NRC·CNRC

Biomanufacturing

The NRC helps biotechs produce their biologics and vaccines, from bench to pilot scale. Our teams can produce thousands of protein variants per year for high-throughput screening. Once a lead is selected, we develop custom clones and processes, scale them up in our pilot plants, purify and analyze the material, and provide documentation and quality assurance. We transfer our expression systems, processes and analytics to cGMP-certified manufacturers to stimulate a strong biomanufacturing sector in Canada.

Protein production in animal cells

- Production of antibodies, proteins, growth factors, receptors and peptides in wave bags up to 25 L
- Proprietary CHO and HEK293 expression systems for transient and stable production
- Cell line development: CHO$^{BRI\ TM}$
  - CHO$^{BRI\ TM}$ parental cell line genome fully sequenced
  - Cumate switch to turn expression on and off
  - CHO pool generation in 2 weeks
  - Selection of fully characterized stable clones within 4 months
  - Clonepix^{TM} and CellCelector^{TM} equipment
  - Animal component-free process from transfection to final clones

Viral vector production in animal cells

- Assembly of viral constructs: plasmids and promoters
- Production in wave bags up to 20 L
  - enveloped and non-enveloped viruses
  - virus-like particles (VLPs)
  - viral vectors (adenovirus, lentivirus, adeno-associated virus) for bioprocessing, vaccine and gene therapy applications
- Proprietary HEK293, A549, and CHO expression systems for transient and stable production
  - Cell line development: HEK293
  - Genes switches to turn expression on and off
  - Technology to increase viral production
- Time-lapse and confocal microscopy
- Flow cytometry analysis
- Virus quantification

Process intensification

- Integrated process development from final clone selection to bench-scale bioreactors (1 to 10 L)
- Fed-batch and perfusion process optimization based on protein-free and animal component-free media and feed development
- On-line monitoring tools
- Scalable processes to facilitate transition between bench and large-scale production

Small-scale production by microbial fermentation

- Engineering and selection of recombinant bacteria (*Escherichia coli, Methylobacterium extorquens*) and yeasts strains (Pichia, Saccharomyces)
- Production of peptides, proteins, nutraceuticals, organic acids, polymers, and probiotics

Scale-up at the NRC's pilot plants: preclinical GLP-quality material for toxicology

- Cell Culture Pilot Plant up to 500 L
- Microbial Fermentation Pilot Plant up to 1,500 L

Purification

- Mammalian, microbial, insect and plant products
- Stainless and single-use technologies
- Clarification, cell breakage and separation
- Chromatography: affinity, ion exchange, hydrophobic, mix mode and size exclusion
- Platform purification for harvests up to 5 L
- Robotic platform for high-throughput protein purification
- Endotoxin removal (microbial and plant)
- Formulation development
- Platform protein conditioning
- Development and pilot-scale runs of purification processes to facilitate transition to large-scale manufacturing

Glyco-engineering

- Improved half-life and stability of target proteins
- Optimized mAb effector functions: Improved Fc sialylation (anti-inflammatory) and reduced Fc fucosylation (ADCC)
- Three stages of optimization:
  - Pre-production: Glycan optimization on CHO cell lines, metabolic engineering, and co-expression of glycosyltransferases
  - During production: Sialidase inhibitor in culture medium
  - Post-production: Enzymes to modify glycosylation patterns on target proteins
- Production of enzymes and sialic acids as glycan remodelling tools

Case study

NRC played an instrumental role in scaling up the primary production and developing the downstream processing of REOLYSIN®, an oncolytic virus being developed by Oncolytics Biotech as a novel cancer therapeutic. REOLYSIN® is currently undergoing Phase 3 trials for head and neck cancer. It is also in various stages of Phase 1 and 2 trials for other indications including breast, lung and pancreatic cancer.

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