VIRAL DETECTION BY TRANSCRIPTOME ANALYSIS AT PATHOQUEST

PathoQuest is the leading expert in NGS services for the biopharmaceutical industry. We have now demonstrated our GMP NGS transcriptome assay can replace in vivo testing allowing you to meet your 3Rs objectives.

PathoQuest

GMP GOOD MANUFACTURING PRACTICE CERTIFIED

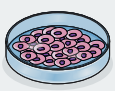
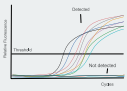
MODALITIES TESTED

- Manufacturing cell banks:
  - Monoclonal antibodies
  - Gene therapy
  - Oncolytic virus
  - Vaccines
- CAR-T and cell Therapy lots

BENEFITS OF NGS FOR VIRUS DETECTION

- ✓ Detection of "live" replicating virus
- ✓ Reduced sample compatibility issues
- ✓ Broader detection capabilities than tradition methods
- ✓ Identification of contamination
- ✓ Removal of animal based methods (3Rs) including MAP, HAP and RAP
- ✓ BMF available for FDA submissions

COMPARISON OF ADVENTITIOUS VIRUS DETECTION METHODS


	In vivo	*In vitro*	PCR	NGS
Speed	★☆☆☆☆	★★☆☆☆	★★★★☆	★★★★☆
Compatibility	★☆☆☆☆	★★☆☆☆	★★★★★	★★★★★
Detection of unknowns	★★★☆☆	★★★☆☆	☆☆☆☆☆	★★★★★
Identification of unknowns	☆☆☆☆☆	☆☆☆☆☆	☆☆☆☆☆	★★★★★
Volume required	★☆☆☆☆	★★☆☆☆	★★★☆☆	★★★★★
Detection of live replicating virus	★★★☆☆	★★★☆☆	☆☆☆☆☆	★★★★★

Traditionally, cell culture and animal models have been used for the detection of adventitious viral contaminants. The advantage of these systems is that both known and emerging viral risks could potentially be identified. However, the detection capability of these systems is limited because of low sensitivity and virus may not propagate. These assays are also very slow. Molecular methods such as PCR overcome many of the issues with speed, sensitivity and sample compatibility. However, PCR cannot discriminate between live virus and inactivated virus or viral fragments.

NGS combines the benefits of PCR with the agnostic capabilities of traditional culture or animal models. Regulatory guidelines now specifically include NGS for viral detection. For example, the ICH guideline Q5A [1] has been revised to state **"NGS is encouraged as a replacement for in vivo assays"**.

Q5A also states that **"because of the assay sensitivity and breadth of virus detection, NGS may also be used to replace cell-based infectivity assays, to overcome potential assay limitations"**. Manufacturers are still concerned about the ability of NGS to discriminate between live virus and inactivated viral or viral fragments – so called "false positives".

PathoQuest's GMP transcriptomic assay can help with 3Rs objectives by replacing in vivo assays in cell characterization packages, including mouse, hamster and rat antibody production assays. Our approach is shown to have superior performance over in vivo methods [2] and detects only live, replicating virus. With equivalent or better sensitivity across a broad range of viruses as well as manufacturing cell lines; including CHO, HEK293, Sf9 and Vero.

SAMPLE REQUIREMENTS*	SHIPMENT & STORAGE	STANDARD TURNAROUND TIME	FASTTRACK TURNAROUND TIME	SENSITIVITY OF DETECTION - ONE INFECTED CELL IN BACKGROUND OF UNINFECTED CELLS**	OUTPUT
Minimum $3x10^5$ cells (recommended $1x10^6$ cells) Backup sample required BSL1 or 2*	Dry Ice / -80°C	5 weeks	4 weeks	$1x10^3$ (Cox A16 and Mumps) to $1x10^7$ (Influenza A)	GMP CoA Any viral sequences are identified in report.

* Biosafety level classifications can vary between regulatory authorities – contact PathoQuest to discuss. Contact PathoQuest for patient or tissue samples.
** NGS sensitivity determined by dilution of infected cell extracts into non-infected cell extracts. Note, all tested viruses detected by NGS; Cox A16 was not detectable in *in vivo assays*, Echo 11, Measles and BVDV1 were not tested *in vivo* for ethical reasons.

REFERENCES

1. ICH Guideline Q5A(R2) on viral safety evaluation of biotechnology products derived from cell lines of human or animal origin.
2. Beurdeley-Fehlbaum, P., et al (2023) Vaccine, https://doi.org/10.1016/j.vaccine.2023.07.019 (Aug 2023)

To read our NGS vs in vivo comparison publication scan here:

To find out how PathoQuest can help you meet your 3Rs objectives visit **www.pathoquest.com/3Rs**

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