PRODUCTION OF VACCINES USING **VIRUS-LIKE PARTICLES** AND THE **BACULOVIRUS-INSECT CELL** EXPRESSION SYSTEM

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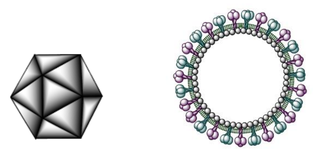
VIRUS-LIKE PARTICLES

Definition

Protein structures that mimic the organization of native viruses but lack the viral genome, becoming potential vaccine candidates

Types

- Number of structural proteins: Simple or complex
- Presence of envelope: Enveloped or non-enveloped



Simple VLP **Complex VLP**

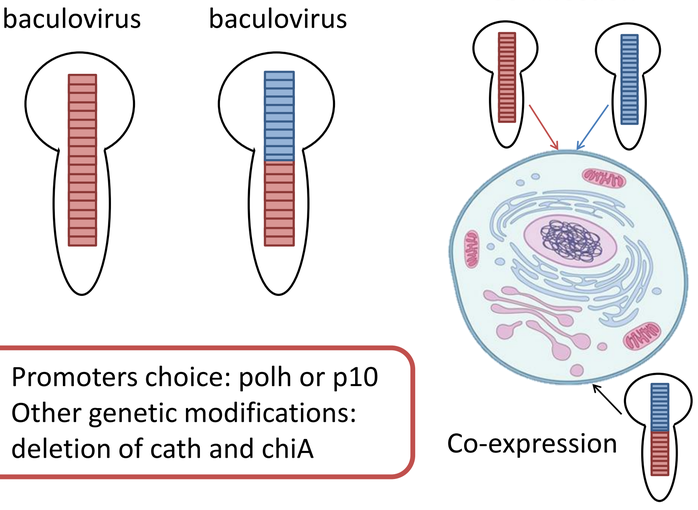
Liu, F. et *al*. Protein Expr. Purif. **90**, 104–116 (2013)

Vaccination role

	Traditional vaccines		Subunit vaccines		Peptide vaccines	Live recombinant vaccines	DNA vaccines
	Attenuated	Inactivated	Recombinant proteins	Virus-like particles			
Safety	Low	Medium	High			Medium	
Price	Cheap	Medium	Expensive		Cheap	Medium	
Administration	Intramuscular						
Immunogenicity	High		Low	High	Low	High	Depends
Adjuvant	Yes			Depends	Yes	No	

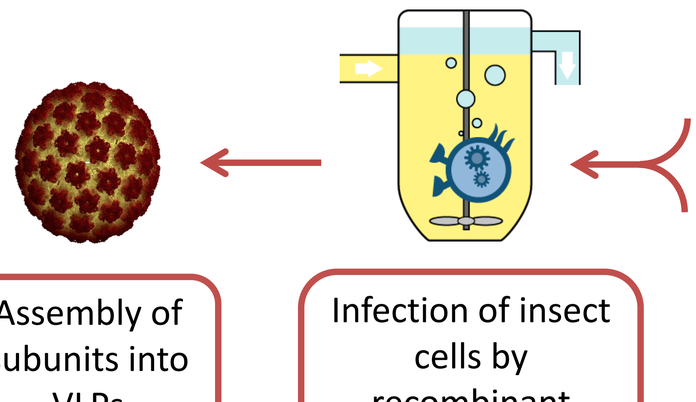
PRODUCTION PROCESS

Design of recombinant baculovirus



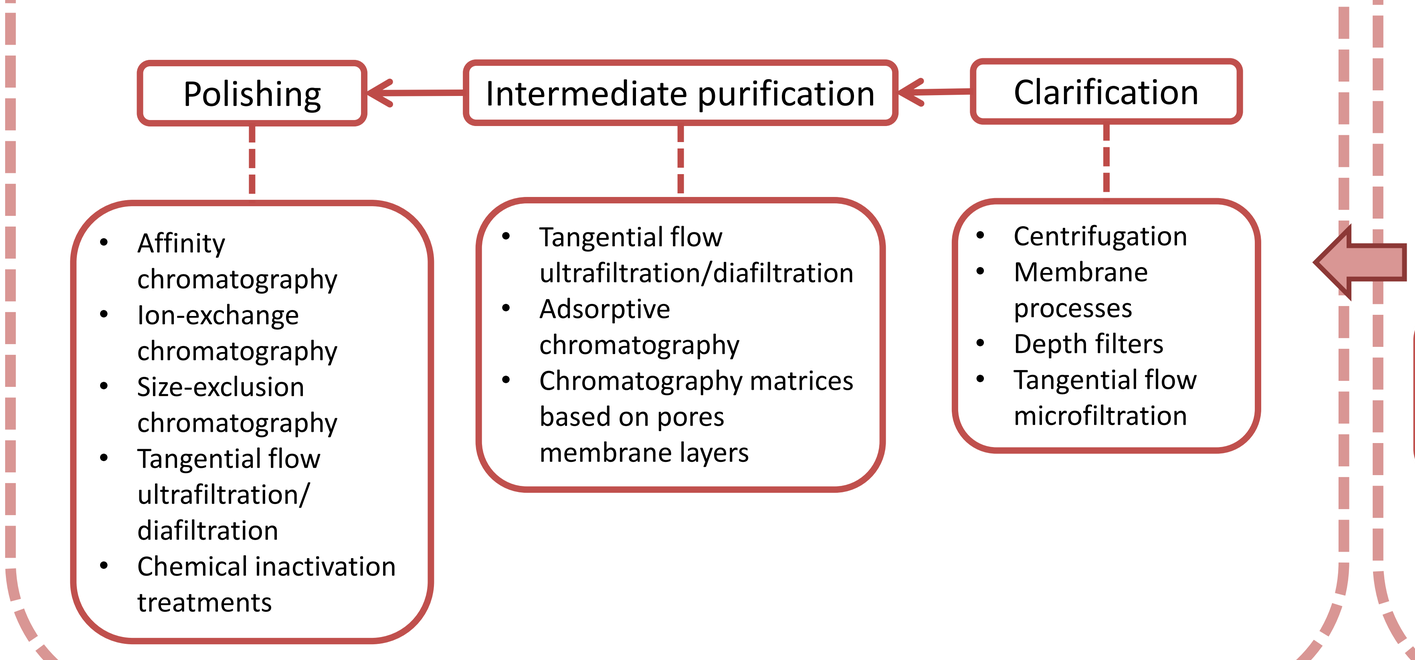
- Promoters choice: polh or p10
- Other genetic modifications: deletion of cath and chiA

Upstream



Systems biology

Downstream



ADVANTAGES AND DISADVANTAGES

Advantages	Disadvantages	Solutions
High versatility	Protein folding	Chaperones or foldases
High complexity	Glycosilation	Genetic modification of insect cells/baculoviruses
Promoters power	Proteolytic processing	Proteolytic preservatives
Disulfide bond formation	Contamination of baculovirus particles	Diversity of downstream strategies
Post-translational modifications		

THE PRESENT: CERVARIX®

Information

- **Recombinant vaccine against Human Papillomavirus**
- **Bivalent:** Against HPV types 16 and 18
- **Simple non-enveloped VLP** composed by L1 protein
- Use of aluminum hydroxide **adjuvant**

Achievements

- The **second VLP-based approved vaccine**
- The **first approved vaccine using BEVS**

- Produced by **GlaxoSmithKline Biologicals**
- Approved by the FDA in **2009**
- Data from **13 clinical studies** involving **30,000 females** were submitted in support of licensure

CONCLUSIONS AND FUTURE PERSPECTIVES

BEVS is the most suitable and advantageous technology to produce VLP vaccines at large-scale

The approval of Cervarix® meant the acceptance of BEVS technology and a boost to more VLP vaccines based on BEVS to reach the market

Systems biology and genetic engineering are expected to improve both vector technology and bioprocess engineering

ABBREVIATIONS

VLP: Virus-Like Particle
BEVS: Baculovirus-insect cell Expression Vector System
HPV: Human Papillomavirus
FDA: Food and Drug Administration

RELEVANT REF.

- Liu, F., Wu, X., Li, L., Liu, Z. & Wang, Z. Use of baculovirus expression system for generation of virus-like particles: Successes and challenges. *Protein Expr. Purif.* **90**, 104–116 (2013)
- Vicente, T., Roldão, A., Peixoto, C., Carrondo, M. J. T. & Alves, P. M. Large-scale production and purification of VLP-based vaccines. *J. Invertebr. Pathol.* **107**, S42–S48 (2011)