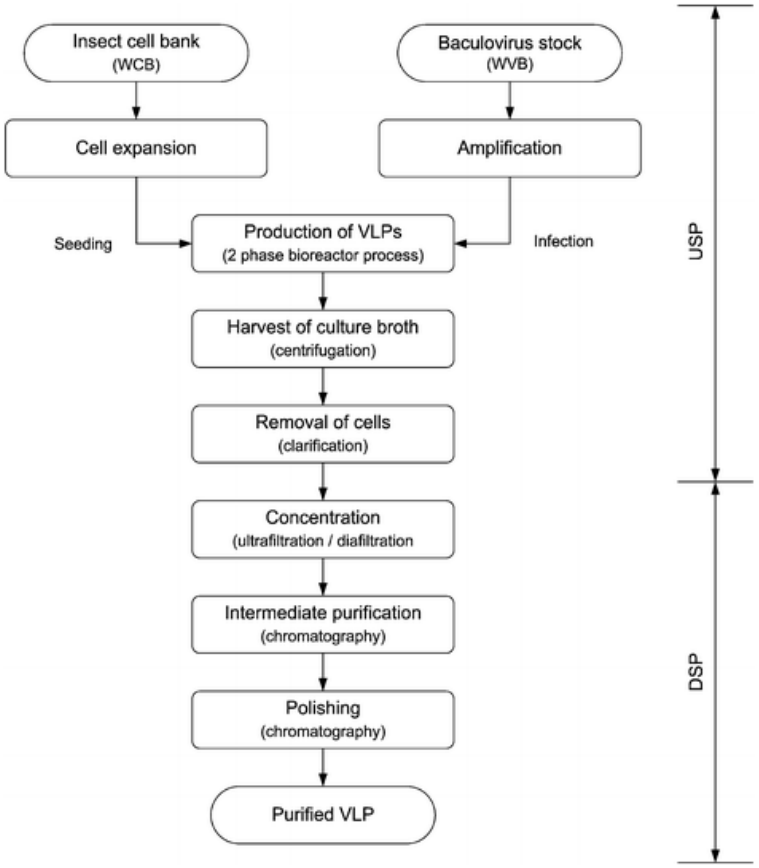
VLP of HA-M1

BEVS translate to LMICs manufacturers - Challenges

Vaccine manufacturing costs is higher than other recombinant protein expression systems – animal cell culture, yeast, bacteria .

- Low expression yields - limited by the slow cellular secretion processes
- Complex steps for purification – using different chromatography systems

BEVS translate to LMICs manufacturers



- Enhancing the antigen expression (New expression systems)
- Using new technologies for Cell Culture Platforms

- Simple Steps for purification (TFF dialysis, Depth Filtration, Size exclusion Chromatography)

Acknowledgements

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- Mrs. Vu Hong Nga
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Thanks for Your Attention!