

## BIOANALYSIS SPOTLIGHT

# Biodistribution & Transgene Expression of Viral Vector Gene Therapies: Assessing Risk and Therapeutic Effectiveness in Preclinical Development

## Understanding Preclinical Biodistribution of AAV and *In Vivo* Gene Therapies to Enable Product Progression into the Clinic

- ◆ *In vivo* gene therapies based on adeno-associated viral (AAV) and adenoviral (AdV) vector-based products are targeted therapies administered systemically or into specific compartments to patients. Safety depends on delivery of the therapeutic to the target tissue. Uptake by non-target tissues occurs readily and can impact safety as well as modulate effectiveness of the therapeutic. To evaluate how a gene therapy is taken up and retained *in vivo*, biodistribution studies are conducted. Understanding the biodistribution of a product in preclinical models is essential for evaluating risk in the development of a gene therapy before entering the clinic.
- ◆ The distribution and persistence of the gene therapy vector is monitored to confirm the uptake and retention of the viral vectors in target and non-target tissues. The expression levels of the therapeutic transgene is also assessed in tissues shown to contain the vector.
- ◆ Combining biodistribution results with determination of transgene expression levels as a function of time enables understanding of correlations between dose, biodistribution, toxicology and unwanted outcomes to inform product development.

## Biodistribution

- ◆ ProtaGene delivers high-quality biodistribution results (Figure 1) and offers extensive experience to help clients evaluate data in conjunction with toxicology studies to better understand safety of the dosed product.
- ◆ We leverage state-of-the-art instrumentation along with extensive experience with designing and conducting biodistribution studies for AAV and other viral vectors dosed in common (e.g., rodents, primates) and other preclinical animal models.
- ◆ Effective and efficient transfer of existing methods from clients is frequently performed. Resultant biodistribution data is then used to gain further understanding of toxicology results.
- ◆ For programs needing additional support, our experts can design and develop methods to enable successful biodistribution assessments. Our team is experienced in designing studies to target genetic modifications to ensure specific amplification of the target molecules.
- ◆ Our new modern facilities, including automation, run under GLP and our senior leadership collaborates with clients in the design of validation approaches.

Figure 1. Vector levels in key preclinical tissues

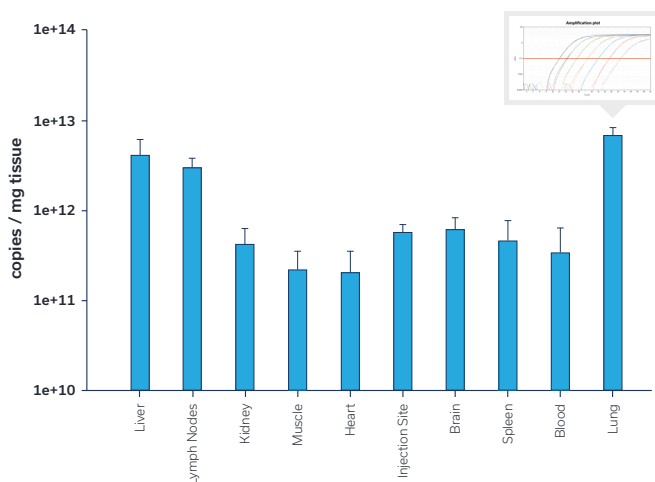


Table 1. Key tissues commonly analyzed with respect to route of administration

Systemic Administration		Ocular Administration	
Liver	Brain	Eye	Tears
Kidney	Heart	Optic nerve	Saliva
Lung	Muscle	Brain	
Gonads	Injection site	Draining lymph nodes	
Lymph nodes	Blood	Blood	

## Transgene Expression Monitoring

- ◆ An important part of evaluating viral vectors in preclinical studies is determining the expression of the transgene post-administration. The level of mRNA expression is quantified using reverse transcription and qPCR-based analysis (RT-qPCR).
- ◆ This approach confirms that the transgene in the delivered vector is successfully transcribed into mRNA, the precursor to expression of the therapeutic protein.

## ProtaGene Advantages

- ◆ Bioanalytical laboratory and workflows designed based on 25+ years of experience in the field
- ◆ Expert understanding of industry expectations for how molecular assays should be developed and validated
- ◆ Future-proofing approach used in preclinical study design to enable use in clinical studies
- ◆ State-of-the-art instrumentation and automation to support biodistribution and transgene expression studies
- ◆ Established processes to maintain the integrity of results generated during sample analysis while minimizing the risk of contamination
- ◆ Projects led and managed by dedicated experts



**With a deep understanding of this complex field and commitment to innovation, we're uniquely positioned to help innovators overcome challenges and bring life-changing therapies to patients.**

**–Paul Byrne**

## Meet ProtaGene's Senior Director of Genomics

**Paul Byrne** has 25 years of industry experience and can frequently be found speaking at symposia on topics such as: analytical development challenges for ATMPs, biodistribution and safety assessment considerations for cell and gene therapies and more. Paul received his BSc (Hons) in biology from the University of Stirling (UK) and his MSc in research from the University of Glasgow (UK).