Gene Therapy Services

Enhance your preclinical research with Scantox' specialized expertise in gene and cell therapy studies of neurodegenerative and rare diseases.

The field of gene therapy is undergoing rapid advancements and thus holds immense promise to revolutionize treatments across a spectrum of genetic disorders. As a leading Contract Research Organization (CRO) specialized in preclinical research, our mission is to facilitate the translation of groundbreaking scientific discoveries into tangible preclinical applications.

Already more than 100 gene therapy *in vitro* and *in vivo* studies have been successfully completed, including studies with:

- Cell therapies (including handling of cells *in vitro*)
- Adeno-associated viruses (AAVs)
- Lentiviruses (LVs)
- Anti-sense oligonucleotides (ASOs)
- RNA therapeutics (e. g., siRNA)

Within Scantox, studies can be performed under BSL-1, BSL-2, and even BSL-3 conditions.

Our capabilities encompass a comprehensive toolbox enabling the optimization of both innovative viral and non-viral delivery systems meticulously crafted to optimize transgene expression and tissue specificity. Leveraging state-of-the-art *in vivo* and *in vitro* models, we strive to identify and validate therapeutic targets with greater precision.

Gene Therapy Services

In vitro

Gene Therapy Services

Optimization of your viral transduction protocol in different cell systems or comparison of transduction efficiency of different viral batches in the following cell types:

- Various neuronal- and non-neuronal cell lines (e. g., SH-SY5Y, HEK293T, HepG2)
- Primary mouse & rat cells
- Mouse embryonic fibroblasts
- Human fibroblasts (diseased & healthy controls)
- Human induced pluripotent stem cells (iPSCs)
- Organoids (in the pipeline)

***In vitro* Gene Therapy Services**

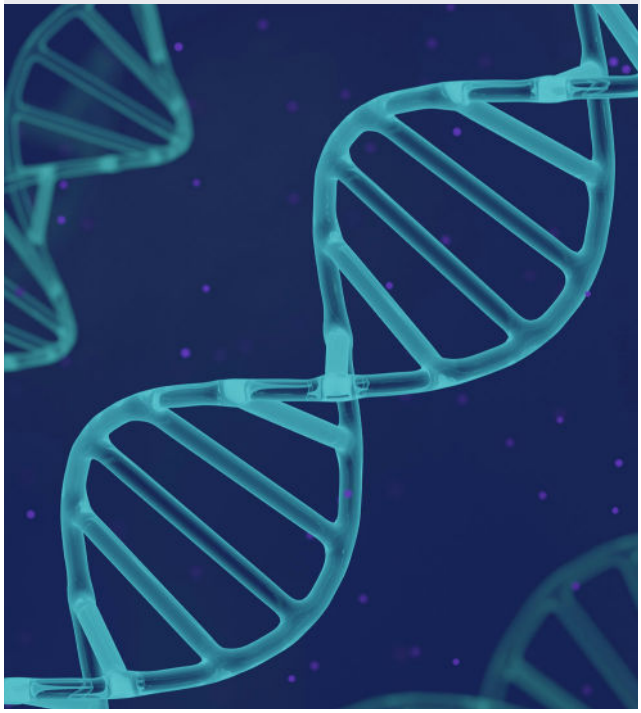
Distinguished by our expertise in surgical techniques, we offer precise administration of gene therapy agents, ranging from parenteral to stereotactic injections with a dual focus on maximizing efficacy while minimizing invasiveness. Moreover, we offer the possibility to administer gene therapy agents to larger animals such as rabbits and soon also to minipigs.

Test your gene or cell therapy in different study types such as:

- Efficacy studies
- Immunization studies
- Toxicology studies
- Biodistribution studies in rats and mice
- Pharmacodynamic (PD)/Efficacy studies in rabbits, rats, mice and transgenic mouse models, e. g., for rare genetic diseases, AD, PD, or ALS

Readouts

- Viability/cytotoxicity
- Life cell imaging
- Neuronal activity / oxidative stress / mitochondrial activity
- Efficacy testing using, e. g.,
  - qRT-PCR
  - Immunocytochemistry
  - Western blot/automated Western blot (WES)
  - MesoScale Discovery (MSD) platform
  - Enzyme-linked immunosorbent assay (ELISA)
  - Magnetic associated cell sorting (MACS)



Scantox can perform all common gene and cell therapy application routes in various preclinical models:

	Mouse	Rat	Guinea Pig	Hamster	Ferret	Rabbit	Minipig
Intracerebroventricular injections	x	x					
Intracerebral in different brain regions	x	x					
Cisterna magna injections	x	x					
Intrathecal (lumbar) injections	x	x					
Intravenous injections	x	x	x	x	x	x	x
Intramuscular injections	x	x	x	x	x	x	x

***In vivo* readouts**

- *In Vivo* Imaging System (IVIS) – mouse

Repeated *in vivo* sampling of blood and CSF in rats and mice enables a longitudinal assessment of various important and translational biomarkers. Provision of high-quality tissue and liquid samples for *ex vivo* analyses:

- Whole brain or individual brain regions
- Spinal cord
- Dorsal root ganglia
- Peripheral organs
- Various muscles
- Repeated and terminal CSF sampling
- Repeated and terminal blood sampling
- Bronchoalveolar lavage

Despite prevailing challenges such as those pertaining to delivery and durability, our commitment to transparency, clarity, and adaptability remains unwavering throughout all phases of gene therapy studies.

Ex vivo

Gene Therapy Services

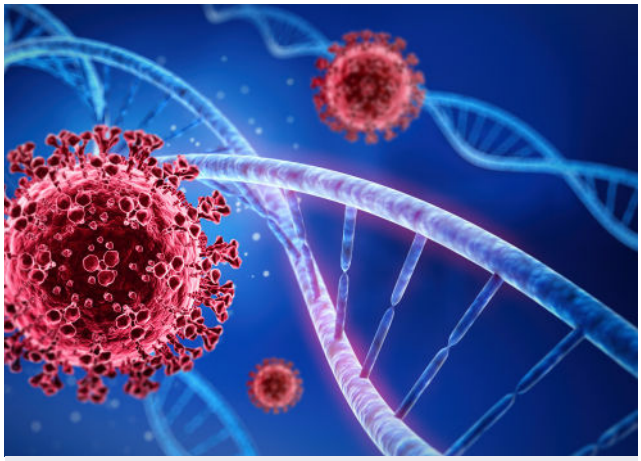
At the core of our proficiency lies our extensive expertise with adeno-associated viral (AAV) vectors, both *in vivo* and *in vitro*, augmented by a highly skilled team specialized in histological and biochemical analyses to support comprehensive *ex vivo* evaluations for gene therapy studies.

Moreover, qRT-PCR can be performed to quantify vector presence and distribution within target tissues. Recently, we established Fluorescence *In Situ* Hybridization (FISH) for the detection of AAV vectors, providing spatial information on vector localization, offering valuable insights into post-administration vector behavior. Additionally, the evaluation of target protein expression can be explored through biochemical and histological approaches, allowing for the assessment of therapeutic efficacy and protein functionality at the molecular and tissue levels.

Finally, we are using MACS for the isolation of specific cell subpopulations such as microglia. These advancements represent significant steps to enhance the precision and effectiveness of gene therapy, paving the way for an improved therapeutic outcome.

Analyze the biodistribution and efficacy of your gene or cell therapy using biochemical and histological readouts. Analysis of samples from *in vivo* studies performed *ex vivo* from the following species:

- Rodents' tissues and fluids (mouse, rat, guinea pig, hamster)
- Non-rodents' tissues and fluids (rabbit, ferrets, dog, Göttingen minipig, externally provided NHP tissue)
- Humans' tissues and fluids

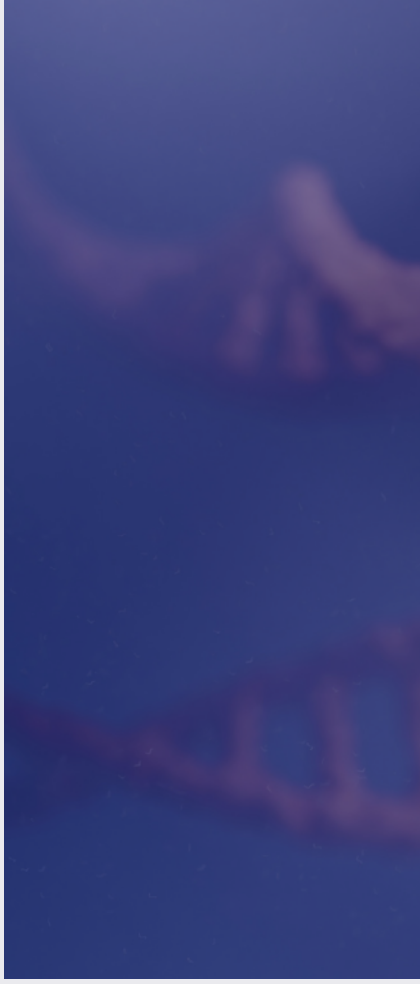


Biochemical readouts

- qRT-PCR
- Immunocytochemistry
- Western blot/automated Western blot (WES)
- MSD platform
- ELISA
- MACS

Immunohistochemical readouts

- Customized sectioning and staining
- Immunohistochemistry including target engagement and biodistribution
- Qualitative and quantitative multichannel immunofluorescence
- FISH – also in combination with immunofluorescence



Toxicology Services
Liver toxicity is a critical concern in the development of gene therapy treatments. Preclinical studies have shown that high doses of viral vectors, such as adeno-associated virus (AAV), can lead to hepatotoxicity, evidenced by elevated liver enzymes and tissue damage. Researchers are working diligently to optimize vector dosage and design safer delivery systems to minimize these adverse effects. By understanding and addressing the mechanisms of liver toxicity, the aim is to advance gene therapy towards safe and effective treatments.

Hepatoxicity screening:
- Liver enzymes (AST/ALT/ALP, GGT, GLDH)
- Bilirubin
- Complete blood count
- Immunofluorescence (to evaluate e. g., inflammation)

Central to our endeavors is the paramount consideration of safety. We present robust data derived from thoroughly conducted preclinical *in vivo* studies, which underscores the importance of accuracy and reliability for all methods applied.

Years of experience with clients worldwide ensure that our preclinical models consistently surpass industry standards, thereby expediting regulatory approval processes and streamlining the journey to market for novel therapies.

Regulatory toxicology (GLP)
We can support programs through the development phase offering studies from maximum tolerated dose (MTD) and dose-range finding studies to full scale chronic toxicity studies up to 26 and 39 weeks of duration for rodents and non-rodents, respectively.

Regulatory toxicology service:
- Genetic toxicology – non-GLP screening, GLP in vitro and in vivo battery and ecNGS approaches
- General toxicology
- Safety pharmacology – core battery to include CV telemetry, CNS and respiratory function
- Reproductive toxicology
- Juvenile toxicology
- Bioanalysis
- Dose formulation analysis
- Histopathology

Studies can be performed in rodents, rabbits, dogs and minipigs.
Further we can support formulation development and preclinical manufacture.

Scantox
Discovery

Important note:
Representative data are shown throughout this document. However, biological variability might cause deviations from shown data.

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