Analytical Capabilities at ElevateBio BaseCamp Utilizing LentiPeak ™

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Abstract

Development of well-characterized, robust assays are key in the growing field of Cell and Gene therapy.

With the increasing number of clinical applications and interest in the field, robust, scalable, and cost-effective platforms for rapid analytics are needed.

Companies are seeking rapid turnaround times to get products to patients faster and ElevateBio BaseCamp's development of platform analytics support a range of release testing for Cell and Gene therapy products using our LentiPeak ™ system.

This poster will describe ElevateBio BaseCamp's platform analytical offerings and development capabilities.

Capabilities at ElevateBio BaseCamp

- ✓ Cutting-edge technology platforms
- ✓ End-to-end process development and cGMP manufacturing
- ✓ Integrated business model
- ✓ Industry-leading talent

Analytical Structure and Team at BaseCamp

- Deep expertise in analytical development at leading cell therapy companies with experience across HSCs, T cells, B cells, NKs and gene therapy modalities
- Early-stage assay development through late-stage assay validation and commercialization at leading industry companies
- Deep subject matter expertise in a **variety of analytical platforms** including but not limited to, **flow cytometry**, molecular biology, **PCR, cell-based assays** including **potency, immunoassays**, protein-based assays, biophysical methods, NGS, and **microbiology**
- Dedicated labs for AD and non-GMP testing
- **Aligned equipment and protocol Is between AD and QC** to allow for seamless assay transfers and qualifications
- **Quality Control** has separate labs for cell therapy and viral vector
- There are also dedicated microbiology labs, raw material program, and dedicated logistics team

Highlighted Assay Platforms in AD and QC Laboratories

- **Molecular**
  - Bio-Rad QX200™/QX ONE™ ddPCR System
  - Thermo QuantStudio™ 5 qPCR
  - Biomérieux BIOFIRE® MYCOPLASMA
- **Flow Cytometry/Cell Analysis**
  - Miltenyi Biotec MACSQuant® 16
  - BD FACSLyric™, 12-color
  - Chemometec NC-200 ™
  - Beckman Coulter Vi-CELL BLU
  - Curiox Auto-1000
- **Immunoassay Plate Readers**
  - Molecular Devices SpectraMax® M5
  - MESO QuickPlex SQ 120
  - Mabtech IRIS
  - ProteinSimple Ella
- **Protein Characterization**
  - ProteinSimple Maurice
  - NanoTemper Prometheus
  - Analytical Ultracentrifugation (AUC)
  - U/HPLC
- **Microbiology**
  - Charles River Endosafe® nexgen-MCS™
  - Biomérieux BACT/ALERT® 3D

LentiPeak ™ Qualified Platform Assays

Assay	Method	Testing Site
Sterility	USP<71>	BaseCamp
Endotoxin	USP<85>	BaseCamp
Mycoplasma	USP<63>	BaseCamp
Residual plasmid DNA	ddPCR	BaseCamp
Residual host cell DNA	ddPCR	BaseCamp
Residual Nuclease	ELISA	BaseCamp
Physical titer	p24 ELISA	BaseCamp
Infectious titer	ddPCR using a cell-based assay	BaseCamp
pH	USP<791>	BaseCamp
Appearance	Visual	BaseCamp
Osmolarity	OsmoTECH Pro	BaseCamp
E1A	ddPCR	BaseCamp
Replication Competent Lentivirus (RCL)	Cell Based	Outsourced
Adventitious virus agents (Bulk Harvest)	Multiple Methods	Outsourced
Proviral Sequence	Sanger Sequencing	Outsourced
Identity	TBD	BaseCamp

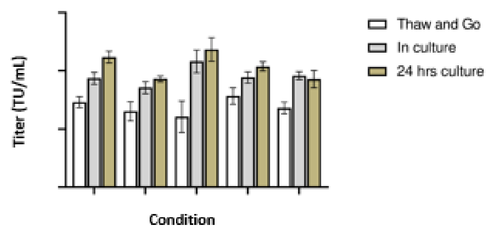
- The AD and QC groups at ElevateBio have worked collaboratively to offer a complete analytical control strategy for partners using our LentiPeak™ platform. Most assays are tested on site to reduce costs and TAT.
- Basecamp AD and QC are involved in life cycle management of all assays to ensure methods are phase appropriate and capable of delivering the highest quality data to partners.
- The team is always evaluating new technologies and automation to improve method performance, reduce costs and improve turn around times.

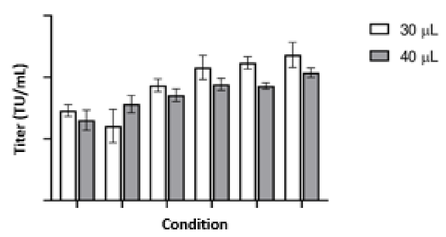
Prequalification and Qualification of a LentiPeak™ Platform Method

Analytical methods are needed to determine product quality. The methods must be scientifically sound and fit for purpose. Method development builds knowledge on method performance.

For example, an infectious titer assay was developed as an early phase potency method as part of the LentiPeak™ platform. The goal of the assay is to determine the genetic change i.e. quantify vector genomes in the drug substance.

During development, parameters such as cell density, volume, incubation times were assessed prior to prequalification of the method.

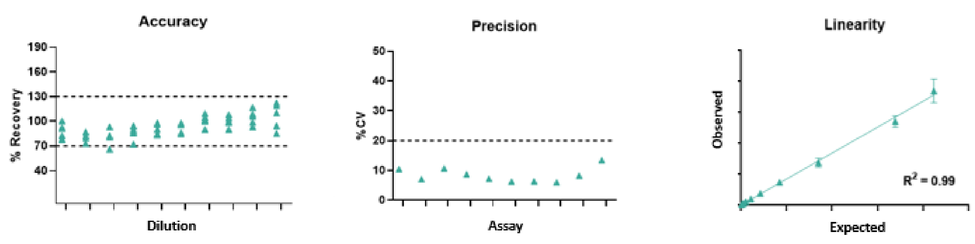




The design and results of the prequalification inform the design of the qualification.

During prequalification and qualification of the methods, **accuracy, precision, linearity, specificity,** and **repeatability** are assessed.

Once prequalified, the method is seamlessly transferred to QC via Basecamp's tech transfer team.



Case Study: LVV MoA Functional Potency

Vector potency tends to be more complicated because there are many other components like selecting a representative cell bank, a suitable target cell, and a representative LVV lot which includes determining a suitable range of vector. A suitable assay control also needs to be established and an appropriate readout.

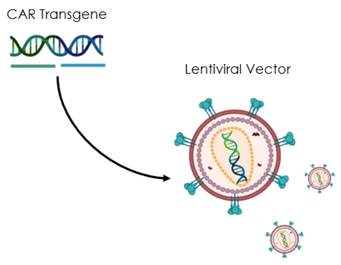
As the interaction between the CAR and target cell occurs, signaling cascade events result in expression of cytosolic enzymes and proinflammatory cytokines. The IFNg secretion is the targeted readout. This readout could be measured by ELISA, MSD, or perhaps western blot. ElevateBio developed an MSD assay for this method.

Critical Assay Reagent

Suitable Cell Bank
To minimize inter-assay variability
Infectivity should be reflective of GMP process

Lentiviral Vector Lots
LVV lot representative of clinical material

Cell Bank Expressing Target Receptor
Single use aliquots
Minimizes inter-assay variability

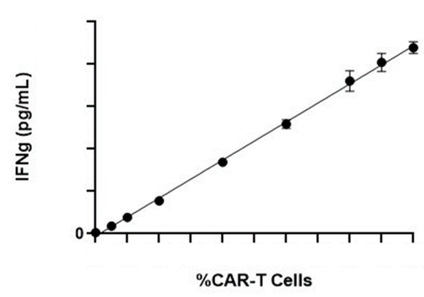


Assay Overview

Step 1: **LVV Transduction**
Requirements: Reference standard, Inter-assay control, Test article

Step 2: **Cell Harvest and Readouts**
Requirements: % CAR expression by Flow cytometry, Vector Copy Number by qPCR

Step 3: **CAR T – Target Cell Co-Culture**
Requirements: Cytokine release (IFN-g) by ELISA (**MoA potency**)



Conclusion

- Analytical methods maintain control of starting materials, in process unit operations, product release testing, and extended characterization, all of which facilitates consistent production of a safe and efficacious therapeutic.
- ElevateBio uses cutting-edge technology platforms, end-to-end process development and cGMP manufacturing formed by an integrated business model utilizing industry-leading talent
- We are dedicated to drive the DESIGN and DEVELOPMENT of GENETIC MEDICINES with our PARTNERS aimed at curing diseases.

Learn More

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