CIC 2014 CCI

December 2-4
2 - 4 décembre
OTTAWA

Canadian Immunization Conference
Conférence canadienne sur l'immunisation

Towards clinical development of a vaccine to prevent Respiratory Syncytial Virus (RSV) infection

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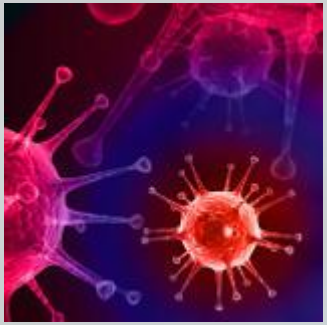
National Research Council of Canada

Disclosure Statement

- I am a member of the Scientific Advisory Board of Folia Biotech Inc

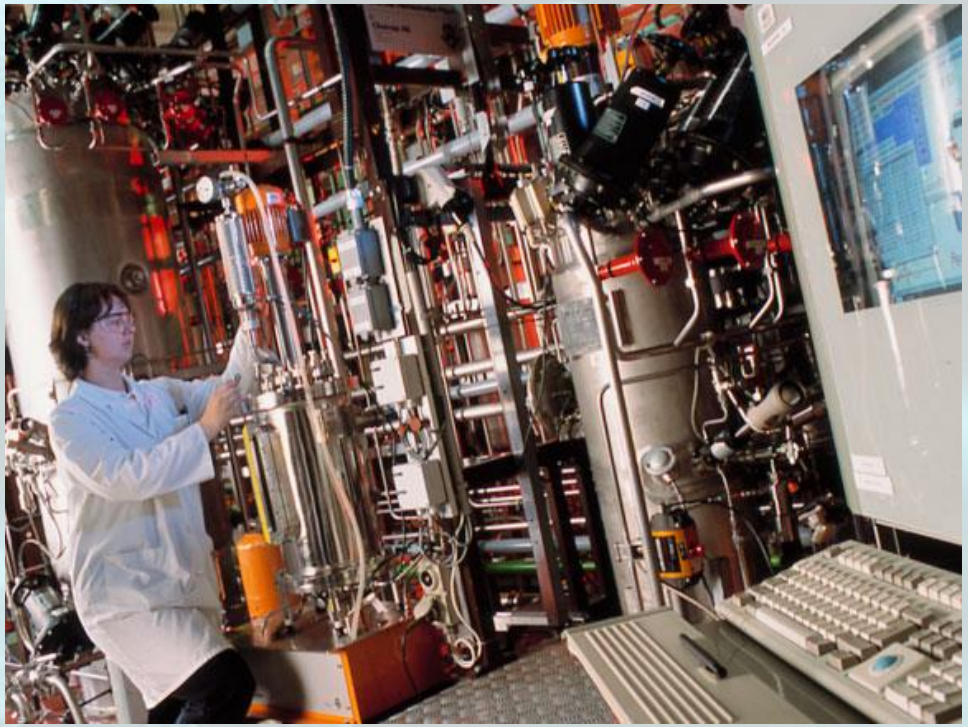
A Canadian Solution



- VIDO-InterVac has developed a vaccine that combines the respiratory syncytial virus (RSV) F-protein immunogen with a patented defined novel adjuvant.
- A partnership with the Pan-Provincial Vaccine Enterprise Inc. (PREVENT)
- NRC was contracted to develop the expression system and process to manufacture RSV F-protein and eventually tech-transfer to a cGMP facility to produce material for clinical studies

NRC unique research facilities, infrastructure and capabilities

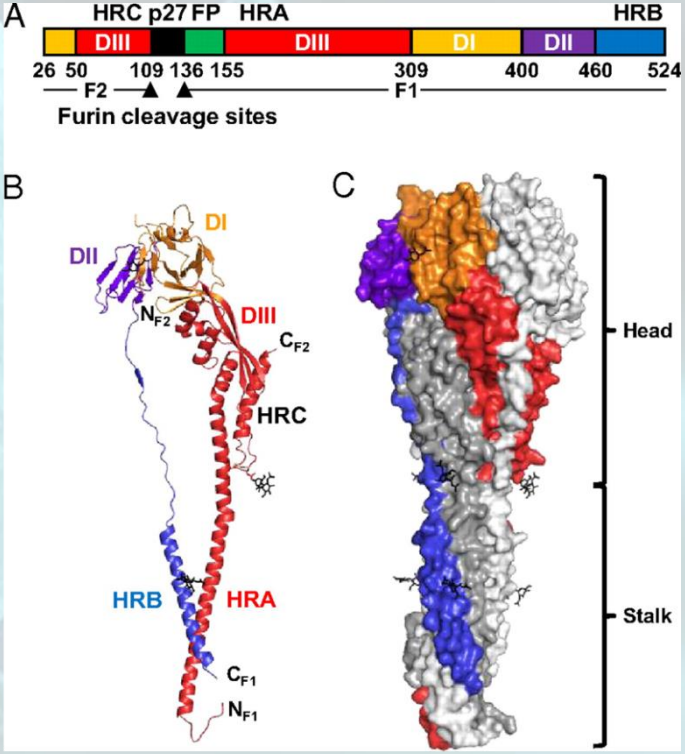
- Scale-up of **bacteria, yeast, mammalian cells, insect cells** and **viruses** in Containment Levels 1, 2 and 3
- **Purification** of GLP-quality material up to 1500 L **for microbial systems and up to 500 L for mammalian cells.**
- **GLP-compatible processes and product** for proof-of-concept in animals
- Process validation, documentation, and **training/ support for tech transfer to GLP- and cGMP-certified facilities**



Microbial fermentation pilot plant, 6100 Royalmount, Montreal, QC

From Bench to Process Development

- Construction and evaluation of RSV-F protein expression vectors for transient expression
- Generation of RSV-F standards for the development of quantification assay based on Sandwich-ELISA, UPLC
- Generation of stable clones to produce RSV- F
- Development of processes for the Production and Purification of RSV-F at 20 L scale



Swanson K A et al. PNAS 2011;108:9619-9624

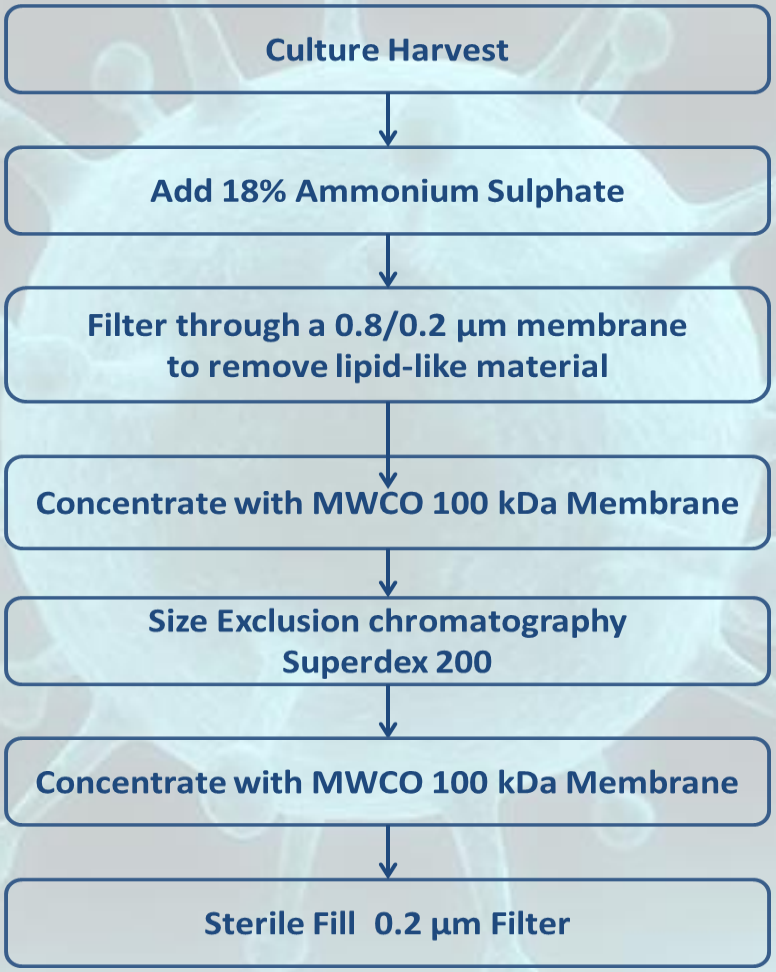
Technology Innovation – Cumate-Inducible Switch

- Development of a production process of RSV-F protein with cGMP-compliant CHO^{BRI} cell line in a serum-free suspension cell culture system using cumate-inducible expression vector
- Harvesting in 8-9 days post induction with viability of >60% in working volumes of 12-20L, where the production is extended by reducing the temperature from 37°C to 30°C

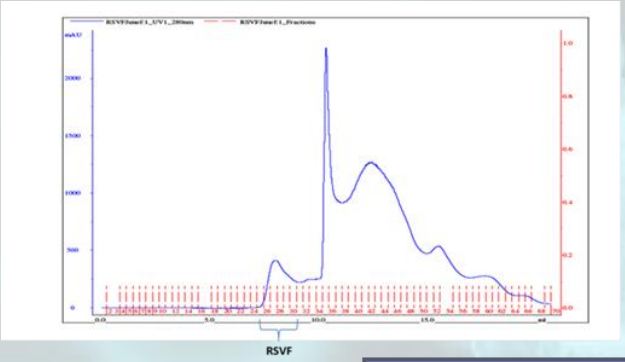
Technology Innovation – Process Development

- **Quantification** - Development of a rapid and robust analytical method based on UPLC
- **Functional Assay** - Development of functional assay based on ELISA
- **Reference standard** - his-tagged variant of RSV-F protein was produced for analytical method development
- **Purity and Identity** –SDS-PAGE / Western

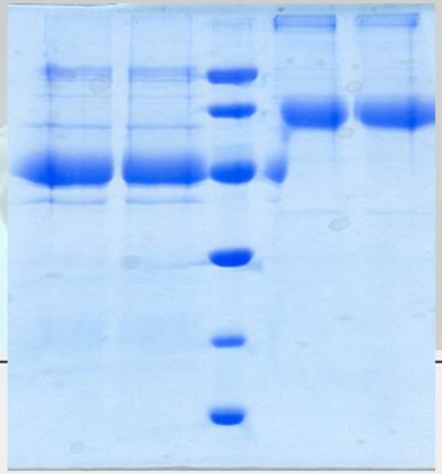
RSV-F Protein Purification Scheme

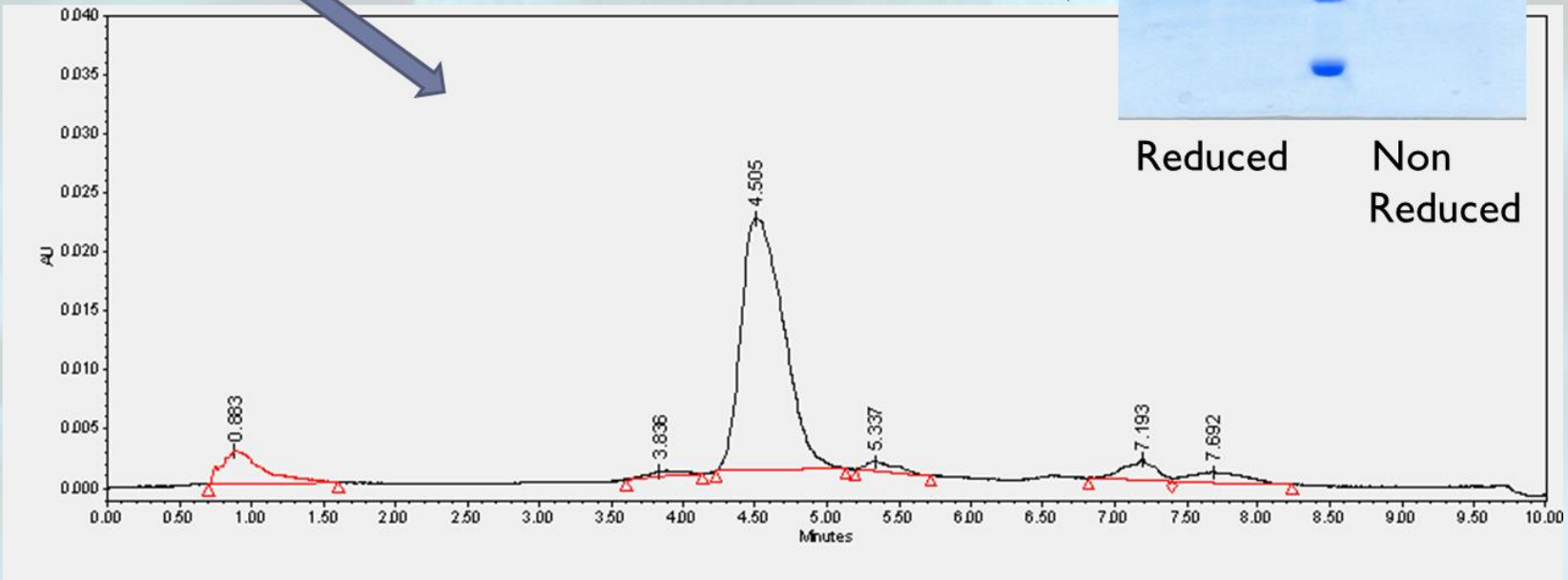


UPLC of RSV-F protein - peak from SEC



Conc by 100KDa MWCO





Conclusions

- Stable clones were generated to produce RSV-F protein by GMP-compliant CHO^{BRI} cell line
- ELISA and UPLC methods were developed to determine the functionality and quantity of RSV-F. Purity was assessed by SDS-PAGE
- A simple and rapid purification scheme was developed to purify RSV-F based on ammonium sulphate precipitation and size exclusion chromatography
- A Production and Purification processes from bench-scale to cGMP manufacturing facility

Acknowledgements

NRC Team

- Parminder Chahal
- Amine Kamen (currently at McGill University)

Yves Durocher, Brian Cass, Sylvie Perret, Louis Bisson, Alaka Mullick, Julien Leroy, Joe Schrag, Gerald Rowe, Hongtao Qi, Hafida Aomari, Sylvie St-Arnaud, Tao Limei, Danielle Jacob, Rosa Tran, Paule Lachance, Josee Plamondon