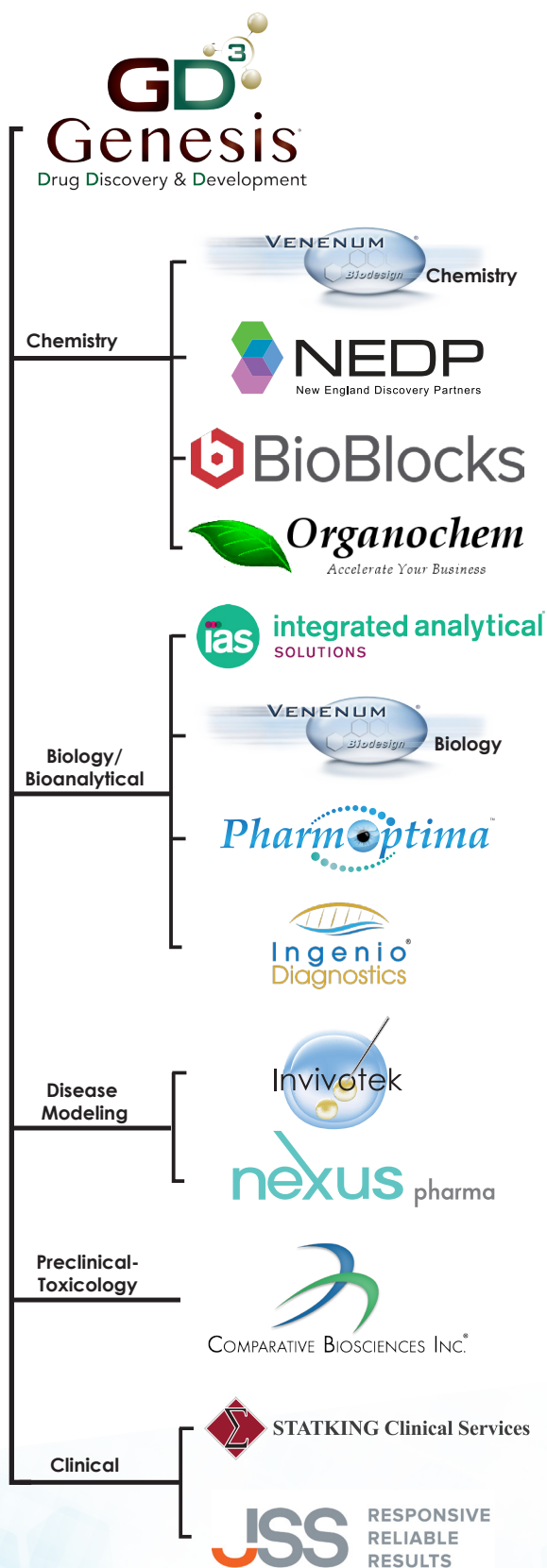




A GENESIS DRUG DISCOVERY & DEVELOPMENT COMPANY

OVERVIEW OF SERVICES



Genesis Drug Discovery & Development (GD³) is a fully integrated CRO providing services to support drug discovery programs of our clients from target discovery through IND filing and managing Phase I-IV clinical trials. GD³ portfolio includes services for HTS and assay development, synthetic organic and medicinal chemistry, DMPK/in-vivo pharmacology and safety pharmacology, toxicology as well as clinical trial services for the regulatory approval of novel drug and medical device products.

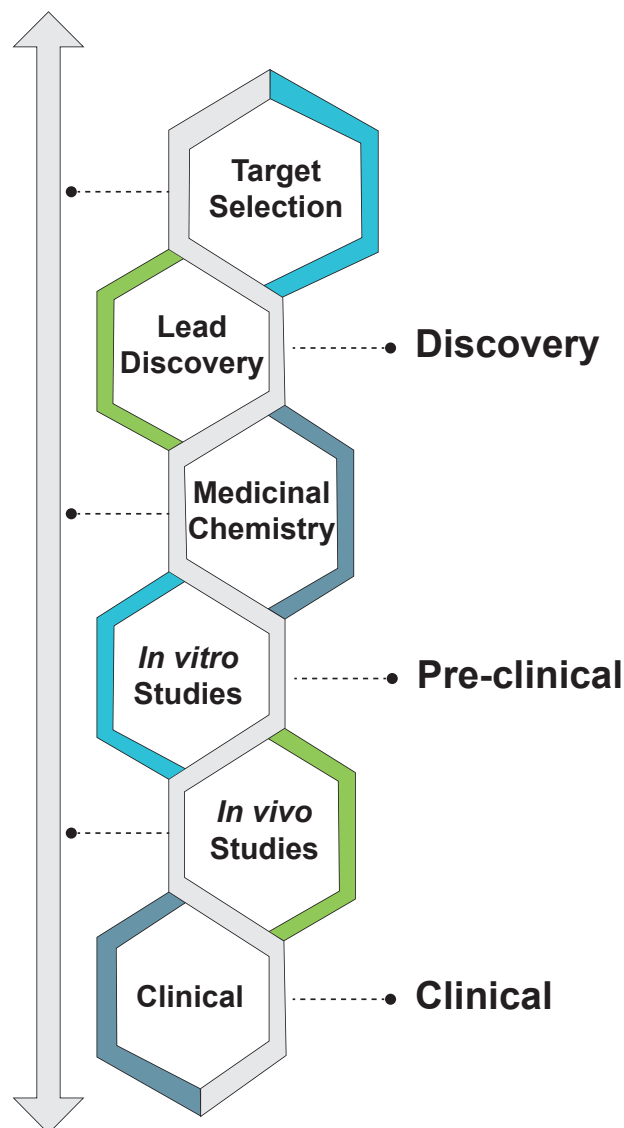
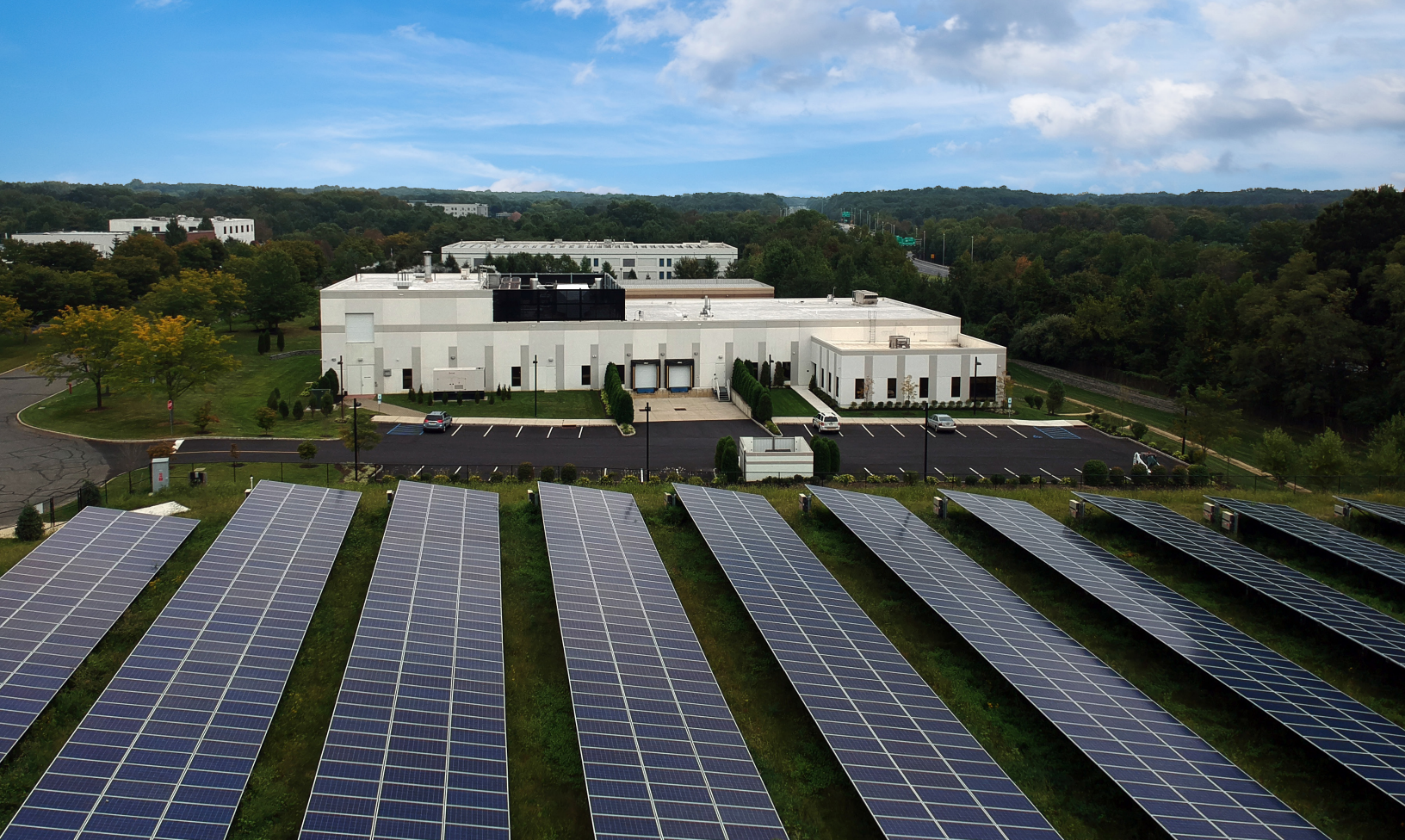


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Invivotek

Our flexibility in designing studies ensures that you will obtain the maximum amount of information to expedite your drug discovery efforts.

We offer both customized and standard preclinical *in vivo* pharmacology services in addition to new model development and validation. Our portfolio includes bioassays to support *in vivo* testing of potential therapeutics in rodent disease models, including Oncology, Immunology and Inflammation, Metabolic Diseases, Ischemia and Fibrosis, and rare disorders. We also have years of experience characterizing novel genetically modified rodents for therapeutically relevant phenotypes. The *in vivo* testing capabilities at Invivotek are supported by biochemical and molecular biology analysis, as well as functional assays using primary cell cultures established from various mouse tissues under disease model and normal conditions. These *in vivo* and *ex vivo* assays provide tools to validate potential drug targets, study the mechanism of action of various therapeutic candidates and explore drug efficacy biomarkers.

Invivotek is a contract research organization (CRO) specializing in the evaluation of therapeutic candidates in rodent models of human disease.

We provide expertise in:

- **Oncology and Immuno-Oncology**

- Efficacy studies

- **Immunology & Inflammation**

- Animal Disease Models
- Non-Disease *In vivo* Bioassays
- *Ex vivo* Bioassays
- Cell Therapy Evaluation
- Flow Cytometry

- **Metabolic Diseases**

- Animal Disease Models
- *In vivo* Energy Homeostasis and Body Composition Assessment
- Glucose Homeostasis
- Lipid Metabolism
- Cardiovascular Function

- **Neuroscience**

- Neurological and affective disorders
- Acute nociception and chronic pain models
- Opioid withdrawal model

- **Clinical Pathology**

Oncology & Immuno-Oncology

Efficacy Studies in Xenograft and Syngeneic Cancer Models in Mice

Our Oncology program for evaluating test compounds in xenograft and syngeneic tumor models in mice offers a unique suite of technologies, scientific expertise, and technical skills for monitoring primary and metastatic tumor growth *in vivo*.

Our capabilities include:

- Years of experience in the fields of Oncology and Immuno-Oncology
- Sophisticated surgery techniques for orthotopic tumor implantation and primary tumor excision
- Experience with xenograft tumor models in humanized mice
- A small animal radiation research platform for testing therapeutics in combination with targeted radiotherapy
- Advanced expertise in FACS analysis of tumor-infiltrating lymphocytes
- Expertise in biophotonic imaging (IVIS) for tracking orthotopic and metastatic tumor growth
- Biochemical capabilities for multiplex analyses of cytokines, hormones, and other analytes
- A multidisciplinary scientific team with extensive experience in the evaluation of a broad range of compounds and biologics in efficacy studies

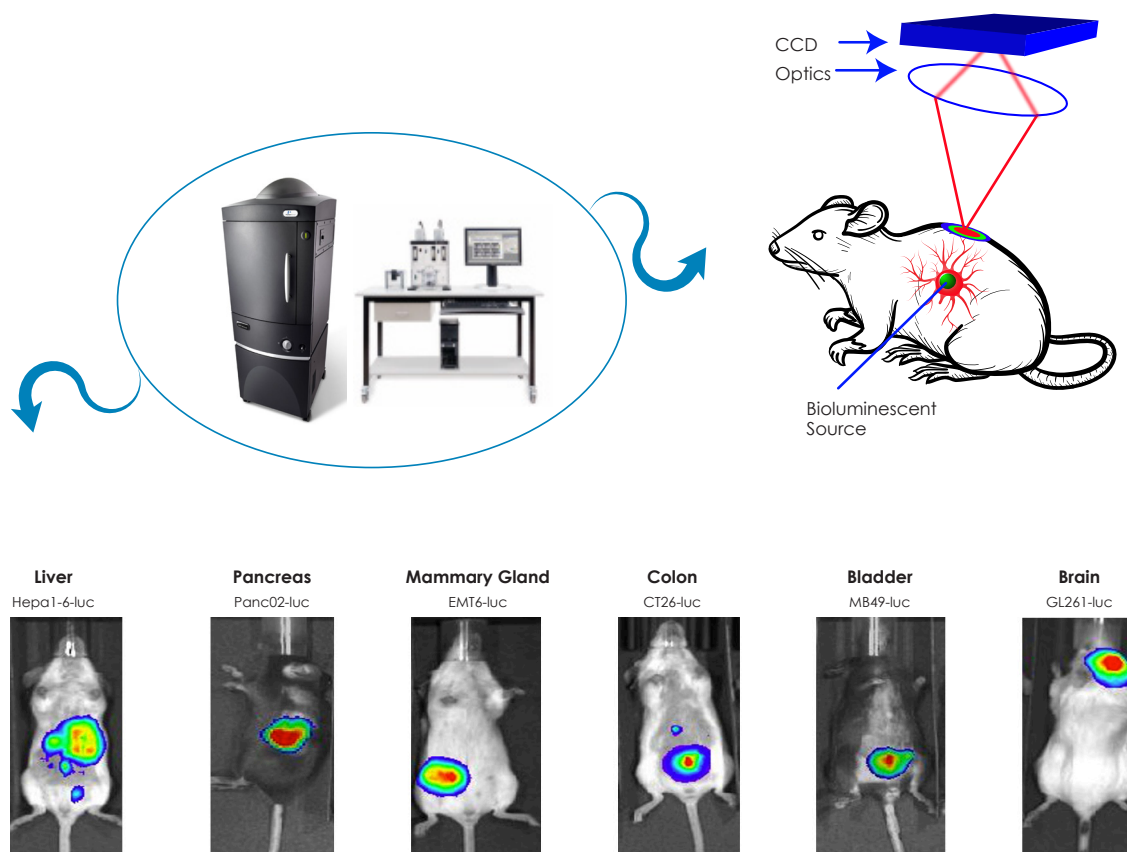
Specifically tailored, individual study designs are optimized to meet individual client needs. Interpretive data analysis and robust summary reports are provided at the completion of each study.

Invivotek provides Xstrahl's industry-leading Small Animal Radiation Research Platform (SARRP) services. This powerful technology incorporates CT imaging with precise radiation delivery to enable researchers to pinpoint an exact anatomical target and more efficiently and effectively incorporate irradiation into their immuno-oncology study designs.

- **Small Animal Radiation Research Platform (SARRP)**
 - Fully CT guided irradiation device
 - Radiotherapy application in small animal models
 - Ideal for studying radiotherapy with immunotherapy to mimic ongoing clinical trials



- IVIS® *In-vivo* Bioluminescence and Fluorescence Imaging System
 - Located within the vivarium to provide real-time non-invasive *in vivo* imaging technology to monitor orthotopic tumor growth and metastases
 - Customizable luciferase tagged tumor cell line generation on request



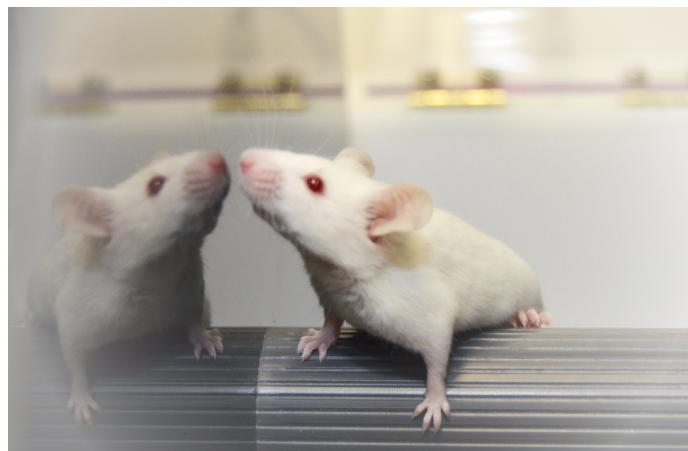
Immunology and Inflammation

Our multidisciplinary scientific team offers a broad spectrum of disease models and bioassays focused on Immunology and Inflammation through specifically tailored, individual studies designed to meet your drug discovery research needs. Interpretive data analysis and complete raw data sets are provided in the final report to accelerate your development process.

The Invivotek Immunology and Inflammation Program offers the following models and bioassays:

Animal Disease Models

- Antigen-induced Rheumatoid Arthritis
- Collagen-induced Rheumatoid Arthritis
- Monoclonal antibody induced Rheumatoid Arthritis
- Experimental Autoimmune Encephalitis (AEA) for Multiple Sclerosis (MS)
- Allergen-induced pulmonary inflammation for asthma
- Lipopolysaccharide (LPS)-induced airway inflammation
- Acute lung injury model (LPS-induced)
- Dextran Sulfate Sodium (DSS)-induced colitis for ulcerative colitis
- Trinitrobenzene sulfonic acid (TNBS)- induced colitis for Crohn's disease
- Allergic Dermatitis [fluorescein isothiocyanate (FITC), dinitrofluorobenzene (DNFB) or Oxazolone -induced]
- Antigen-induced Myasthenia gravis
- Graft vs. Host Disease



Non-Disease *In Vivo* Bioassays

- Non-lethal endotoxemia with LPS
- Antigen-dependent *in vivo* T cell proliferation by BrdU uptake
- OVA-stimulated *in vivo* antibody production (IgG1, IgG2a, IgG2b)
- KLH-stimulated *in vivo* antibody production (IgM, IgG)
- Delayed-type hypersensitivity induced by methylated bovine serum albumin (mBSA) or Keyhole limpet hemocyanin (KLH) with adjuvant
- Delayed-type hypersensitivity induced by SRBC
- Monocyte or neutrophil infiltration induced by thioglycollate, zymosan, curdlan, or trypsin
- Cutaneous wound healing

Ex *Vivo* Bioassays

- Serum and tissue cytokine profiling in animal disease models
- FACS analysis of lymphoid organs and tissue infiltrates
- Hematology five-part differential cell count
- Proliferative responses of T and B cells *in vitro*
- *In vitro* cytokine production assays
- T cell differentiation assay

Cell Therapy Evaluation

- Expertise and experience with cell based therapeutics
- Pluripotent Stem cell therapies for multiple indications in:
 - Oncology
 - Neuroinflammation
 - Autoimmune disorders
- CAR-T cells

Flow Cytometry

Invivotek provides state-of-the-art flow cytometry services from experimental design to specimen processing, acquisition, and data analysis for all stages of drug development programs. We can customize our assays, rapidly set up and develop your flow cytometry project with accurate reporting in a cost-effective and timely manner.

- All of our flow cytometry studies are conducted on a BD Biosciences LSRFortessa™:
 - The five laser apparatus allows for multichannel evaluation of up to 20 markers in a single tube
- Basic to comprehensive immuno-profiling available including lymphoid and myeloid panels for mouse and humans.
- Full service analytical team available for on-demand data analysis using FlowJo version 10.6.2.
- Invivotek uses the gentleMACS Dissociator Instruments from Miltenyi Biotec to generate single cell suspensions of tissues for FACS analysis.

Validated protocols are developed for the following tissues:

- | | |
|---------------|-------------------------|
| • Blood | • Brain and spinal cord |
| • Spleen | • Liver |
| • Bone Marrow | • Adipose Tissue |
| • Lymph Nodes | • Intestine |
| • Tumor | • Skin |

Multi-Color Panels for FACS Staining

- Treg Panel
- MDSC Panel
- Lymphocyte Panel
- Inflammatory Infiltrate Panels
- M1/M2 Monocyte/ Macrophage Panel
- White Blood Cell Profiling Panel
(T and B cells, monocytes, NK cells)



Metabolic Diseases

Invivotek offers a comprehensive evaluation of energy balance, glucose homeostasis, and lipid metabolism in normal and disease-model mice as well as models to replicate conditions such as nonalcoholic steatohepatitis (NASH) and nonalcoholic fatty liver (NAFL).

Animal Disease Models

- Diet-Induced obesity
- Streptozotocin (STZ)-induced diabetes
- Genetic models of diabetes and obesity
- Nonalcoholic steatohepatitis
 - Choline-deficient, amino acid defined High Fat Diet (CDA-HFD)
 - Neonatal streptozotocin HFD model
 - High fat (palm oil), high cholesterol, high fructose obesity model
- Genetic models of atherosclerosis and dyslipidemia

In vivo Energy Homeostasis and Body Composition Assessment

- Longitudinal body weight gain
- Body composition by DEXA:
 - Fat mass/ % fat/ lean mass/ % lean/ total tissue mass/ tissue area
 - Bone mineral density and content/ bone area
- Assessment of regional adipose depots
- Food intake
- Indirect calorimetry and locomotor activity:
 - O₂ consumption/ CO₂ production/ respiratory exchange ratio (RER)
 - Total horizontal / ambulatory/ non-ambulatory/ vertical activity

Glucose Homeostasis

- Glucose and insulin levels in glucose tolerance tests
- Gastric emptying
- Insulin tolerance test
- Tissue glycogen levels
- Pancreatic insulin content
- Glucagon, adiponectin, GLP-1 and other circulating hormones

Lipid Metabolism

- Triglyceride levels in oral lipid tolerance tests
- De novo lipogenesis *in vivo*
- Hepatic triglyceride export
- Serum leptin levels
- Serum ketone levels
- Serum and hepatic triglyceride levels
- Serum free fatty acids
- Serum and hepatic cholesterol levels
- Cholesterol distribution: VLDL, LDL, HDL
- Serum corticosterone levels

Cardiovascular Function

- Non-invasive blood pressure & heart rate with and without L-NMMA Challenge
- Exercise capacity
- Histological assessment of atherosclerosis

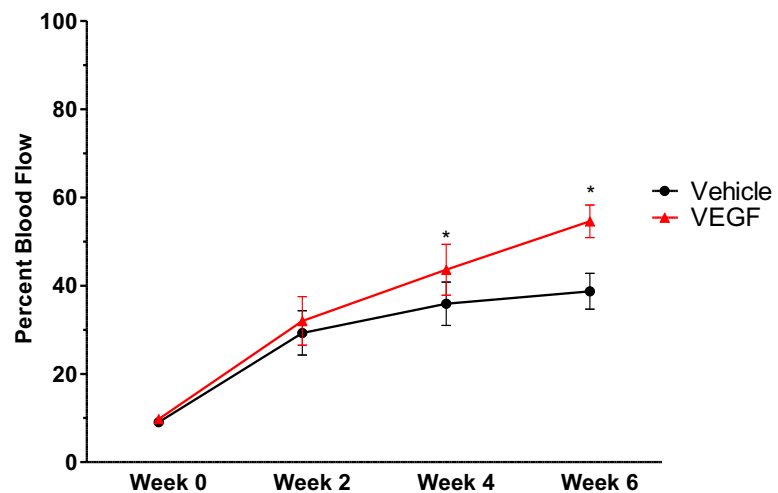
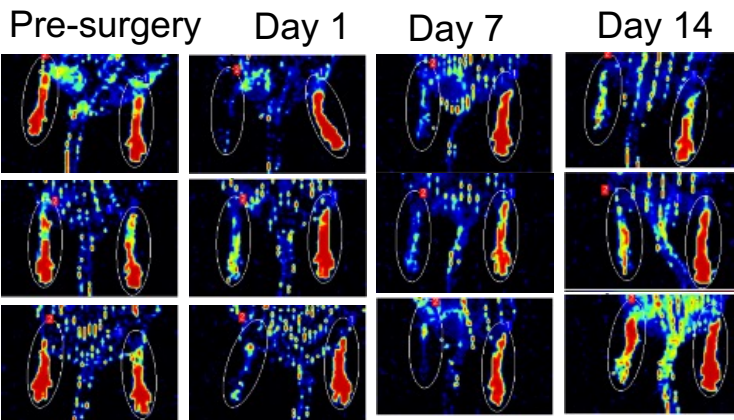
Arteriogenesis

- Hind-limb ischemia-
 - Includes laser Doppler measured cutaneous blood flow
 - Functional clinical score
 - Immunohistochemical analysis

Blood flow before and after surgery



Hind-limb ischemia model



Neuroscience

Our neuroscience research services provide a comprehensive approach to the assessment of neurological diseases through a wide range of behavior, pain and motor function tests for the purposes of testing efficacy and toxicity.

The Invivotek Neuroscience Program offers the following models:

- **Neurology**

- Locomotor activity (open field, long-term locomotor activity in home cage)
- Rotorod
- Grip strength
- Behavioral Battery

- **Pain**

- Acute nociception
 - Hot plate
 - Acetic acid
 - Tail flick
 - Hargreaves
- Chronic pain models
 - Inflammatory neuritis-carrageenan induced sciatic nerve in rats
 - Inflammatory pain – carrageenan and complete Freund's adjuvant foot pad injection



- **Opioid withdrawal model**

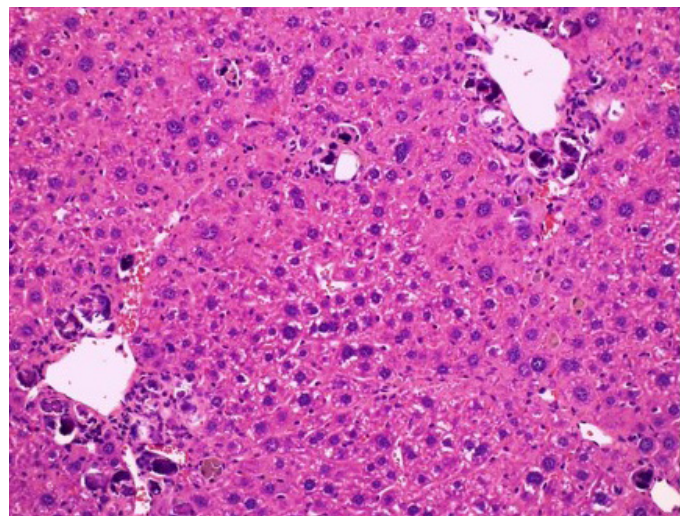
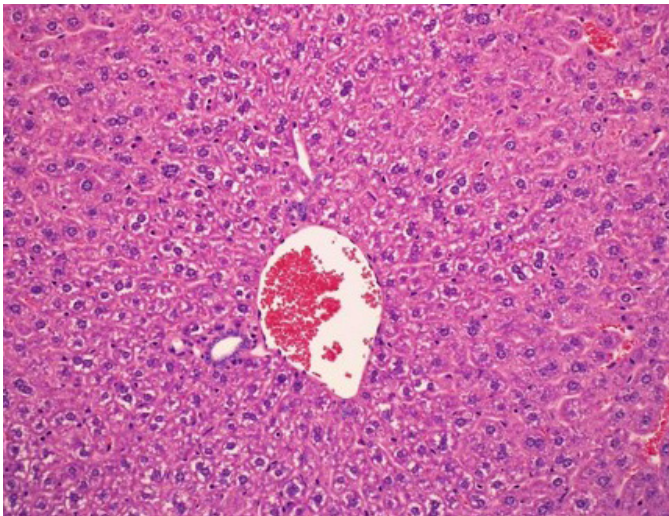
- **Affective Disorders**

- Elevated Plus maze
- Open field
- Novel environment induced feeding suppression

Clinical Pathology

Invivotek offers clinical pathology services to support animal models including:

- Irwin Behavioral Battery
- Serum and Urine Clinical Chemistries (Alfa Wasserman, Vet Axcel)
 - Standard liver function, kidney function and metabolic analytes
 - Serum and urine measurements
 - Specialized chemistries
- Hematology (complete blood cell count with differential) on Hemavet
- Histopathology necropsy and tissue preparation



Scientific Management

Rukiye Nazan Eraslan Ph.D. **Chief Scientific Officer**

Dr. Eraslan brings 20 years of experience in Immunology and Oncology working with multidisciplinary matrix teams comprised of colleagues from various groups including Discovery, Safety, Clinical, and Regulatory to develop and deliver biomarker strategies and potential combination therapies for Immuno-Oncology and autoimmune diseases assets. She has in-depth experience developing and implementing preclinical assessments tailored to target biology and mechanism of action for the evaluation of immune modulators in oncology and autoimmune diseases. She previously held positions at Xenogen/Caliper Life Sciences, Taconic, Inc., and Bristol Myers Squibb (BMS), leading Immuno-oncology and Inflammation platforms. Dr. Eraslan received her Ph.D. in Immunology from the University of Illinois at Chicago and did her postdoctoral fellowship at the Northwestern University Medical School in Chicago.

Vladimir, Khazak, Ph.D. **Head of Oncology**

Dr. Khazak is an experienced biologist with more than 20 years of experience working in multiple biopharmaceutical companies with a fundamental understanding of genetics and molecular oncology with particular emphasis on protein-protein interactions, gene regulation/expression, and signal transduction. He also has extensive experience in implementing and carrying out high-throughput screens, preclinical analysis for oncology lead compounds, and hands-on development of proprietary patient-derived xenograft (PDX) models. Dr. Khazak has a strong publications record in peer-reviewed journals and is an inventor of multiple patents in assay development, small molecule therapeutics, and molecular oncology.

Emily Arcamone B.S., RLATG **Manager, Resource Coordination**

Emily has over 20 years of experience working in biotechnology, including more than 15 years in a management role. She joined Invivotek's management team as Resource Coordination Manager from Taconic Biosciences, where she had a similar title (Resource Coordinator). Emily has extensive experience in the planning, scheduling, and allocation of resources to maximize the efficiency of the team, including in vivo and in vitro Research Associates. She has extensive experience in liaising and providing critical support to the Study Directors and their studies. Emily was involved in the AALAC accreditation process in multiple facilities. She is an AALAS Registered Laboratory Animal Technologist (RLATG). Ms. Arcamone received her B.S in Animal Sciences from Rutgers University.



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