IMGM®
LABORATORIES

ABOUT IMGM AND OUR SERVICE PORTFOLIO

Located in Martinsried, Germany, IMGM offers advanced genomic services tailoring each project design to the needs of our customers coming from pharma, diagnostics, biotech, clinics and academia. IMGM is certified service provider for Agilent, Affymetrix, and Ion Torrent PGM and holds an ISO 17025 accreditation for Sanger sequencing as well as for gene expression analysis and SNP genotyping using both real-time PCR and microarray technology. Beyond biodistribution, our services focus on:

BIOMARKER DISCOVERY

Associate biological markers on DNA or RNA level with the specific condition or disease of your research focus.

- Gene/miRNA expression analysis (Microarray, qPCR, RNA-Seq, small RNA-Seq)
- Sequencing of whole genomes, gene panels or specific target regions
- HLA typing

METAGENOMICS

Take a comprehensive view into the diversity and metabolic profile of your microbial community of interest.

- Phylogenetic identification by amplicon sequencing of e.g. 16S and 18S rRNA, ITS or other functional genes
- Generation of super-long reads with up to 1,000 bases
- Metabolic profiling with Shotgun Metagenomics and Metatranscriptomics

PHARMACOGENETICS

Study the effect of genetic variants (SNPs, CNV, InDels etc.) on drug efficacy and safety from basic research to clinical phases.

- DMET Plus Microarray (Affymetrix, covering 1'936 markers in 231 genes)
- qPCR (e.g.TaqMan) pre-designed and custom assays
- Sanger and targeted next generation sequencing
- GCP-compliant analyses and documentation

Customer satisfaction is our definition of success!

DAkkS Deutsche Akkreditierungsstelle D-PL-13105-01-00

Agilent Certified Services Provider Microarray-based Genomics Analysis

affymetrix Authorized Service Provider

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your outsourcing partner for
genomic services

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BIODISTRIBUTION SERVICES AT IMGM

Track where your gene therapy vectors, small RNA molecules or injected cells travel in your study subjects.

Why study biodistribution?

Have you ever sent a love letter to your finance office or a tax return to your sweetheart? Consequences to be imagined… What is obvious for messages is obligatory for gene and cell therapeutics: You have to make real sure that they arrive at the right place to result in the desired effect. Misdirection of letters will hopefully have reversible consequences which are mild compared to potential results of gene or cell therapeutic activity in the wrong place. Unfortunately, their unique potential to treat hereditary and other genetic disorders is accompanied by severe risks as tumorigenesis or chromosomal instability caused by unintended localization in the body or genome.

Imagination of scientists and licensing authorities and sadly, also gene and cell therapy cases in reality have delivered many scenarios and examples giving more than enough reasons to stringently control that the therapeutics' potential is unfolded in the right place only. In addition, the dosage i.e. the amount of therapeutic at the right or wrong place can be crucial for positive and negative effects.

How to study biodistribution?

The described paramount importance of the right dosage at the right place make it absolutely necessary to **most accurately** analyze both aspects for each gene or cell therapy candidate before its application in patients. Exactly this is done in a pre-clinical **biodistribution study**: After application in a model organism, the amount of the nucleic acid therapeutic in target and non-target tissues is absolutely quantified by qPCR, typically indicated as copy number or femtograms per milligram organ. Considering the significance of accuracy for biodistribution studies, licensing authorities have strict guidelines for the workflow and require **GLP-compliant* documentation** including study plans and reports.

Look inside and find out how a biodistribution study at IMGM provides accuracy and GLP-compliant* documentation in submission-ready format.

*NOTE: IMGM has successfully applied for the GLP certificate, which is expected in the second quarter of 2015. All of IMGM's working processes are already performed according to GLP requirements.

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your outsourcing partner for
genomic services

A biodistribution study at IMGM LABORATORIES

Project Design

Consulting and experimental design in close communication between you and your project manager at IMGM. Requirements of your project and specifications by licensing authorities are considered with topics including:

Nucleic acid therapeutic characterization

- Type of analyzed DNA or RNA molecule
- Optimal target region for qPCR primer positioning

Study volume and sample preparation

- Number of study animals
- Number and type of sample sources (organs, body fluids, the injection site etc.)
- Optimal preparation of each sample type
- Appropriate reference materials

Study overview and timeline

- From first sample to final results
- Realistic time frames for documentation, quality management and communication
- Validation and main study requirements

IMGM LABORATORIES Biodistribution Benefits:

- Free of charge and in-depth consulting
- Detailed project design by IMGM's biodistribution experts
- Consideration of licensing authorities requirements

Validation Study

The method of detection is established and validated for your specific target and sample sources. Calibration curves using reference material ensure accurate and reliable absolute quantification of your target nucleic acid by TaqMan assays.

Establishment of nucleic acid extraction

- Optimization of nucleic acid purification for each tissue type
- Minimal risk of contamination by stringent working conditions
- Quantity and quality control of every nucleic acid extract

IMGM LABORATORIES Biodistribution Benefits:

- High quality, project-optimized nucleic acid extraction
- Reliable yields by standardized, tissue-specific workflow

Contracting Audit

Project Consulting

Validation Study Plan

Establishment of nucleic acid extraction

TaqMan assay design and validation

Definition of quality control acceptance criteria

Validation Study Report

Main Study Plan

Preparation and analysis of main study samples

Main Study Report Data transmission

Documentation

Study plans and reports are of central importance for every biodistribution study. IMGM's extensive GLP-compliant* documentation clearly outlines project design and results and facilitates convenient communication with licensing authorities.

- Study plans and reports for validation and main study detailing all methods, experimental steps and results
- Approval by customer and IMGM's quality assurance (QA) ensures successful study accomplishment
- Data format is ready for submission at regulatory authorities

IMGM LABORATORIES Biodistribution Benefits:

- GLP-compliant* documentation in submission-ready format
- Comprehensive reporting and detailed graphics
- High quality study plans and reports ensured by extensive review process

TaqMan qPCR assay design and validation

- Design of a specific TaqMan assay for the nucleic acid therapeutic
- Wet-lab validation of optimal PCR conditions by analysis of PCR amplification plots and efficiencies
- Generation of calibration curve with defined target concentrations in appropriate background matrices
- Quantification of validation study samples with validated TaqMan assay in triplicates

Main Study

The nucleic acid therapeutic is quantified in the main study samples applying the validated TaqMan assay and QC criteria from the validation study. Extensive GLP-compliant* documentation in submission-ready format facilitates convenient communication with licensing authorities.

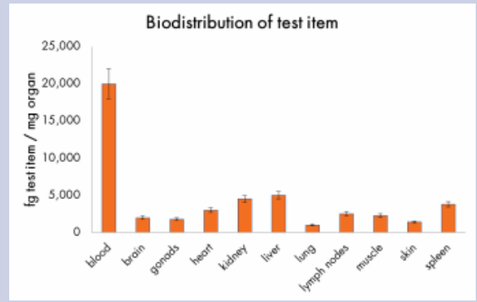

Figure 1: Biodistribution of test item in various tissues in fg/mg organ.

Analysis of main study samples

- Absolute quantification of nucleic acid therapeutic by qPCR in triplicates
- Quality controlled and validated qPCR conditions
- Highly accurate determination of therapeutic as absolute amount (fg) and copy numbers per mg organ (Fig. 1)

IMGM LABORATORIES Biodistribution Benefits:

- Maximum qPCR accuracy by validation and internal controls
- Highly precise absolute quantification of therapeutic as amount (fg) and copy numbers per mg organ

Definition of quality control acceptance criteria

- Clear-cut threshold values for qPCR accuracy and precision, sensitivity and selectivity
- Definition of limit of detection and quantification (LOD, LOQ)
- Precise determination of nucleic acid therapeutic recovery rate and stability
- Consideration of all regulatory specifications

IMGM LABORATORIES Biodistribution Benefits:

- GLP-compliant, detailed validation of qPCR assays
- Clearly defined quality control acceptance criteria and analytical range
- Reliable target detection and quantification

*see front page