NRC·CNRC

Antibody generation, characterization, and optimization

The NRC's Human Health Therapeutics Research Centre can help you develop therapeutic, diagnostic, and carrier antibodies against cancer, infectious diseases, central nervous system (CNS) diseases, and other indications. We offer R&D services in antibody generation against a wide variety of target classes, as well as antibody characterization and lead optimization.

Our expertise

Your project will be guided to success by our experts, who have over 30 years of experience working with monoclonal, bi-specific, and multi-specific antibodies, as well as antibody-drug conjugates. In addition, our research teams possess deep expertise in human and camelid single-domain antibodies (sdAbs), whose unique features can be harnessed by clients seeking a wider range of options in their antibody development.

Target classes

We have experience generating antibodies against hundreds of different antigens, including:

- G protein–coupled receptors (GPCRs)
- Immunomodulators
- Ion channels
- Transporters
- Kinases, phosphatases and other enzymes
- Antibody idiotypes
- Protein complexes
- Histones
- Peptides
- Glycans
- Small molecules

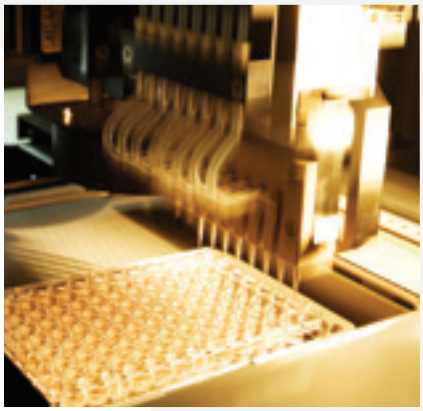
Antibody generation: Single-domain antibodies

Libraries

- Naïve libraries from camels, alpacas, and llamas: selection of sdAbs (VHHs) against non-immunizable targets
- Immune libraries from llamas: protein immunization, DNA immunization, whole-cell immunization, multiplexed / batch immunization
- Large synthetic human sdAb libraries: variable heavy (VH) and variable light (VL) sdAbs with engineered scaffolds (size: $>10^{10}$)
- Consistent isolation of sdAbs from immune libraries in low nM – pM affinity range

Screening and panning

- Panning for cell-surface molecule binding sdAbs, cell internalizing sdAbs, cross-species and isoform-specific sdAbs, high affinity binders, binders with high stability, pH-specific binding, and binders to a specific epitope (competitive elution)
- Panning against immobilized proteins, protein-domains, and immobilized proteins in specific orientation
- Next-generation sequencing (NGS) to identify binders



Antibody generation: Monoclonal antibodies

- Protein immunization, DNA immunization, whole-cell immunization, multiplexed / batch immunization
- Immunization of mice and rats
- Genetic immunization for complex proteins: single-pass and multiple-pass transmembrane proteins, and other proteins
- Panning for cell-surface molecule binding antibodies, cell internalizing antibodies, cross-species and isoform-specific antibodies
- Panning against immobilized proteins, protein-domains, and immobilized proteins in specific orientation
- High-throughput hybridoma generation: multiplexed immunization, electrofusion, secretor cloning and clone picking

Antibody characterization

Biophysical characterization

- Melting temperature (Tm)
- Long-term stability
- Aggregation
- Secondary and tertiary structure
- Refoldability
- Sequencing
- Immunoglobulin (Ig) subclass determination
- Kinetics and affinity
- Epitope binning / mapping

In vitro functional screening

- High-throughput cell binding
- High-throughput cell internalization
- Enzyme inhibition
- Ligand competition / blockade

Computational characterization

- Antibody structure modeling
- Binding affinity analysis
- Protein-protein docking
- Molecular dynamics simulations
- Protein electrostatics

Lead optimization

Engineering

- Stability improvement
- Affinity improvement
- Incorporation of tags for labeling or conjugation
- Generation of multi-valent and multi-specific sdAb formats
- Half-life extension using anti-serum albumin sdAbs

Molecular modeling and design

- Humanization for reduced immunogenicity
- Virtual affinity maturation: Assisted Design of Antibody and Protein Therapeutics (ADAPT) platform
- Computational developability assessment: stability, immunogenicity, aggregation

Equipment

- Mirrorball microplate cytometer
- Clonepix FL mammalian cell clone picker
- FACS Aria II cell sorter
- Surface plasmon resonance (SPR) instruments: Biacore T200s and Biacore 3000s
- Isothermal titration calorimetry (ITC)
- Circular dichroism spectroscopy (CDS)
- Size exclusion chromatography (SEC)
- Plate washers, dispensers, readers
- KingFisher purification system
- BSL-2 laboratories

Preclinical antibody development and biomanufacturing

Efficacy and safety of therapeutic antibody candidates can be validated through our functional characterization and analytics expertise, and at our preclinical *in vivo* facility. Production of antibodies is offered by the NRC's biomanufacturing experts, with scale-up at our microbial fermentation pilot plant and cell culture pilot plant.

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