Frederick National Laboratory
for Cancer Research

Operational Update on FNLCR

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The Frederick National Laboratory is a federally funded research and development center operated by Leidos Biomedical Research, Inc., for the National Cancer Institute
DEPARTMENT OF HEALTH AND HUMAN SERVICES • National Institutes of Health • National Cancer Institute

Scientific Mission Support at FNLCR

What we do

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	Contractor-provided Research Support	Contractor-executed Research Projects	Contractor-executed Sub-contracted Projects	Contractor- Directed & Executed Projects
	Type 1	**Type 2**	**Type 3**	**Type 4**
Technical	Lab partner and personnel support for the NCI intramural community and other ICs	Provide collaborative research resources for Government-directed research activities.	Extramural Projects execute primarily through subcontracts for Government-directed research projects.	National Lab-Directed Research to meet government-approved mission needs
Infra-structure	Tailored infrastructure to meet research support activities including specialized laboratories	Tailored infrastructure to meet research support activities including specialized laboratories	Office and IT infrastructure	Specialized laboratories and computer infrastructure.
Business Services	Procurement support for core services.	Procurement support for core services	Agile subcontracting to reach the extramural talent.	Procurement support, agile subcontracting , and partnership development

Examples of Different Types of Programs

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Type 1 : Research Support

Center for Cancer Research - Technical staff (reporting to a Leidos Biomed manager) work in CCR PI laboratories supporting their research

Type 2 : Research Programs

Multiple Divisions, Offices, and Centers – The Laboratory Animal Sciences Program provides all phases of animal husbandry, model development, imaging, immunology, treatment evaluation

Type 3 : Sub-contracted Programs

Division of Cancer Treatment and Diagnosis - Cancer Biology Consortium member institutions participate on project teams through task order agreements administered as subcontracts by Leidos Biomed as a part of the NCI Experimental Therapeutics Program (NExT).

Type 4 : Contractor-directed and -executed Programs

Office of the Director – The RAS Initiative advances the understanding of RAS and therapeutic approaches to treating RAS-driven cancers

NCI Mission Support Types
FY16 Science Costs

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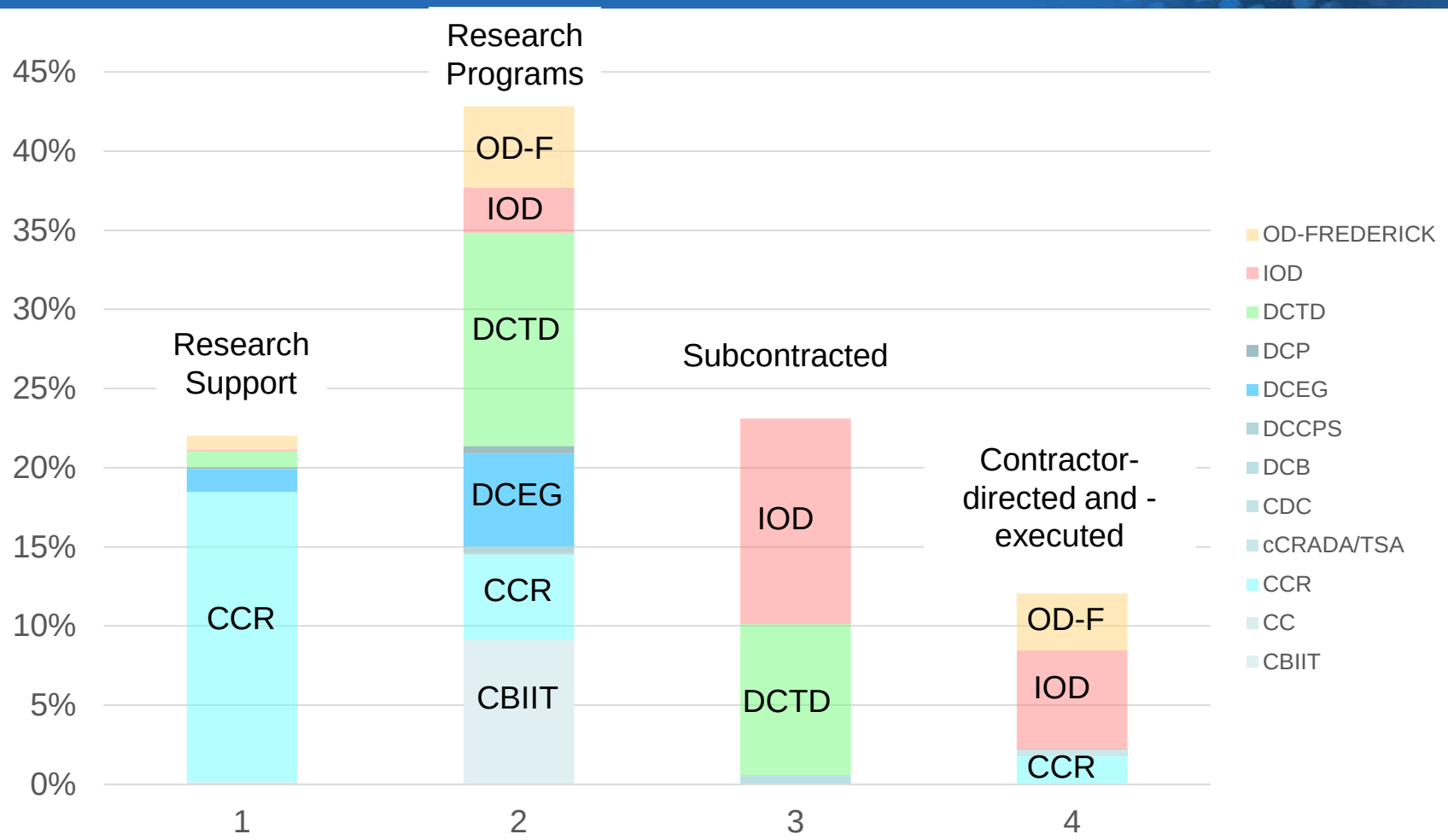

OD-Frederick - Office of the Director, NCI-F
IOD – Immediate Office of the Director
DCTD – Division of Cancer Treatment and Diagnosis
DCP – Division of Cancer Prevention
DCEG – Division of Cancer Epidemiology and Genetics

DCCPS – Division of Cancer Control and Population Sci.
DCB – Division of Cancer Biology
CCR – Center for Cancer Research
CC – Clinical Center
CBIIT – Center for Biomedical Informatics and Info.Tech.

Evolution of NCI Direct Science Costs

Normalized to each Fiscal Year's Direct Science Costs

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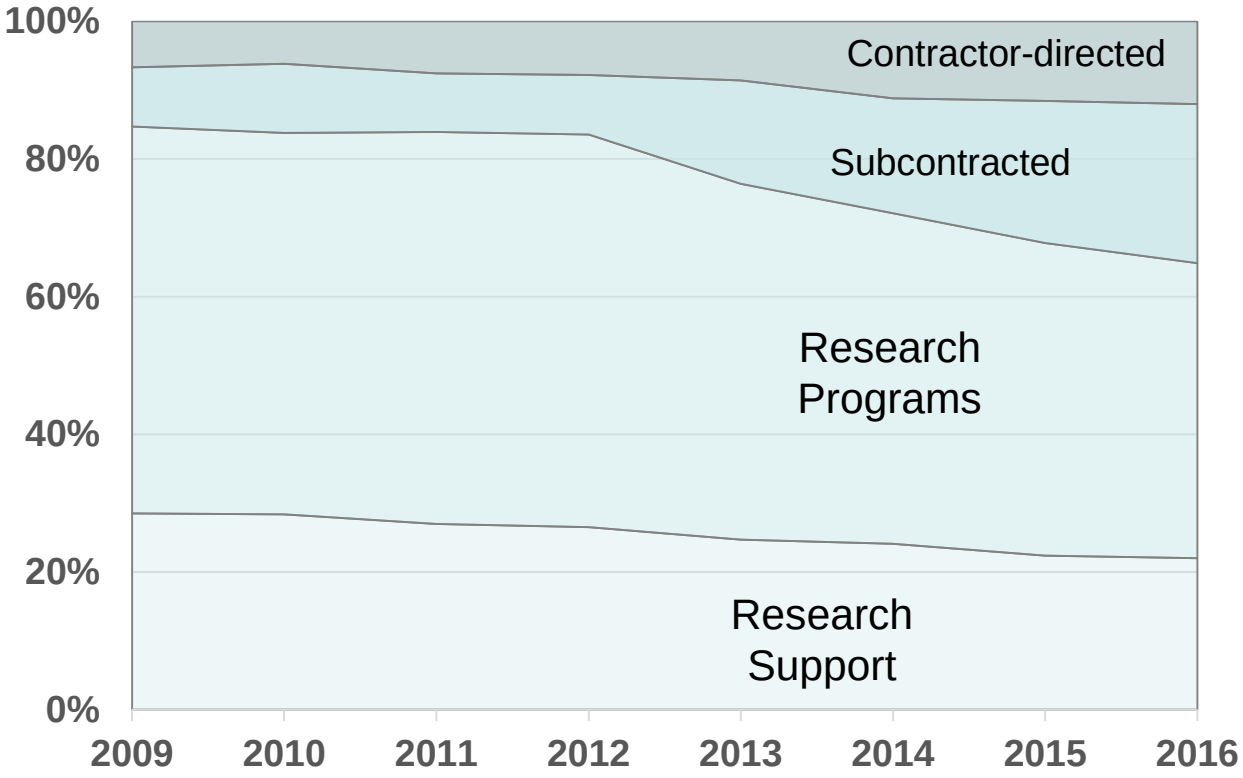

As a percentage, growth in Subcontracted and Contractor-directed and –executed programs

Laboratory Animal Sciences Program

An Essential Core Capability (Type 2) of FNLCR

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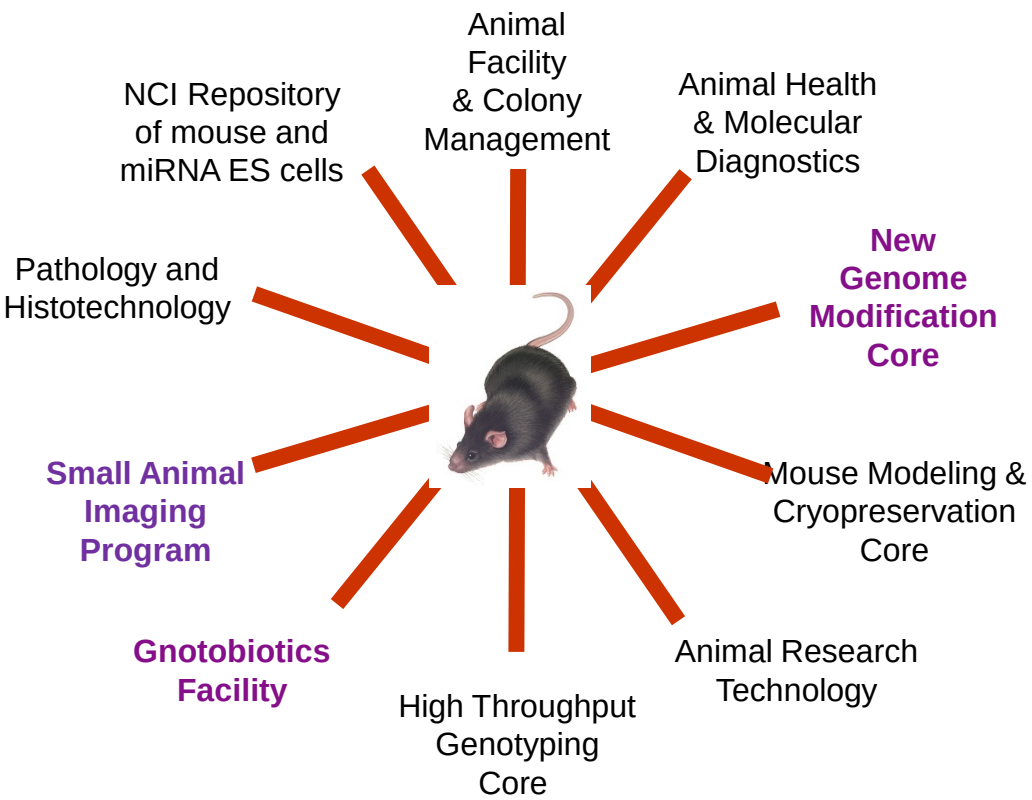
LASP operates the NCI animal facilities and provides routine and specialized husbandry services for Investigators on the Bethesda and Frederick campuses.

- Management of 27 rodent and nonhuman primate research facilities (22 Frederick, 5 Bethesda).
- Maintenance of 133,400 animals occupying 49,228 cages.
- 315 LASP associates (234 Frederick, 81 Bethesda)
- Support of 206 investigators encompassing 551 active animal study protocols.
- Provides support for Frederick and Bethesda ACUC.



LASP staffs and operates many state-of-the-art cores and other facilities to assist NCI Investigators in performing their animal-based cancer and AIDS research.

https://frederick.cancer.gov/science/technology/laboratory-animal-sciences-program

The LASP Genome Modification Core

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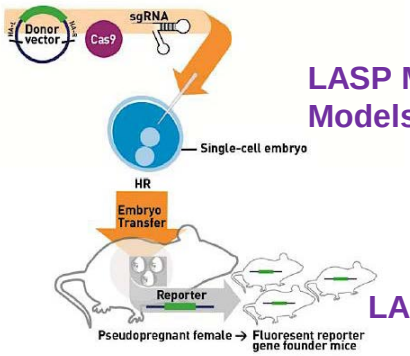
Genome Modification Core (GMC): a new Core that will collaborate with NCI investigators to:

- Design nucleases approaches (including CRISPR) to modify genes in cell lines, primary cells and in animals.
- Generate and validate nuclease components for Investigator use.
- Design CRISPR transduction modalities (viral, liposomal, etc.) and assist Investigators in performing genetic screens.
- Develop “next-gen” nuclease technologies to further enhance our abilities to modify the genome and epigenome.
- Interface with other LASP Cores to facilitate the seamless transition from experimental design to results.

LASP Genome Modification Core



LASP Mouse Models Core

LASP Genotyping Core

LASP Small Animal Imaging Core

The LASP Small Animal Imaging Program

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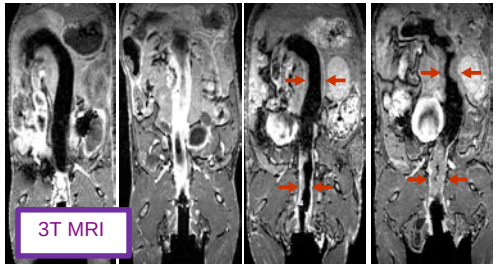
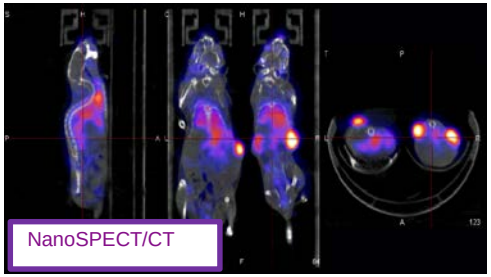
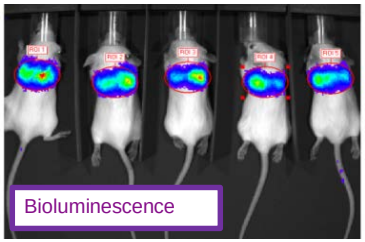
Small Animal Imaging Program (SAIP) collaborates with NCI investigators in:

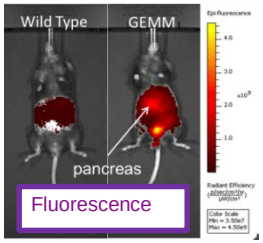
- The development and non-invasive monitoring of GEM and PDX mouse models of human cancers.
- The development of novel molecular imaging probes.
- Performing drug efficacy studies to treat primary and metastatic tumors utilizing *in vivo* imaging techniques.

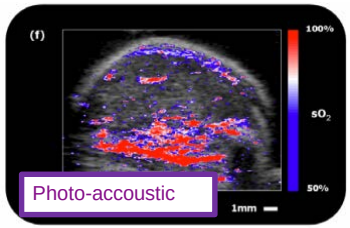
SAIP assays include x-ray/CT scan, nuclear PET, ultrasound, photo-accoustic, bio-luminescence, fluorescence, magnetic resonance, and molecular tomography.











The recent addition of Hyperpolarized Metabolic Imaging permits real-time analysis of biochemical and metabolic changes in cancer by improving MRI sensitivity by more than 20,000-fold.

The LASP Gnotobiotics Facility

from *gnostos* "known" and *bios* "life"

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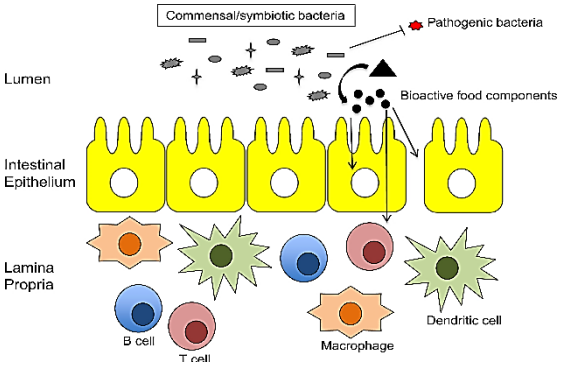
Gnotobiotics Facility (GF) assists

NCI investigators to:

- Develop and monitor germ-free (axenic) or germ-specific (gnotophoric) mouse colonies.
- Explore the role of the microbiota in inflammation and the development of gastric or colon cancer.
- Examine the effects of the microbiota on mouse models of lung cancer, including K-Ras; p53-conditional mutant mice.



The GF doubled in cage capacity last year, and now performs ABSL-2 procedures within the isolators.

standard mouse facility

1950's GF

Present day- LASP Gnotobiotic Facility

FNLCR Support of Beau Biden Cancer Moonshot Program

FY17 NCI Research Activities

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- **Fundamental Science**
  - Technology Development
  - Big Cancer Challenges
  - Creation of Human Tumor Atlas
  - Fusion Oncoproteins in Pediatric Cancer
  - Therapeutic Target Identification to Overcome Drug Resistance
- **Treatment and Cures**
  - Network for Direct Patient Engagement
  - Cancer Immunotherapy Translational Science Network
  - FDA Oncology Center of Excellence
  - Partnership for Accelerating Cancer Therapies
  - Retrospective Analaysis of Biospecimens
- **Health Promotion and Disease Prevention**
  - Symptom Management Research
  - Implementation of Evidence-based Approaches to Prevention
  - Creation of a Data Ecosystem for Sharing and Analysis

Five non-severable Task Orders and 3 severable projects supporting 8 of NCI's Research Activities

Research Activities adapted from presentation by Dr. D. Lowy Mar 28 2017

NCI-DOE High-Performance Computing Collaboration

Building collaborations with world-class DOE National Laboratories

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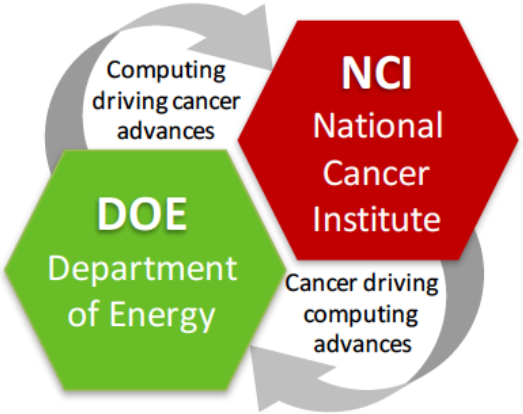


Integrated Precision and Predictive Oncology

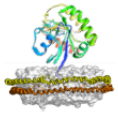
Pilot 1
Pre-clinical Model Development

Aim 1: Predictive Models of Drug Response (signatures)

Aim 2: Uncertainty Quantification and Improved Experimental Design

Aim 3: Develop Hybrid Predictive Models

Pilot 2
RAS Therapeutic Targets



Aim 1: Adaptive time and length scaling in dynamic multi-scale simulations

Aim 2: Validated model for Extended RAS/RAS-complex interactions

Aim 3: Development of machine learning for dynamic model validation

Pilot 3
Precision Oncology Surveillance

Aim 1: Information Capture Using NLP and Deep Learning Algorithms

Aim 2: Information Integration and Analysis for extreme scale heterogeneous data

Aim 3: Modeling for patient health trajectories

Crosscut: Uncertainty Quantification (UQ) and CANDLE exascale technologies

https://frederick.cancer.gov/news/extreme-scale-computing-project-aims-advance-precision-oncology

Creation of the Accelerating Therapeutics for Opportunities in Medicine (ATOM) consortium with Lawrence Livermore National Laboratory, GlaxoSmithKline, and UCSF

Goal : From Target Identification to Clinical Trial in *1 year*

ATOM Consortium

Accelerating Therapeutics for Opportunities in Medicine

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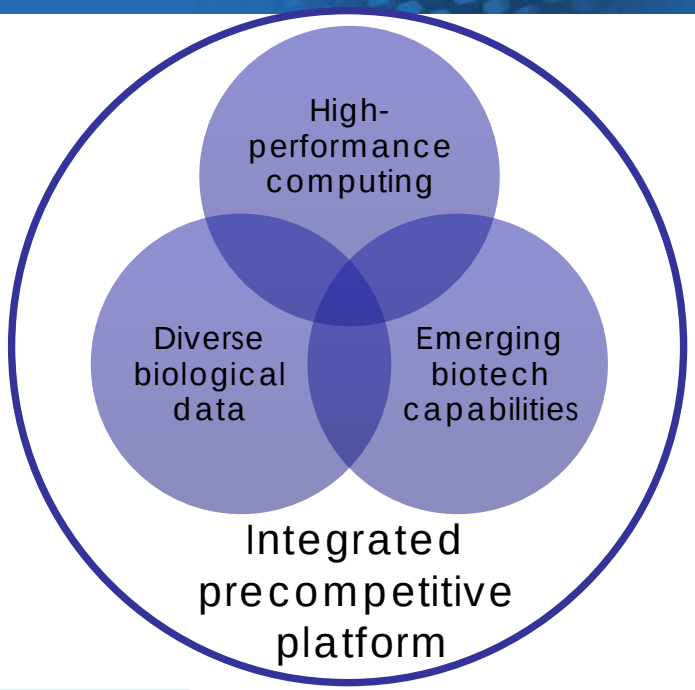
Mission

To accelerate the development of more effective therapies for patients

Vision

A new starting point:
Transform drug discovery from a slow, sequential, and high-failure process into a rapid, integrated, and patient-centric model

How?



3 year goal

Starting from a validated oncology target, deliver a patient-ready cancer therapy in <1 year, a process that currently takes an average of 6 years

Our journey

Establishing a public-private partnership

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June: Partnership between GSK, DOE, and NCI announced as one of the Cancer Moonshot task forces

December: Congress passes 21st Century Cures Act, including funding for the Cancer Moonshot

June – December 2016

GSK, DOE, and NCI sign a Memorandum of Agreement to establish ATOM

January 2017

October 2017

Founding Members

GSK, LLNL, FNLCR, and UCSF sign a cCRADA establishing the ATOM Consortium

Model allows **expansion** to make additional partnerships with qualified pharma, biotech, technology, academic, government, and other organizations

Lawrence Livermore National Laboratory

gsk

UCSF

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Three-year ATOM plan

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2017

- Bring in additional members and participants
- Locate staff to ATOM office space in Mission Bay area of San Francisco
- Execute startup plans to enable the secure sharing of data and building of research tools & capabilities

2018-2019

- Move into ATOM lab space in Mission Bay area of San Francisco
- Continue to bring in new members and participants
- Continue to build tools and capabilities

2020

- Demonstrate technology readiness; embark on POC project from Target to IND

Mission Bay, SF

Photo source: chasecenter.com; rendering of 2019 Golden State Warriors arena in Mission Bay

Accelerated drug discovery concept

Vision of ATOM workflow in practice

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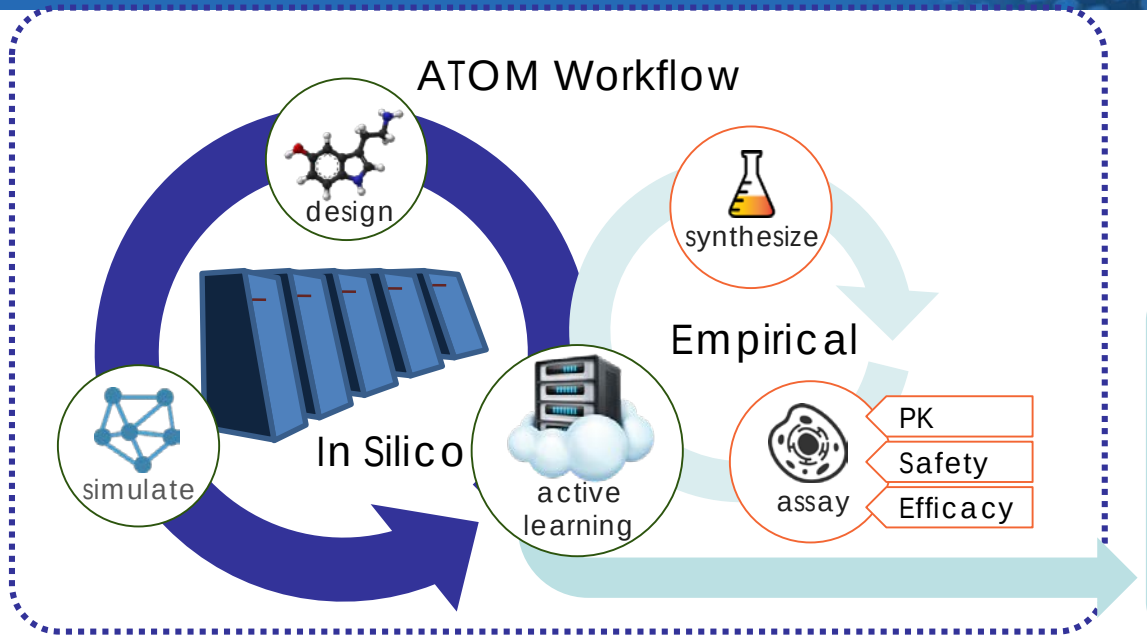
Patient-specific data and samples input to workflow to develop new therapeutics

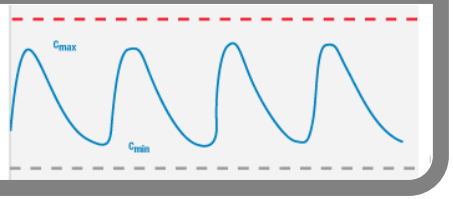


Released to public after a 1-year member benefit

Open source models and generated data

Members use workflow for internal drug discovery

Models of drug behavior in humans



Therapeutic Candidates

Commercialization by members for patient benefit

The ATOM platform vision

Our moonshot goals

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Predict the effects of a therapeutic at the protein, cell, tumor, tissue, organ and organism level

Complex in vitro models and in silico modeling to reduce reliance on animals in preclinical research

ATOM

Empirical testing will become a tool to validate and optimize computational predictions – not the primary platform for preclinical research

Regulatory agencies engage to accelerate filing process that is supported by in vitro data and in silico predictions

ATOM Consortium Membership

Actively seeking additional members who share the vision

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Elements of membership:

1. Augment knowledge and capabilities
2. Senior leadership participation
3. Data, equipment, and/or resources
4. Staff with expertise to work at the ATOM lab
5. Financial support for the consortium
6. Commitment to a new pre-competitive balance

Examples of contributions from founding members

gsk	Lawrence Livermore National Laboratory	Frederick National Laboratory for Cancer Research	UCSF	
2M compounds and associated data from terminated projects and screening collections	Access to DOE supercomputers for purposes of carrying out Consortium related activities	Scientific expertise in cancer, computational chemistry and biology, data science, and predictive oncology	Access to UCSF facilities, expertise from UCSF faculty, cancer center	…n

The ATOM Consortium is actively seeking new members

https://frederick.cancer.gov/science/ATOM

Conclusions

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- **The Mission Support Model demonstrates the breadth and evolution of the science that FNLCR delivers to NCI and NIH**
- **The Laboratory Animal Sciences Program exemplifies the technically advanced core services of FNLCR**
- **The ATOM Consortium represents a unique government / industry / academia collaboration with the extraordinarily ambitious goal of revolutionizing drug discovery in Oncology**

Questions?