LASP operates the NCI animal facilities and provides routine and specialized animal husbandry services for NCI Investigators on the Bethesda and Frederick campuses.

**Animal Care and Facility Management**

Management of 30 rodent and non-human primate vivaria.

Maintenance of 133,400 animals occupying 49,228 cages.

316 LASP associates (237 in Frederick, 79 in Bethesda).

Support of 206 investigators with 551 active animal study protocols.

Provides support for Frederick ACUC and Bethesda ACUC.

Provides outstanding (board-certified) veterinary care for research animals.

LASP also provides many state-of-the-art cores or facilities to assist NCI Investigators in performing their animal-based research into cancer and AIDS.
LASP – Cores and Facilities

Laboratory Animal Sciences Program

- Animal Facility and Colony Management
- Support for the Center for Advanced Preclinical Research (CAPR)
- Pathology/Histotechnology Laboratory (PHL)
- Small Animal Imaging Program (SAIP)
- The ARTS Gnotobiotics Facility (GF)
- Animal Diagnostics Laboratory and Genotyping Core (ADL)
- Genome Modification Core (GMC)
- Mouse Modeling and Cryopreservation Core (MMC)
- Support for the NCI Repository of Mice and miR ES Cells
- Animal Research Technology Support (ARTS)
1. Animal Health Diagnostics Lab (AHDL):

Comprehensive animal health monitoring and diagnostic services for rodents and non-human primates.

- Viral serology: MFIA, HI, ELISA, and IFA.
- Bacteriology: includes culture in anaerobic and special gas environments.
- Parasitology: direct examination for the presence of ecto- and endoparasites.
- Necropsy: routine and clinical health evaluations.
- *Mycoplasma* PCR and biochemical tests (*MycoAlert™*) to help evaluate the viability of contaminated *mycoplasma*. 

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*Dr. Wang-Ting Hsieh*
2. Animal Molecular Diagnostics:

Assists AHDL in health monitoring and offers many other advanced molecular services.

- Molecular diagnostics to detect murine and non-human primate viral/bacterial pathogens.
- Molecular Testing of Biological Materials (MTBM): PCR-based MAP test.
- Accelerated production of congenic mouse strains by microsatellite marker-assisted backcrossing.
- Custom speed congenics - marker assisted backcross breeding to produce congenic mice.
- Microsatellite DNA and single nucleotide repeat (SNP) detection for genetic background evaluation
- Custom molecular assay development for Investigators.

3. High-Throughput Animal Model Genotyping (HTAGL)
The newly-formed **Genome Modification Core (GMC)** is a CCR-dedicated facility providing:

1. Expert guidance on editing procedures to create genetic and epigenetic modifications.
2. The generation and validation of nuclease-based reagents.

The GMC provides technical advice and expertise for gene-editing in primary cells and cell lines, and interacts closely with the LASP Mouse Modeling Core to facilitate the generation of CRISPR-mediated GEM models.

**Dr. Raj Chari**

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Mouse Model Development

- Generation of transgenic mice.
- Generation of CRISPR modified mice.
- Gene targeting in mouse ES cells and generation of GEM models.
- Several hundred models generated annually for NCI, NIAID, NIAMS, NIA, NEI, and NICHD.
- Culturing and expansion of modified cell lines for injections
- Xenograft and Allograft modeling.

Cryopreservation

- Cryopreservation of mouse strains and assisted reproduction (IVF).
- Regeneration of frozen mouse germplasm to live mice.
- Rederivation of mice to pathogen-free status via embryo transfer.
MMC and the NCI Mouse Repository

- Resource supported by NCI’s Mouse Models of Human Cancers Consortium (MMHCC) and/or the Division of Cancer Biology (extramural community).

- Cryopreservation and distribution of frozen germplasm for >150 mouse models for cancer research.

Repository of Tet-inducible miRNA-Expressing ES Cells

- Cryopreservation and distribution of 1500+ lines of mouse ES cells bearing tet-responsive (reversible) microRNA expression constructs, including a GFP reporter gene.

- These mini-genes contain the mature miRNA species in its endogenous context or embedded in a miR30 precursor to control the effect of microRNA processing on overall miRNA expression levels.
Animal Research Technology Support (ARTS) Core:

- Provides comprehensive rodent breeding, experimental and colony management services.
- Assist Investigators in induction and characterization of tumors in preclinical animal models.
- Assist Investigators in immunizations and assessment of immune functions by transplantations.
- Performs metabolism studies, including food and water consumption and collection of body fluids.
- Tissue collections, including perfusion and sample preservation.
- Perform surgical procedures on Investigators’ animals, including tumor excision, thymectomy, splenectomy, partial hepatectomy, colon resection/colonoscopy, ovariectomy, vasectomy, and the implantation of osmotic pumps and slow-release devices.

PRECLINICAL EVALUATION

**Compound efficacy**

- Vehicle
- Cytarabine
- RO 5-3335
- RO 24

**Days post induction (p.i.)**

-7 0 7 14 21 28 35 42 49 56

**Percent survival**

- 0 20 40 60 80 100

**Compound toxicity, pharmacokinetics, bio-distribution, metabolism**

Dr. Simone Difilippantonio
**Gnotobiosis** (from *gnostos* "known" and *bios* "life"); all life forms present within an organism are known. Typically gnotobiotic organisms are germ-free (axenic) or gnotophoric (having only one biologic agent), though reconstitution of an axenic mouse with patient microbiomes is also becoming prevalent.

The ARTS Gnotobiotic Facility (GF) works with NCI investigators to:

- Development and monitor germ-free mouse colonies.
- Explore the role of the microbiota in inflammation and cancer.
- Examine the effects of microbiota on mouse models of human cancer.
**LASP – Small Animal Imaging Program (SAIP)**

**Small Animal Imaging Program (SAIP)** collaborates with NCI investigators in:

- The development and monitoring of mouse models of human cancer.
- Performs drug efficacy studies (collaborates with LASP-ARTS) utilizing non-invasive *in vivo* imaging techniques.
- The development of new molecular imaging probes.

**Assays:**

- Perfusion (Ultrasound + microbubbles + dynamic susceptibility contrast MRI)
- Anatomical volumes (Ultrasound and MRI)
- Angiogenesis (Ultrasound using tagged microbubbles)
- Glucose metabolism $[^{18}\text{F}]$FDG (PET/CT)
- Permeability (Dynamic Contrast Enhanced DCE-MRI)
- Hypoxia (Oxygen saturation) (Photo-acoustics)
- Cell Proliferation $[^{18}\text{F}]$FLT (PET/CT)
- Cell Trafficking (Fluorescence, Bioluminescence)
- Metastasis (Bioluminescence and MRI)
- Cardiac Function and Blood Flow (Ultrasound and Doppler)
- Probe bio-distribution (Gamma-well counter)

**Other Techniques:**

- Virtual Colonoscopy (MRI)
- Image Guided Injections (Ultrasound)
- Measuring Tracer kinetics (SPECT/CT, Fluorescence, PET/CT, and MRI)
Histotechnology:

- Animal necropsies.
- Processing of wet tissue (fixed and/or frozen).
- Embedding and microtomy, with physical and enzymatic slide staining.
- Molecular histology assay development: immuno-staining.
- In situ hybridization using nucleic acid probes.
- Laser-capture tissue micro-dissection and nucleic acid isolation.
- Image capture (bright-field and fluorescence).
- Hematology and blood chemistry.
Veterinary Pathology:

- Image capture and analysis (bright-field, fluorescence).
- Digital imaging and annotation, including quantitative molecular analysis.
- Assistance with protocol development.
- Phenotypic and toxicologic analysis of GEMs and xenograft models.
- Specimen classifications and selection for micro-dissection and micro-array.
- Assistance with study design and consultation throughout the study.
- Baktiar Karim, DVM, PhD & Elijah Edmondson, DVM, PhD
The Center for Advanced Preclinical Research (CAPR) is a research lab with dedicated staff drawn from NCI and LASP. CAPR evaluates diagnostic and therapeutic regimes in well-established pre-clinical mouse models of human cancer. CAPR interfaces with many other LASP Cores to perform pharmacokinetics and bio-distribution studies of therapeutics in animal models and to provide rigorous evaluations of therapeutic candidates in efficacy studies.
LASP serves as a comprehensive resource for those NCI scientists performing animal-based research by providing the highest level of animal care, by offering robust and cutting edge scientific support for animal studies, and by ensuring that all Investigators’ animals in Bethesda and/or Frederick, are cared for and studied in a humane and highly professional manner (and in accordance with all regulatory guidelines).

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