Science Applied Where It Matters

We believe that current viral vector optimization technologies fall short because they fail to address a fundamental challenge: **innate cellular antiviral defenses**. Viral vectors used in gene therapy and vaccine applications trigger these antiviral defenses which prevents optimal production, leading to lower yield, efficiency, and limited scalability. Virica has developed a unique approach to address this challenge.



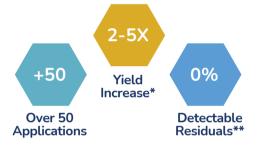


UNLOCK YOUR POTENTIAL WITH VIRAL SENSITIZER TECHNOLOGY (VSE™)

Virica has developed a library of Viral Sensitizers (VSEs) that reduce these antiviral defenses during production. VSEs alter cellular signaling and dampen antiviral defenses. This unlocks the potential for higher yields, consistent scale-up, and improved critical quality attributes (CQAs) based on application.

WHAT ARE VIRAL SENSITIZERS (VSEs)?

VSEs are patented small molecules that transiently attenuate antiviral pathways in cells thus enhancing virus production. VSEs are a simple additive introduced at time of infection or transfection and leaves no residual trace after purification.



I've been researching the concept of innate cellular responses and felt it was imperative to test VSEs. I didn't anticipate how significant their magnitude of enhancement would be both in terms of yield and full particle encapsidation."

-Brian Tomkowicz, Senior Director, Vector Engineering & Manufacturability "We set up a collaboration with Virica to test on human embryonic kidney cells producing AAV8...to see if VSEs drive productivity in a dynamic system, not just flatware"

> - Emmanuelle Cameau, Strategic Technology Partnership Leader, Cytiva

APPLICATIONS

Our VSEs have been validated in over 50 viral vector manufacturing applications across a wide range of cell lines and viral products. VSEs are primarily used to enhance viral titer, and vector quality attributes through scale-up. Virica has developed a compound library, along with high-throughput workflows, to formulate the optimal VSE combination for each cell substrate and target viral product.

*Yields are application dependent. VSEs must be evaluated in each application to determine actual yield

**Residuals after purification were found to be below limits of detection of both HPLC and Mass Spectrometry based assays

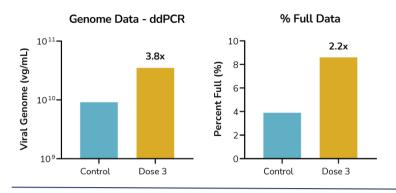
Typical Applications

Cell Substrate Product
HEK293 AAV
HEK293T Lentivirus
Eggs Influenza
BHK-21 MVA

VSEs have been evaluated in over 50 applications

Case Study: Scale-Up Validation of VSE-Assisted AAV Production

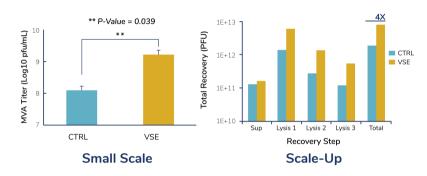




VSE formulation originally validated in Ambr[®]15 scale was successfully scaled to a 5L suspension bioreactor (3.75L working volume).

VSE addition resulted in multi-fold enhancement in total capsids (ELISA- data not shown), genomic titer (ddPCR) and % full AAV particles.

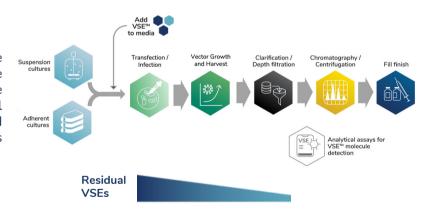
Case Study: MVA Production



Addition of a VSE formulation to a small-scale culture improved MVA yield by up to 10X across multiple strains. In a scale up model using an iCellis Nano (0.53-4.0m2), addition of the VSE formulation improved yield by 4X without any optimization, suggesting that scaling up of the technology is feasible.

Implementing VSEs

VSEs are a simple upstream process additive that have been shown to leave no residual traces** as they are rapidly metabolized by cells, and remaining traces are removed using standard purification methods. Residual testing is performed using specially developed and highly sensitive analytical assays such as mass spectrometry and HPLC.



The Virica Advantage

Virica has developed standard workflows to help clients evaluate the benefits of VSEs with options for in-house or Virica conducted testing. The end result is a tailor-made formulation optimized for each application with support, if needed, to help meet the necessary regulatory requirements.

Regulatory Support

Filing Support

Material Traceability

Residual Studies

Toxicology Studies

Typical VSE Evaluation Workflow



