Comparative Biosciences, Inc.

A TRANSLATIONAL APPROACH TO PRECLINICAL RESEARCH

SERVICES/PROJECTS

OVERVIEW

www.compbio.com

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786 Lucerne Drive • Sunnyvale, California 94085 • tel: 408-738-9260 • fax: 408-738-9278

Introducing Comparative Biosciences, Inc

Comparative Biosciences, Inc. was founded in 1996 with the mission to provide expert resources and quality service to all sectors of the biomedical community. We have grown each year steadily, increasing and expanding our capabilities and areas of expertise. In 2004, we moved into our state-of-the-art purpose built facilities in Sunnyvale, CA.

CBI features almost two decades of extensive experience offering GLP and non-GLP preclinical toxicology, efficacy, pharmacology, pharmacokinetics-pharmacodynamics, histopathology and safety studies on all laboratory species. We are fully-staffed, state-of-the-art, AAALAC-accredited purpose built facility with both an in house histopathology laboratory and a full time quality assurance unit. We are registered with the FDA, USDA, and OLAW and located in the heart of the Silicon Valley admist many biotech companies.

Our particular areas of expertise include ocular, dermatology, fibrosis, ototoxicity, wound healing and burns, stem cells, oncology, renal, inflammation, immune-mediated, CNS, cardiovascular, infection models, and devices, as well as contract histopathology, immunohistochemistry and custom model development. Our clients range from the smallest virtual company to pharmaceutical giants, academia, defense, and government.

Learn more about our **mission,** our core **management team,** and **scientific professionals**.

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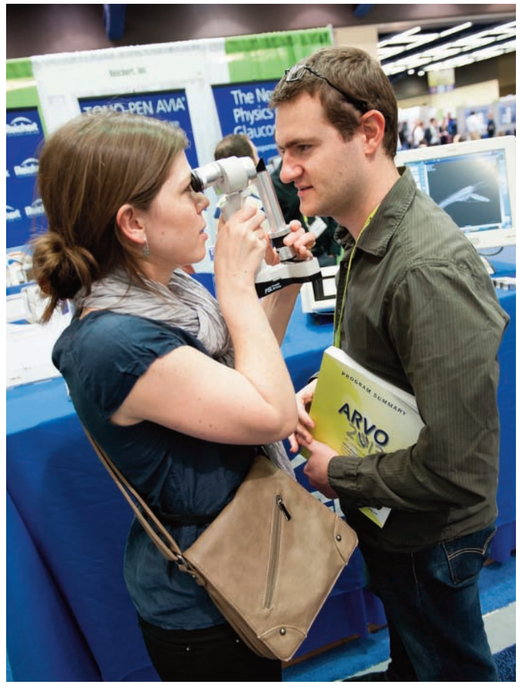
Scientific Overview

We specialize in developing a custom study plan in order to best meet your preclinical research needs and prepare for regulatory submission.

We offer expertise in the following areas:

- Toxicology
- Pharmacokinetics
- Pharmacology
- Efficacy
- GLP and Non-GLP Studies
- In-house Histopathology, Immunohistochemistry and TCR

Meet Carol Meschter, DVM, PhD, DACVP — CEO



Trade Shows

Toxicology — Pharmacokinetics — Pharmacology

Toxicology Studies

We offer a complete program of preclinical research services to support a range of toxicology. Beginning with early assessment of new molecules including single dose, multiple dose, and targeted studies, as well as directed or investigative toxicology, complete IND enabling toxicology programs, and finishing with long term carcinogenicity studies, CBI provides expertise, attention, and care on every study. Our study directors are experienced, communicative, and attentive, and we produce high-quality GLP reports in a very timely manner.

CBI provides expertise in the following preclinical contract toxicology services:

- Discovery Toxicology
- Investigative, Custom, and Special Toxicology
- Efficacy - Toxicity Studies
- Regulatory Toxicology

Toxicology Studies

Discovery Toxicology
CBI offers a number of fast, inexpensive research programs designed to assess, characterize, and rank new molecules for toxicity and efficacy, and to assist in the selection process. For early discovery toxicology projects, CBI also offers a range of nonGLP exploratory toxicity studies for early assessment of molecules including single dose, multiple dose, and targeted studies, as well as directed or investigative toxicology.

Investigative, Custom and Special Toxicology
There is often a need for specialized and complex toxicology studies, generally to address unanticipated or unusual toxicologic or pharmacological events or to conduct tolerability, efficacy or pharmacology studies that are of a novel, difficult or unusual nature. These studies are directed, hypothesis driven, and may have specialized or unusual techniques or methods. In some cases they are requested by the FDA or by clinicians. If you have such a problem, the skilled scientists at CBI can facilitate the protocol.

Efficacy-Toxicity Studies
GLP and nonGLP efficacy and efficacy-toxicity combination studies include assessment of systemic effects, toxicity, histopathology and immunohistochemistry of muscle and nerve, reversal by botulinum toxicity therapies such as therapeutic antibodies.

Regulatory Toxicology
We feature rapid study initiation and report preparation to meet sponsor deadlines or milestones. We comply with FDA, USDA, OECD, and ICH guidelines. Our PhD study directors are experienced, communicative, and attentive, and we produce high-quality GLP reports in a very timely fashion.

REGULATORY TOXICOLOGY STUDIES

SPECIES

All Species

ROUTES OF ADMINISTRATION

Standard Routes	Ocular	Infusion	Intra-thecal
Intravesicular	Aural-Otic	Dermal	Intra-cerebral
Intravaginal	Buccal	Topical	Intra-tumoral
Intra-rectal	Patches	Wounds	Intra-cardiac
Intra-nasal	Devices	Sublingual	Intra-intestinal
Intradermal	Device-drug combination	Nanoparticles	Others upon request
		Device Stem cell combination	

TYPES OF TOXICOLOGY STUDIES

Acute Studies	**Subacute & Subchronic**	**Chronic & Carcinogenicity**	**Special or custom toxicology**
Dose ranging	1-week subacute	3-month chronic	1-year chronic
Maximum tolerated dose	2-week subacute	6-month chronic	2-year chronic
Acute	4-week subchronic	9-month chronic	Transgenic carcinogenicity
Single dose	8-week subchronic	1-year carcinogenicity	Surgical toxicity
Limit dosing		2-year carcinogenicity	Stem Cells
			Others upon request

Pharmacokinetic Studies

CBI provides a complete range of research services in the area of pharmacokinetic, toxicokinetic, bioavailability, bioequivalence, and ADME studies.

We feature rapid study initiation and report preparation to meet sponsor deadlines or milestones. We comply with FDA, OECD, and ICH guidelines. Our capabilities in Pharmacokinetics include early exploratory, investigative, or screening studies, cassette dosing studies, juvenile studies, disease model studies, and formal studies that support regulatory submission. We specialize in unusual and customized studies.

Pharmacokinetic Studies

PHARMACOKINETIC STUDIES

ANIMAL SPECIES

- Mice
- Immunocompromized mice and rats
- Rats
- Cotton rats
- Guinea pigs
- Chinchillas
- Gerbils
- Hamsters
- Ferrets
- Pigs
- Juveniles and neonates
- Dogs
- Cats
- Diseased animals/animal models/tumor models

ROUTES OF ADMINISTRATION

- Routine systemic
- Dermal/topical
- Ocular (topical, intraocular, periocular)
- Otic, external and inner ear
- Infusion
- Depot
- Mechanical or osmotic pumps
- Intra-arterial
- Intra-articular or bone
- Intranasal
- Intracerebral (stereotaxic)
- Intrathecal
- Intra-tracheal
- Intra-intestinal
- Intra-rectal
- Intravaginal
- Intravesicular
- Surgical routes
- Other unusual routes

Pharmacokinetic Studies in Disease Models

Disease states can alter the metabolism of some test articles as can treatment with multiple drugs. Consequently, pharmacokinetic assessments in disease models and treatment states may be important. We offer custom pharmacokinetic studies in all the animal models and tumor models that CBI offers.

Large Animal and Colony Studies

CBI maintains a standing colony of healthy dogs, cats, and pigs for use in PK studies for our clients. Alternatively, CBI can also maintain dedicated colonies of dogs, cats or pigs specifically for individual sponsors. Dedicated colonies assure the sponsor that PK studies can be scheduled and conducted very rapidly, usually with a 1-2 week turn around between scheduling and delivery of specimens for analytical assessment.

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Pharmacology & Efficacy Studies

Pharmacology

CBI provides a range of pharmacology capabilities across a spectrum of indications that ensure reliable results in the drug-discovery and translation process. Assessment and analysis modalities are fine-tuned to meet the specific requirements demanded in each targeted area of scientific investigation.

Our specialities in Pharmacology and Efficacy Studies include:

- Pharmacology and efficacy modeling in multiple areas
- Custom model development
- Surgical modeling
- Investigative studies
- Combination GLP efficacy and toxicology studies

Animal Disease Models for Multiple Indications:

- Ocular
- Otic
- Cardiovascular
- Inflammation
- Dermatology
- Arthritis
- Allergic and Immune Mediated Studies
- Wound Healing and Scarring
- Fibrotic: skin and lung
- Anti-infective studies
- Oncology and xenograft
- Botulinum
- Central nervous system
- Rengenerative medicine
- Atherosclerosis
- Metabolic Diseases

Dermatology

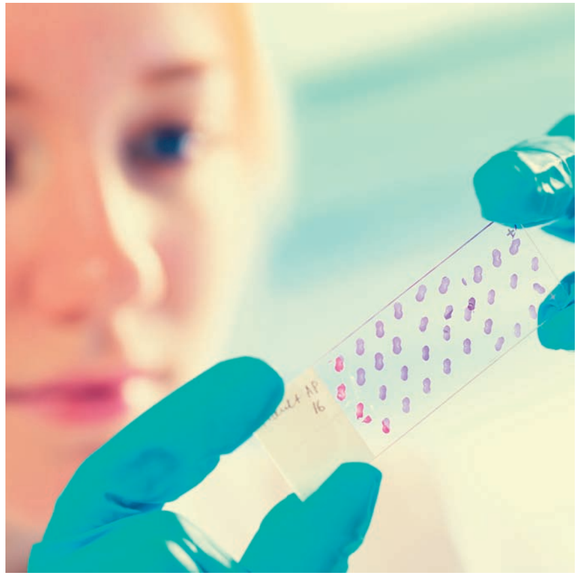
Comparative Biosciences, Inc. has demonstrated expertise in all phases of the drug development process in preclinical contract dermatology studies. Due to CBI's unique and extensive experience in dermatology studies and state-of-the-art facilities, we have the skill and expertise to accelerate new dermatology drugs, biologics, and devices from discovery through the drug development process, to regulatory submission and studies in man.

CBI conducts dermal studies in all species. Minipigs are the most used species for dermatologic assessments. Minipig skin is a close correlate to human skin in comparison to the skin morphology of other animals. CBI has over 10 years experience with minipigs in toxicology, dermatotoxicology, and dermal efficacy studies and recommends them as the nonrodent species of choice for dermatologic toxicology, pharmacokinetics and pharmacology.

- **Dermal Toxicology Studies**
- **Dermal Pharmacokinetics or Bioavailability Studies**
- **Dermal Pharmacology and Efficacy Studies**

Pharmacology: Dermal and Efficacy Studies

CBI provides a wide range of established and validated dermal pharmacology and efficacy studies in all species in normal and in diseased animals, and with single, multiple or infusion/slow release dose administration with small molecules, biologics, stem cells, nanoparticles and devices. CBI also offers custom studies and custom model development.



Our Dermal capabilities include:

- Dermal inflammation
- Delayed type hypersensitivity
- Dermal sensitization (Beuhler, Magnusson-Kligman methods)
- Dermal scarring and wound healing
- Keloid formation
- Delivery devices
- Dermal infection
- Botulinum

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Wound Healing Models

Whether it is a small nick, a large surgical incision, or a burn, healing is dependent upon the body's ability to heal itself. A vital role is played by our own natural biomolecules in the healing process, including their contribution to the growth of new cells and the development of new blood vessels that provide nutrients to those cells. Here at Comparative Biosciences, Inc. we are developing the models to test the therapeutics that could accelerate the wound healing process.

Wound Healing

Ocular Studies

CBI has demonstrated expertise in all phases of the drug development process in preclinical contract ocular studies. Our highly specialized staff is experienced in providing exploratory/proof-of-concept, GLP toxicology, pharmacokinetics, in vivo animal models, pharmacology, and histopathology/immunohistochemistry studies related to the eye.Due to CBI's unique and extensive experience in preclinical contract ocular studies and state-of-the-art facilities, we have the skill and expertise to accelerate new ocular drugs from discovery through the drug development process to regulatory submission. CBI is committed and dedicated to providing ophthalmology research and offers a complete range of services to pharmaceutical, biotech, and medical device companies in the following areas:

Ocular Toxicology Studies
Ocular Pharmacokinetics Studies
Ocular Modeling and Pharmacology
Optical Coherence Tomography (OCT)

Ophthalmic Pharmacology

CBI Offers a wide variety of validated ocular efficacy and pharmacology models related to retinal neovascularization, dry eye, inflammation, glaucoma, and pain.

Neovascular and vascular models

- Laser induced macular degeneration induction in mice, rats and rabbits
- Oxygen induced retinopathy in neonatal mice and rats
- STZ induced retinopathy in diabetic rats
- Angiotensin II induced retinal vascular leakage
- Corneal pocket or suture model
- Vegf-induced retinal vascular leakage

Dry eye models

- Scopolamine-induced dry eye in mice
- Botulinum-induced dry eye in mice
- ConA-induced model in rabbits
- Glycopyrrolate-induced model in rabbits
- Benzalkonium chloride-induced model in rabbits

Inflammation

- LPS-induced acute uveitis in rodents and rabbits
- F40 80-induced acute uveitis in rabbits
- Albumin-induced conjunctivitis in rabbits

Immune-mediated inflammation

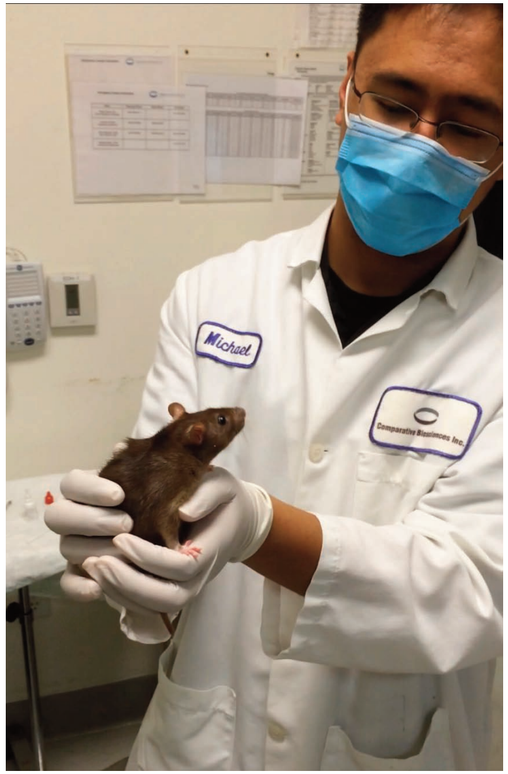
- Melanin associated antigen induced anterior uveitis in rats
- IRBP or S-antigen induced posterior uveitis in mice and rats

Glaucoma and ocular hypertension

- Laser induced glaucoma in rodents
- Corticosteroid-induced
- Water loading
- Chymotrypsin

Ocular Pain

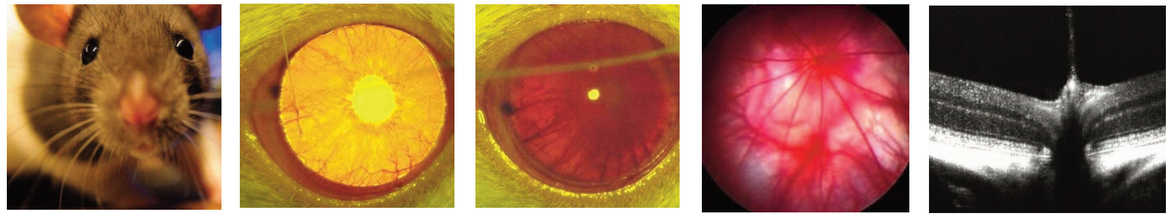
- Capsaicin-induced
- Formalin-induced



Ocular Studies

In vivo assessments may include clinical signs, Draize scoring, McDonald-Shadduck scoring, biomarkers, body weights, phenol red thread test, TBUT test, Schirmer test, slit lamp biomicroscopy, funduscopy, IOP, pachymetry, retinal scanning with the Phoenix retinal scanner, ERG, OCT, ultrasound and ocular photography.

- Clinical Signs
- Body weights
- Draize scoring
- McDonald Shadduck scoring
- IOP
- Pachymetry
- Ultrasound
- Ocular photography
- Tonovet
- Schirmer Test
- Phenol red thread test
- Tear Break up test
- Slit Lamp Biomicroscopy
- Funduscopy
- Phoenix retinal scanner
- ERG
- OCT
- Angiography
- Fluorescein dye corneal examination
- Aqueous or Vitreal Protein
- Aqueous or vitreal cell count



Normal rat eye, Grade 4 inflammation following MAA treatment

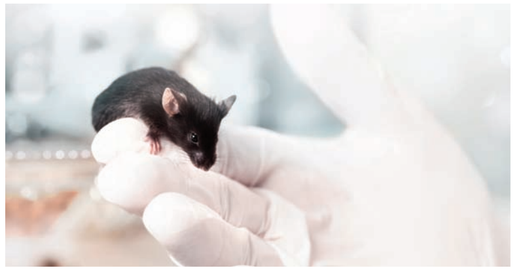
Brightfield

Optical Coherence Tomography OCT

STZ Studies

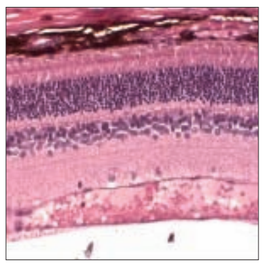
STZ Studies

CBI offers a robust and validated model of STZ-induced hyperglycemia and retinopathy in rats. Streptozotocin-induced hyperglycemia results in changes in the retinal pigmented layer consisting of increased thickness of the middle retinal layers, increased new vessel formation, reactive endothelium, dilated capillaries distended with either blood or edema fluid, acute inflammation composed of intravascular neutrophils, and neutrophils adhered to vessel walls and extravascularly by 4 weeks or longer post-STZ treatment. These changes were clearly evident histologically and were supported by Optical Coherence Tomography and retinal angiography. Examination of the retina via fluorescein angiographs reveals increases in retinal vascularity in streptozotocin-treated rats with areas of leakage particularly surrounding the optic nerve. These changes were compatible with and correlated with the histopathologic findings of increased vascularity of the retinal pigmented layer. OCT assessments clearly demonstrating thickening of the retina, primarily the middle layers following STZ induction. Treatment with triamcinolone significantly reduced STZ-induced retinal thickness as well as other ocular changes.

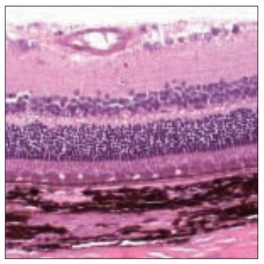


STZ Assessments include:

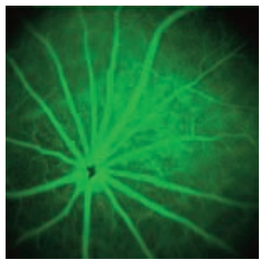
- Clinical observations
- Body weights
- Blood glucose
- Blood insulin
- Angiography
- OCT
- Histopathology
- Immunohistochemistry



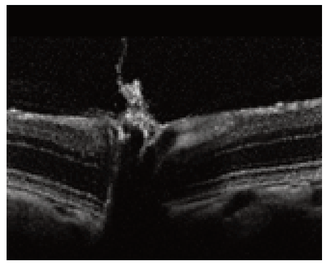
404: Histology, Normal Retina



202: Histology, STZ retina with increased vascularity and inflammation



Green and White:
Angiography of STZ retina
(Micron Scanner)



Black and White:
OCT of rat retina

Streptozotocin (STZ) is an antibiotic that can cause pancreatic β–cell destruction, so it is widely used experimentally as an agent capable of inducing insulin–dependent diabetes mellitus (IDDM), also known as type 1 diabetes mellitus (T1DM). These models for diabetes can be employed for assessing the mechanisms of T1DM, screening potential therapies for the treatment of this condition, and evaluation of therapeutic options.

Optical Coherence Tomography (OCT)

Optical Coherence Tomography

CBI is proud to announce that it is now offering optical coherence tomography (OCT) for research and toxicology studies in laboratory animals. Optical coherence tomography (OCT) is an optical signal acquisition and processing method that captures micrometer-resolution, three-dimensional images from within biologic tissues and in particular, eyes. Our Envisu R2200 SDOIS Imaging System (Bioptigen, Inc) allows us to assess the retina, optic nerve, retinal vasculature, lens and anterior segment. Doppler assessment of ocular venous and arterial blood flow is also available.

CBI is ready to include OCT assessments in both ocular pharmacology studies and ocular toxicity studies in a research or regulatory environment.

OCT Overview

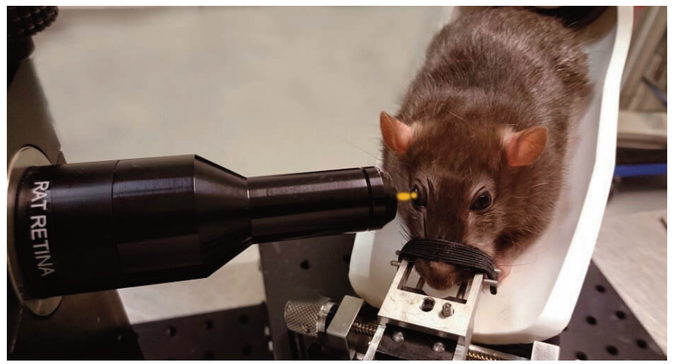
Optical Coherence Tomography, or 'OCT', is a technique for obtaining sub-surface images of translucent or opaque materials or other biological regions at a resolution equivalent to a low-power microscope. It is effectively "optical ultrasound,"
imaging reflections from within tissue to provide both frontal and cross-sectional images. Further, with appropriate software, these regions maybe comprehensively measured at micron levels.

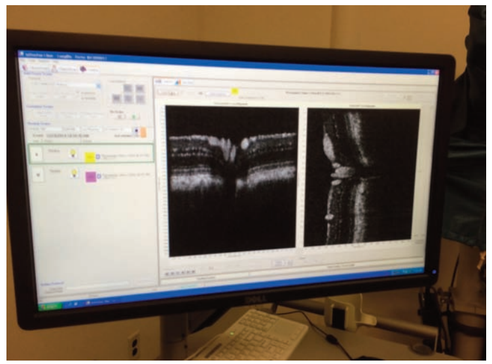
OCT is attracting interest among the research community, because it provides tissue morphology imagery at much higher resolution (less than 10 μm) than other imaging modalities such as MRI or ultrasound.

OCT imaging captures a wide range of subtle in life changes in the retina and optic nerve, and to visualize lesions such as laser-induced subretinal plaques, neovascular proliferation, diabetic retinopathy, intraocular devices, intra-ocular depositions such as stem cells or subretinal depot injections, measure structures, and examine, in detail, the cornea, iris, ciliary process, angles, and lens. Further, the FDA is very interested that OCT be conducted in ocular toxicity studies.

CBI Dermal OCT Scanning is used in our biomedical research, cosmeticsand pharmaceuticals.
Applications currently being investigated include:

- SKIN MODELS
- TISSUE ENGINEERING
- EMBRYOLOGY
- FAT
- LLTech Images





Otic Studies

Otic Studies
CBI has demonstrated expertise in all phases of the drug development process in preclinical contract otic studies. Our highly specialized staff is experienced in providing exploratory/proof-of-concept, GLP toxicology, pharmacokinetics, in vivo animal models, pharmacology, and histopathology/immunohistochemistry associated with the outer, middle and inner ear.

Due to CBI's unique experience in preclinical contract otic studies and state-of-the-art facilities, we have the skill and expertise to accelerate new ear drugs from discovery through the drug development process to regulatory submission.

We have conducted studies relating new drugs that prevent hearing damage from loud sounds, such as:

• Battlefield Injury • Ear Infections • Parasitism • Chemotherapeutics • Antibiotics
• Acute and Chronic Tympanic Membrane Perforations and Surgical Manipulations

Drug delivery includes systemic local to the ear canal or tympanic membrane or by infusion into the middle or inner ear. Special techniques include peri-lymph collection, cytocochleograms, hair cell analysis, behavioral analysis, and auditory brainstem response testing (ABR).

Stem Cell Research

Stem Cell Research Specialized

Stem cells are undifferentiated biological cells that can differentiate into specialized cells and can divide (through mitosis) to produce more stem cells. They are found in multicellular organisms. In mammals, there are two broad types of stem cells: embryonic stem cells, which are isolated from the inner cell mass of blastocysts, and adult stem cells, which are found in various tissues. In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues. In a developing embryo, stem cells can differentiate into all the specialized cells—ectoderm, endoderm and mesoderm (see induced pluripotent stem cells)—but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues.

There are three known accessible sources of autologous adult stem cells in humans:

1) Bone marrow, which requires extraction by harvesting, that is, drilling into bone (typically the femur or iliac crest).
2) Adipose tissue (lipid cells), which requires extraction by liposuction.
3) Blood, which requires extraction through apheresis, wherein blood is drawn from the donor (similar to a blood donation), and passed through a machine that extracts the stem cells and returns other portions of the blood to the donor.

FDA requirements for Stem Cell Regulatory Packages

Our scientists are well versed in the FDA requirements for Stem Cell Regulatory Packages, including recommendations on species selection, proof of concept studies, and duration of studies. Pivotal issues in Stem Cell research study design include clinical relevance, appropriate comparative anatomy and physiology, relevant clinical route of administration, and immune tolerance. Stem Cell Research toxicity studies are often conducted in the relevant disease model. Key comprehensive assessments include disposition and tolerability of the stem cells following injection, possible formation of ectopic tissues, teratoma-tumor formation, site reactions, and functional impact. CBI is also versed in stem cell-device or delivery combinations. We have conducted multiple CIRM-funded studies.

Our experience in Stem Cell Research includes, but is not limited to:

TOXICITY STUDIES	EFFICACY STUDIES
• Acute, Subacute, Chronic, Local Tolerability	• Custom or functional studies (GLP or non GLP)
• 1, 3, 6, 9, 12 and 24 month chronic	• Ocular
• Carcinogenicity and tumorogenicity	• Cardiopulmonary, intracardiac administration
• Biodistribution	• Diabetes
• Radiolabel and PCR	• CNS-brain, spinal cord
• Histology	• Oncology
• Immunohistochemistry	• Reproductive
• Combination device and stem cell toxicity	• Bone marrow
• Custom toxicity studies	• Combination device cells

Heymann Nephritis

Heymann Nephritis or membranous glomerulonephritis (MGN) is a slowly progressive immune-mediated disease of the kidney affecting mostly patients between ages of 30 and 50 years, usually Caucasian. It is the second most common cause of nephrotic syndrome in adults, with focal segmental glomerulosclerosis (FSGS) being the most common. It is not curable, but may be managed with dialysis and immunosuppressive drugs.

Immune-mediated FX-1A-induced glomerular nephritis in rats

Immune-mediated FX-1A-induced glomerular nephritis in rats is an excellent translational model of immune-mediated membranous glomerular nephritis in humans. Administration of sheep antibody to rat proximal tubular epithelial cell brush border antigen (ant-Fx1A) induces a uniform and severe glomerular nephritis characterized by proteinuria and characteristic histologic changes in the kidney. At CBI, we have optimized and validated the model and we have a robust, uniform model that is suitable for assessment of disease mechanisms and test article activity:

- Heymann Nephritis Immune mediated FX-1-induced glomerular nephritis is an established, robust, reproducible model at CBI
- Rats are administered the FX-1 antibody
- Urine changes-marked increases in urinary protein, creatinine and protein/creatinine ratios due to glomerular damage beginning within one week and increasing over 2-3 weeks
- Glomerular histologic changes of glomerular hypercellularity, inflammation and deposition visible by 3 weeks histologically

Heymann Nephritis

Immune-mediated FX-1-induced glomerular nephritis

Urine protein excretion increases beginning about Day 8

Veterinary Preclinical Studies

Veterinary Preclinical Research
Comparative Biosciences Inc., is committed to providing expert high-quality contract research services to the veterinary and animal health industry. Extensive experience industry provides our staff with a solid track record in preclinical veterinary research and drug development capabilities. We work closely with both sponsors and Veterinary Clinical Research horse-Organizations to support studies that are needed to support regulatory submissions to the USDA and FDA. We offer toxicology, pharmacokinetic and pharmacology studies in all relevant veterinary species (juvenile and adult) such as dogs, cats, minipigs, pigs, and also mice, rats, hamsters, guinea pigs, chinchillas, ferrets, gerbils, and rabbits, limited studies with small ruminants and horses are also possible. We offer a wide range of routes of administration as well as unusual and specialized routes of administration for a wide variety of test articles including small molecules, large molecules, biologics (vaccines, antibodies, proteins, toxins, viral, stem cells, radiolabeled products), and other related test articles and devices.

Toxicology
Beginning with early assessment of new molecules including single dose, multiple dose, and targeted studies, as well as directed or investigative toxicology, and finishing with complete FDA or USDA enabling toxicology programs, CBI provides expertise, attention, and care on every study. Our study directors are experienced, communicative, and attentive, and we produce high-quality reports in a very timely fashion.

Pharmacokinetics
CBI offers a complete range of research services in the area o pharmacokinetic, toxicokinetic, bioequivalence, bioavailability, and ADME studies in normal and in disease states.

Histopathology
CBI offers histology and pathology, incuding immuno histochemistry, plastics, devices and histomorphometry in both a GLP and nonGLP environment for studies generated within CBI as well as from animals from field and academic studies. We welcome tissues from both companion animals and large farm or exotic animals.

Pharmacology and Efficacy

We provide a range of pharmacology capabilities across a spectrum of indications that ensure reliable results in the drug-discovery-development process for companion animals and farm animals. Assessment and analysis modalities are fine-tuned to meet the specific requirements demanded in each targeted area of scientific investigation.
Our specialties in Veterinary Pharmacology include:

- Anti-infectives
- Arthritis
- Anthelmintics
- Arthropods
- Bioequivalence
- Bone and joint orthopedics
- Cardiovascular
- Cancer chemotherapy
- Dermal allergy and atopy
- Devices and implants
- Flea allergy dermatitis
- Inflammation
- Neonatal and juvenile
- Neurologic
- Ocular
- Pain
- Parasites
- Pulmonary
- Reproductive
- Surgical modeling
- Wound healing
- Vaccines
- Special Problems:
  Our scientists will develop any model needed to a ddress special problems in preclinical development.

Biocompatibility and Devices

Biocompatibility and Devices

CBI offers comprehensive biocompatibility testing, and compliance with ISO-10993, 9394 USP & CFR Compliant Testing in rapid and cost effective manner.

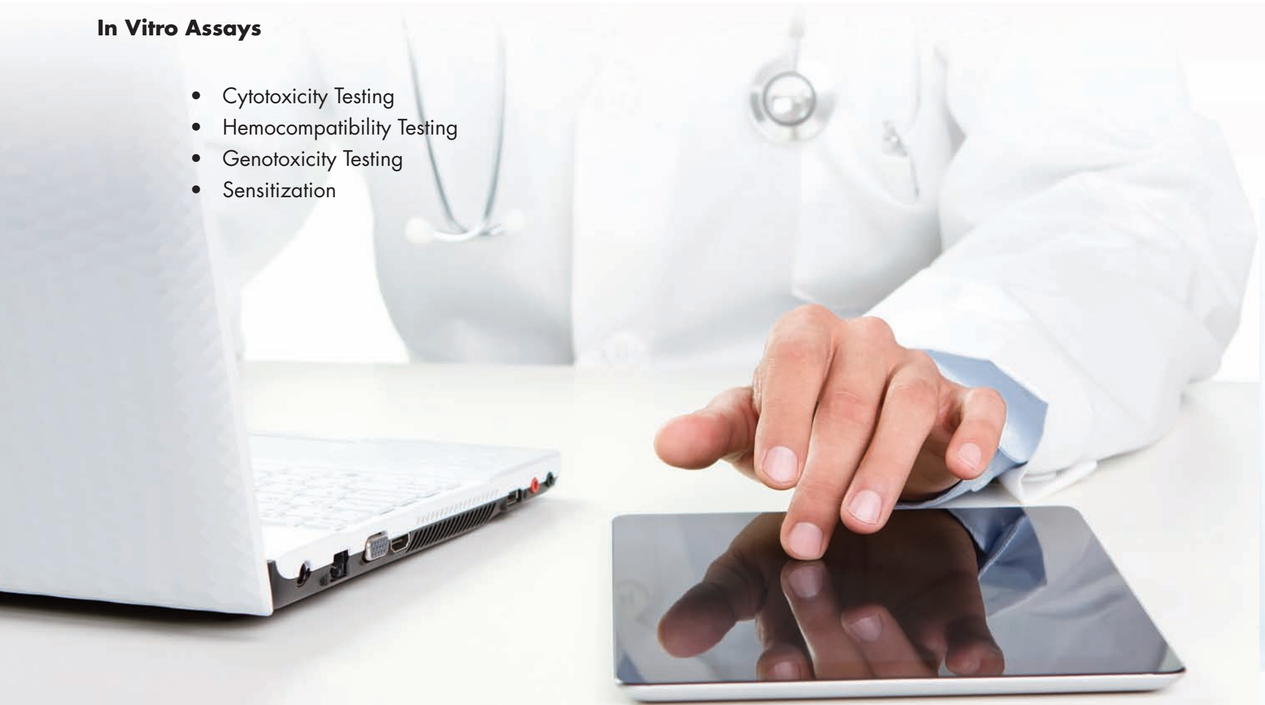
In Vivo Assays

- Acute, systemic, subacute, chronic and carcinogenicity toxicity studies
- Dermal, ocular, mucosal irritation testing
- Contact Lens testing-ISO-9394
- Muscle, bone, subcutaneous, and intradermal implantation
- Topical, intracutaneous, ocular, and primary skin irritation testing
- Beuhler, Draize and Magnussen-Kligman Maximization testing
- Long-term surgical implantation studies
- Biocompatibility
- Device-drug combinations
- Device-stem cell combinations
- Bone and joint, orthopedic biocompatibility

CBI has conducted numerous biocompatibility studies related to dural, amnionic, pericardial and other patches, coated films, sutures, matrices, osteoinduction materials, cartilage regeneration, morselized bone, spinal fusion, bone regeneration and tendon repair.

In Vitro Assays

- Cytotoxicity Testing
- Hemocompatibility Testing
- Genotoxicity Testing
- Sensitization



Oncology and Xenograft Studies

Oncology and Xenograft Studies

We have evaluated many potential anti-cancer compounds in mice and rats. Our in-house expertise allows us to optimally design studies that provide critical preclinical efficacy data. CBI provides a variety of validated cell lines for the assessment of anti-tumor agents. We can help you advance your product by conducting the following evaluations:

- Numerous cell lines validated
- Subcutaneous, intravenous and orthotopic implantation, including infusion
- Immunocompromized and immunocompetent rodents, including knockout and transgenics and syngeneics
- Angiogenesis, gene therapy, nanoparticle and stem cell capabilities
- Maximization of test article effectiveness and minimum effective dosage
- Combination therapy
- Comparison of formulation and routes of administration
- Maximum tolerated dose and pharmacokinetics/pharmacodynamics
- ATCC and custom tumor cells lines
- Supporting capabilities: clinical pathology, immunology, histopathology, immunohistochemistry

Validated Tumor Cell Lines at Comparative Biosciences, Inc.

BREAST	MDA MB-231, MCF-7, MDA-MB-435, 4T1
COLON	Caco-2, HCT-116, COL 205, L5174T Carcinoma
LUNG	A549, LS174T, Lewis Lung (syngeneic)
PROSTATE	LNCAP, PC-3, DU-145
MELANOMA	B16F0, B16F10 (syngeneic)
OVARIAN	SK-OV-3, OVCAR 3, A2780, Hela
CNS	U87-MG
MYELOID	Daudi, GRANTA-519, Jeko-1, Kasumi-1, HL-60
PANCREATIC	PANC-I, PANC-II, ASPC1
LIVER	Milo, Lymphoma

Histopathology, Immunohistochemistry, and Pathology Services

CBI provides contract histology, immunohistochemistry, and pathology services to the biopharmaceutical industry. Founded in 1996, CBI is a prestigious, independent, privately owned, nationally and internationally recognized histology and pathology laboratory. Whether preparing a single biopsy or a complete carcinogenicity study, CBI offers high quality slide preparation, pathological evaluation, and report preparation in a timely and cost effective manner. We are committed to providing the highest quality histology and pathology services to our clients.

Our resources include state-of-the-art laboratories, highly trained and experienced board-certified veterinary pathologists, skilled and detail-oriented technical personnel, and full-time quality assurance staff. All CBI studies are conducted within our laboratories, under the direct supervision of our pathologist, QAU, and PhD-level scientific managers.

For preparation of histology and pathology studies for regulatory submission, CBI follows FDA, OECD, EPA, STP, NTP, MHW, FISA, and EMEA guidelines. Our Quality Assurance Unit audits all critical phases of GLP studies and all phases of slide preparation are overseen by a board certified veterinary pathologist assuring the highest quality slide preparation.

Our clients include pharmaceutical and biotechnology companies, universities, colleges of veterinary medicine, NIH/NIEHS/NPT and other federal grant funded organizations, hospitals, and basic researchers.

Histopathology Services

Histology Laboratory Capabilities

The CBI histology laboratory offers a wide range of preclinical contract histology and pathology research and development services spanning all aspects of paraffin, frozen and plastic slide preparation, staining, and evaluation.
The histology laboratory offers the following services:

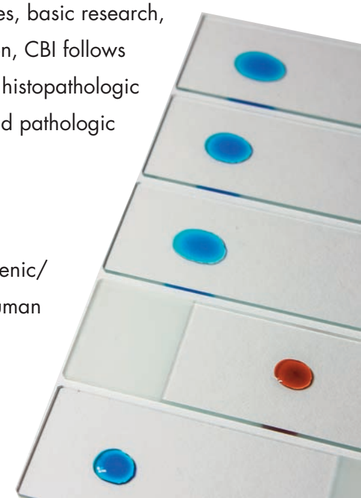
- Routine paraffin slide preparation: gross trimming, processing, embedding, sectioning, staining
- Routine and special histochemical staining
- Frozen sections, cytology, and smears
- Devices, plastic, resin, and ground sections
- Retinal whole mounts
- IHC staining method development, verification, and validation
- Tissue whole mounts with immunohistochemistry
- Standard IHC on tissues from all species from fixed and frozen tissues and cytospin preparation
- Immunohistochemistry, Immuno-fluorescence, and In Situ Hybridization
- Tissue cross reactivity:
    - GLP Tissue cross-reactivity studies
    - Research cross reactivity studies
- Special techniques including ocular, tissue/organ whole mounts, retinal whole mounts, brain mapping, gelatin techniques, stem cells, and oncology
- Complete human and primate tissue bank-including a wide variety of human tumors, diseased and normal tissues
- Digital image analysis, histomorphometry, and photomicroscopy
- ACVP board certified veterinary pathologists
- High-quality and complete reporting, GLP
- All species including human, veterinary, and laboratory animals

Regulatory Studies

The Histopathology Laboratory at CBI provides expert contract histologic slide preparation and evaluation of tissues from both animal and human supporting GLP toxicology studies, pharmacology and efficacy studies, basic research, and diagnostics. For preparation of histology and pathology studies for regulatory submission, CBI follows FDA, OECD, EPA, STP, NTP, MHW, FISA, and EMEA guidelines for preparation of tissues for histopathologic examination. Our professional staff is experienced and capable in both slide preparation and pathologic evaluation in all relevant species.

Research Tissues

CBI maintains a complete tissue bank of human, primate, dog, pig, rabbit, rodent and transgenic/knockout mice species. We also have diseased tissues, tumors, frozen and fixed tissues for human tissue cross reactivity studies as well as research animal and veterinary studies.



Histopathology Services

Pathology

Comparative Biosciences, Inc, offers contract research pathology services. Skillful and accurate interpretation of histology and pathology specimens is critical to consistent success in efficacy, pharmacology, and toxicology studies. The oversight of a board-certified pathologist is essential to evaluate both research and GLP histology and pathology specimens. Whether evaluating studies that are generated in house, evaluating contract histopathology studies that are sent in, or conducting peer review, CBI's ACVP Board Certified Veterinary pathologists provide the highest quality contract research pathology interpretation services and report preparation. Our contract research pathology reports include data acquisition using FDA Part 11 compliant pathology data acquisition systems to collect and manage pathology data, thereby assuring the highest quality assessment and reporting of pathology data.

Pathology Capabilities

- GLP toxicology studies with all species
- Pharmacology and efficacy studies
- Peer-review studies
- Image analysis and histomorphometry
- Digital photomicroscopy
- IND report preparation
- Expert reports
- Validated, Part 11 compliant pathology data acquisition programs (StarPath).
- GLP compliance in all phases

Our state-of-the-art technology and extensive experience with biologics, antibodies, large molecules, small molecules and devices enable us to offer a comprehensive and sophisticated pathologic assessments and interpretations.

ACVP Pathologists

- DVM, PhD, Diplomate, American College of Veterinary Pathologists
- Experienced in all phases of toxicologic and research pathology from discovery to NDA
- Over 100 peer-reviewed publications
- Scientific reviewer for peer-review publications
- Highest quality reports delivered in a timely fashion

Histopathology Services

Tissue Cross Reactivity Studies

Tissue Cross Reactivity (TCR) Studies are key in the development of monoclonal antibodies and other related biologics. The purpose of the tissue or antibody cross reactivity study is to assure that the experimental antibody or biologic, does not bind to epitopes other than the target site as this could lead to treatment-related toxicity in human subjects or animals. TCR studies are also useful in identifying target species for toxicology studies as well as target organs.
We provide complete and comprehensive TCR studies to support both research efforts and IND enabling studies for FDA submission in accordance with the FDA's recommendation ("Points to Consider in the Manufacture and Testing of Monoclonal Antibody Products for Human Use", FDA Guidance Document).

Phase 1: Initial Characterization and Optimization

For the initial characterization and optimization, the optimal specificity and staining conditions for the experimental antibody is determined. Multiple dilutions (usually 5) and appropriate positive and negative control tissues are used to optimize and validate antibody dilution and relevant staining conditions.

Phase 2: Preliminary Tissue Cross Reactivity Screening

Using the optimal specificity and staining conditions, a preliminary study with the standard 32 tissues is conducted and evaluated.

Phase 3: Full Cross Reactivity Study

Following optimization in Phase 1 and 2, a full cross reactivity study can be performed in accordance with the FDA's recommendation ("Points to Consider in the Manufacture and Testing of Monoclonal Antibody Products for Human Use", FDA Guidance Document). This study includes:

- Tissues from 3 unrelated donors
- Experimental antibody at two dose levels
- Isotype control antibody
- β2 microglobulin on each tissue for staining control
- Evaluation by ACVP board certified veterinary pathologist and staining intensity scored
- Conducted under GLP conditions with audits of critical phases
- Final report suitable for FDA submission
- Archiving

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Exciting News

CBI, leaders in Stem Cell Pharmacology and GLP Toxicology, congratulates our Friends and Colleagues at Viacyte for their successful IND and upcoming Clinical Trials

Type 1 Diabetes Treatment Funded by California Stem Cell Agency Cleared To Begin Clinical Trial

August 19, 2014

San Francisco, CA – ViaCyte Inc., a regenerative medicine company headquartered in San Diego, has been given approval to begin a clinical trial for a promising treatment for type 1 diabetes, a program that is funded by the California Institute for Regenerative Medicine (CIRM), California's stem cell agency.

CBI conducts Stem Cell research, toxicology and efficacy studies for the biopharmaceutical, veterinary, and academic research organizations. As a premier Stem Cell Research CRO, our highly trained staff is experienced in the area of GLP contract research studies in stem cell toxicology, pharmacokinetics, biodistribution, combination device, radiolabel, pharmacology, histopathology, and immunohistochemistry.

VIACYTE
Regenerating Health™

Collaborators

Thank you for visiting us!

Here are sites of professional colleagues that we are associated with, as well as some sites around the web that we recommend.

Veterinary Vision, Inc.
veterinaryvision.com

Quality Veterinary Laboratory LLC
qualityvetlab.com

Marin Biologic Laboratories, Inc.
marinbio.com

American College of Veterinary Pathology
acvp.org

Society of Toxicologic Pathology
toxpath.org

Food and Drug Administration
fda.gov

Association for Research in Vision and Ophthalmology
arvo.org

Integrated Analytical Solutions, Inc.
ianalytical.net

Multispan
multispaninc.com

BioLaurus
biolaurus.com

ProNovus Bioscience, LLC.
pronovusbio.com

Animal Eye Specialists
animaleyespecialists.com

Rollinson Advertising Design
rollinsonadvertising.com

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