NxGEN
VECTOR SOLUTIONS

TRANSFORMATIVE TECHNOLOGY

OUR MISSION

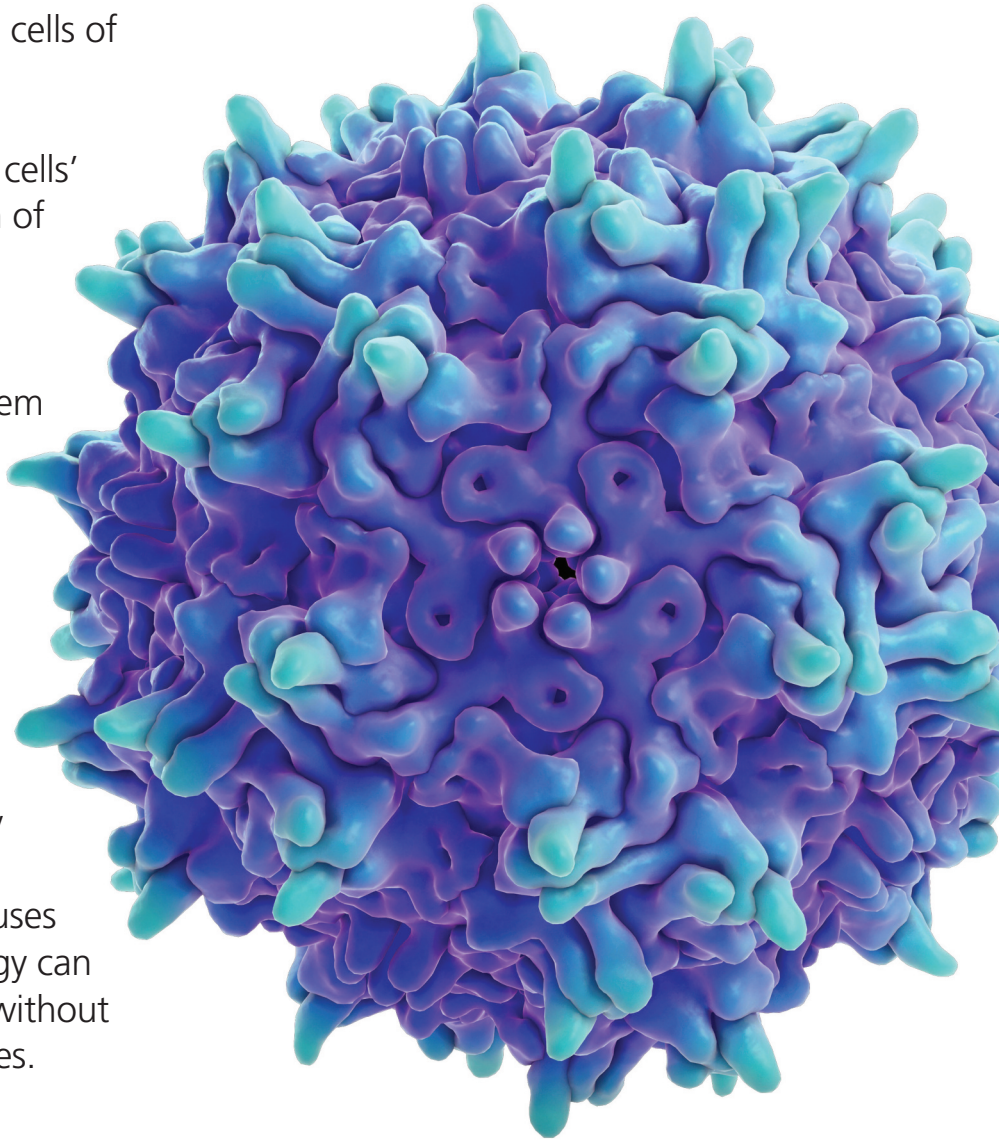
Our Scientists have discovered how to build viruses that are stealthy, healthy and under the radar.

Millions of patients worldwide suffer from diseases and disorders that can be cured with gene therapy, a technique by which viruses are used to introduce new, healthy, genes into the cells of patients.

The challenge lies in human cells' response to the introduction of new genes. The body views new genes introduced by viruses as potential threats, and the body's immune system fights off the viruses with the healthy genes.

NxGEN technology solves this problem. Our Scientists have discovered how to build viruses that are stealthy, coming in under the body's immune radar. By reducing or eliminating the body's immune reaction, viruses built using NxGEN technology can deliver their healing power without activating the body's defenses.

NxGEN Vector Solutions, LLC, is a gene therapy technology company focused on recruiting strategic partners to license cutting edge gene therapy vector technologies that revolutionize and transform the field and improve the lives of patients with genetic disorders.



Transformative technology that overcomes the challenge to effective gene therapy.

OUR TECHNOLOGY

Some people's cells have genes that are malfunctioning, or missing altogether, leading to a variety of serious diseases. Patients with these problems can be treated by delivering new, functional genes into their cells using carefully engineered viruses, which can be built to carry the desired genetic material into the body and incorporate it into the patient's cells.

Unfortunately, the human body's defenses respond to the engineered viruses just as they would to natural ones: as if they were a potentially deadly threat. These defenses have presented a substantial challenge to effective gene therapy: how to deliver the precious genetic cargo to cells without activating the body's natural defenses.

Our transformative technology overcomes this most significant challenge. The breakthrough came by identifying the precise reason that viruses were setting off the body's alarm bells. By removing the chemical signatures that were discovered to be the culprits, viruses could be designed to deliver the curative genes without activating the body's immune system.

THE SCIENCE

Adeno-associated viral vectors (AAV) are leading candidates for gene therapy. However, in Phase I clinical settings, immune responses toward the delivery vehicle or trangene product have compromised safety and long-term gene replacement success. Toll-like receptor 9 (TLR9) has the potential to recognize unmethylated CpG motifs in the therapeutic expression cassettes packaged in an AAV capsid and to induce a pro-inflammatory immune response. The inventors of NxGEN technology identified TLR9 as a critical element in immunoreactivity toward AAV associated antigens following intramuscular gene transfer, and the absence of TLR9 signaling resulted in suppressed Th1 (IFN-gamma) responses toward capsid and transgene antigen, minimal cellular infiltrate, and stable, enhanced transgene expression in target muscles. These findings were subsequently translated into a CpG-depleted AAV vector utilized for skeletal muscle gene transfer into WT mice. Both vectors contained a cytoplasmic lacZ open reading frame expressed from a mammalian-derived promoter flanked by AAV2 inverted terminal repeats (ITRs) and differed only in the abundance of CpG motifs: the AAVCpG+ vector contained a total of 324 CpGs, while the AAVCpG- vector total CpG content was 16. Muscle gene transfer experiments revealed that the AAVCpG- vector established long-term, enhanced transgene expression, evaded inflammatory T cell responses, and minimized infiltration of effector T cells. These findings show the remarkable ability of AAV gene therapy vectors built using NxGEN technology to escape the immune responses that have challenged the field of gene therapy for decades, leading to safe and effective gene transfer.

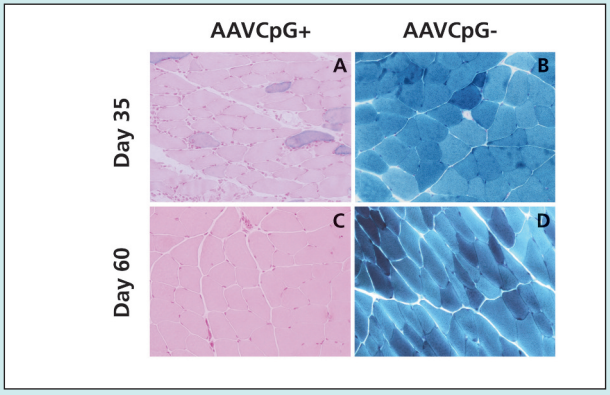


FIGURE 1: AAVCpG+ transduced muscle exhibits a progressive loss of detectable β-gal expression, while the muscle sections from CpG-depleted AAV-transduced mice display robust and stable transgene expression. To test the hypothesis that CpG-depleted AAV vectors would exhibit prolonged transgene expression, WT mice were injected intramuscularly with 1×10^{11} GC of AAVrh32.33CpG+ (AAVCpG+) or AAVrh32.33CpG– (AAVCpG–) vectors and muscle was recovered on day 35 (A and B) and day 60 (C and D) and stained for X-gal.

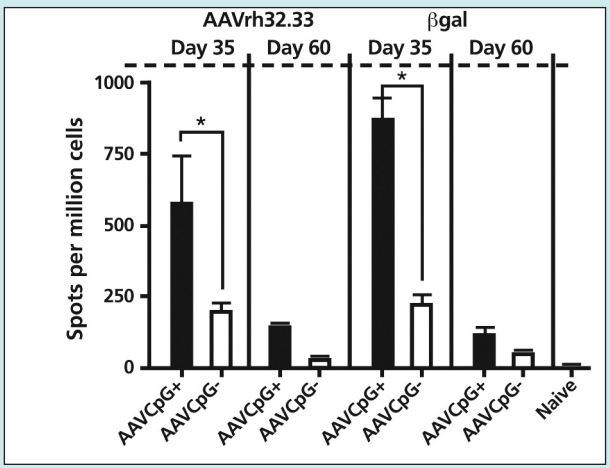


FIGURE 2: A significant decrease of primed transgene and capsid antigen–reactive IFN-γ ELISPOT responses was observed in mice that received the AAVCpG– but not AAVCpG+ vector. Splenocytes were recovered and processed for ELISPOT assays to quantify primed CD8+ AAVrh32.33 capsid and LacZ T cell immunodominant peptides. Results represent the mean ± SD of cytokine-producing cells.

CONTACT US/LICENSING

Gene therapy is an investment for now and in the future. Can you afford to build your vectors without investing in NxGEN technology?

NxGEN Technology is recognized as being one of the most important translational advances in gene therapy both in terms of therapeutic potential and commercial investment. The technology was cited by Sci-Bx: Science-Business eXchange, a publication of Nature Magazine, which features the ***"scientific content and commercial potential of the most important translational research papers from across the life science literature and provide knowledgeable perspectives on the key innovations and trends in translational science."***

Experts in the field agree. ***"The best trade-off one can currently imagine is to engineer rAAV vectors with better transduction efficiency, carrying optimized therapeutic transgenes and with reduced immunogenic profiles (CpG depleted genome, [Faust et al.], inert capsids, contaminant-free batches, minimum amounts of empty capsids, etc.). Such vectors would provide a higher therapeutic index, as they would permit therapeutic efficiency at doses sufficient to bypass pre-existing humoral immunity, but not high enough to trigger deleterious cellular immunity"*** (Vandamme et al., 2017).

We are in a new era of gene therapy, but the way the body views therapeutic genes introduced by AAV vectors as potential threats to human cells is anything but new. It remains a significant challenge. NxGEN technology overcomes this challenge, building stealthy AAV vectors that come in under the body's immune radar to deliver their healing power without activating the body's defenses.

NxGEN Vector Solutions, LLC
455 Massachusetts Ave., N.W., Suite 369
Washington, DC 20001
p: 202.765.7475
www.nxgenvectorsolutions.com