



NATIONAL CANCER INSTITUTE

Grant Number: 2P30CA010815-50

FAIN: P30CA010815

Principal Investigator(s):

Dario C Altieri, MD

Project Title: Consolidated Basic Cancer Research Program

Blodgett, Jessica
Director, Research & Administrative Services
3601 Spruce Street
Philadelphia, PA 191044265

Award e-mailed to: NOGA@wistar.org

Period Of Performance:

Budget Period: 04/17/2019 – 02/29/2020

Project Period: 04/01/1997 – 02/29/2024

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of \$2,749,311 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to WISTAR INSTITUTE in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Cancer Institute of the National Institutes of Health under Award Number P30CA010815. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website <http://grants.nih.gov/grants/policy/coi/> for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Alice Chi Wong
Grants Management Officer
NATIONAL CANCER INSTITUTE

Additional information follows

SECTION I – AWARD DATA – 2P30CA010815-50**Award Calculation (U.S. Dollars)**

Salaries and Wages	\$925,069
Fringe Benefits	\$345,980
Personnel Costs (Subtotal)	\$1,271,049
Consultant Services	\$10,299
Other	\$200,585
Subawards/Consortium/Contractual Costs	\$68,250

Federal Direct Costs	\$1,550,183
Federal F&A Costs	\$1,199,128
Approved Budget	\$2,749,311
Total Amount of Federal Funds Obligated (Federal Share)	\$2,749,311
TOTAL FEDERAL AWARD AMOUNT	\$2,749,311

AMOUNT OF THIS ACTION (FEDERAL SHARE) **\$2,749,311**

SUMMARY TOTALS FOR ALL YEARS		
YR	THIS AWARD	CUMULATIVE TOTALS
50	\$2,749,311	\$2,749,311
51	FUTURE COSTS, RECOMMENDED COSTS	
52		
53		
54		

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name: Cancer Centers Support Grants
 CFDA Number: 93.397
 EIN: 1236434390A1
 Document Number: PCA010815K
 PMS Account Type: P (Subaccount)
 Fiscal Year: 2019

IC	CAN	2019	2020	2021	2022	2023
CA	8423165	\$2,749,311	FUTURE COSTS, RECOMMENDED COSTS			

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:

PCC: ORMD / OC: 414B / Released: CHIA01 04/11/2019
 Award Processed: 04/17/2019 12:05:11 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 2P30CA010815-50

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at <http://grants.nih.gov/grants/policy/awardconditions.htm>

SECTION III – TERMS AND CONDITIONS – 2P30CA010815-50

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

- The grant program legislation and program regulation cited in this Notice of Award.
- Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
- 45 CFR Part 75.

Obtained by Rise for Animals. Uploaded 08/19/2020

- d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
- e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
- f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at <http://grants.nih.gov/grants/policy/awardconditions.htm> for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2. As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is excluded from Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See <http://grants.nih.gov/grants/policy/awardconditions.htm> for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) P30CA010815. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

This award is not subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: <http://publicaccess.nih.gov/>.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than \$10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

Clinical Trial Indicator: No

This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

REQUIREMENT: The awardee is required to adhere to the [Cancer Center Support \(CCSG\) Guidelines](#).

REQUIREMENT: The requirements contained in the document, "Intellectual Property Option to Collaborator," are incorporated by reference as a condition of this award. The "Intellectual Property Option to Collaborator" document may be accessed at http://ctep.cancer.gov/industryCollaborations2/docs/Intellectual_Property_Option_to_Collaborator_s.doc or may be obtained from the Regulatory Affairs Branch, Cancer Therapy Evaluation Program, Division of Cancer Treatment and Diagnosis, NCI at (240) 276-6580.

REQUIREMENT: The awardee is required to follow the Data Sharing and Model Sharing plans included in the competing application and may not implement any changes in the plan without the written prior approval of the National Cancer Institute.

INFORMATION: In accordance with the National Cancer Institute's (NCI's) Fiscal Year (FY) 2019 funding policies, this award has been issued at 98.09% of the adjusted requested level*. Support recommended for future years has been adjusted accordingly.

*adjusted requested level: The requested level of support with adjustments made in accordance with the budget narrative in the summary statement and applicable grant policies.

INFORMATION: This project involves hazardous or potentially hazardous agents. Attention is called to the Health and Safety Regulations and Guidelines (Section 4.1.12) of the [NIH Grants Policy Statement](#).

INFORMATION: This award involves Human Subjects Research. See "Assurance Requirements and Institutional Review Boards" under Part II, Subpart A, Human Subjects, in the [NIH Grants Policy Statement](#), for specific requirements and grantee responsibilities related to the protection of human subjects, which are applicable to and are a term and condition of this award.

This award reflects the National Cancer Institute's acceptance of the certification that all key personnel have completed education on the protection of human subjects, in accordance the [NIH Grants Policy Statement](#), "Education in the Protection of Human Research Subjects."

Any individual involved in the design and conduct of the study that is not included in the certification must satisfy this requirement prior to participating in the project. Failure to comply can result in the suspension and/or termination of this award, withholding of support of the continuation award, audit disallowances, and/or other appropriate action.

INFORMATION: This award includes funds awarded for consortium activity. Consortia are to be established and administered as described in the [NIH Grants Policy Statement \(NIH GPS\)](#).

INFORMATION: Although the budget period start date for this award is April 17, 2019, this award includes funds for twelve months of support. Future year budget periods will cycle on March 1st. Allowable preaward costs may be charged to this award, in accordance with the conditions in the [NIH Grants Policy Statement \(October 2018\)](#), and with institutional requirements for prior approval.

INFORMATION: This award, including the budget and the budget period, has been discussed between Rogers Gross II of the National Cancer Institute and Marianne O'Neill on March 29, 2019.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program

Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Rogers Gross
Email: rogers.gross@nih.gov **Phone:** (240) 276-7589

Program Official: Sonya Roberson
Email: robersos@mail.nih.gov **Phone:** 240-276-6347 **Fax:** 240-276-7682

SPREADSHEET SUMMARY
GRANT NUMBER: 2P30CA010815-50

INSTITUTION: WISTAR INSTITUTE

Budget	Year 50	Year 51	Year 52	Year 53	Year 54
Salaries and Wages	\$925,069	FUTURE COSTS			
Fringe Benefits	\$345,980				
Personnel Costs (Subtotal)	\$1,271,049				
Consultant Services	\$10,299				
Other	\$200,585				
Subawards/Consortium/Contractual Costs	\$68,250				
TOTAL FEDERAL DC	\$1,550,183				
TOTAL FEDERAL F&A	\$1,199,128				
TOTAL COST	\$2,749,311				

Facilities and Administrative Costs	Year 50	Year 51	Year 52	Year 53	Year 54
F&A Cost Rate 1	78.6%	FUTURE COSTS			
F&A Cost Base 1	\$1,525,608				
F&A Costs 1	\$1,199,128				

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)

5. APPLICANT INFORMATION		Organizational DUNS*: 0755245950000
Legal Name*:	The Wistar Institute	
Department:		
Division:		
Street1*:	3601 Spruce Street	
Street2:		
City*:	Philadelphia	
County:	Philadelphia	
State*:	PA: Pennsylvania	
Province:		
Country*:	USA: UNITED STATES	
ZIP / Postal Code*:	19104-4265	
Person to be contacted on matters involving this application		
Prefix:	First Name*:	Middle Name:
	Jessica	
		Last Name*:
		Blodgett
		Suffix:
Position/Title:	Director, Research & Administrative Services	
Street1*:	3601 Spruce Street	
Street2:		
City*:	Philadelphia	
County:	Philadelphia	
State*:	PA: Pennsylvania	
Province:		
Country*:	USA: UNITED STATES	
ZIP / Postal Code*:	19104-4265	
Phone Number*:	215-495-6972	Fax Number: 215-898-6812
		Email: NOGA@wistar.org
7. TYPE OF APPLICANT*		
M: Nonprofit with 501C3 IRS Status (Other than Institution of Higher Education)		
Other (Specify):		
<input checked="" type="radio"/> Small Business Organization Type <input type="radio"/> Women Owned <input type="radio"/> Socially and Economically Disadvantaged		
11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*		
Animal Shared Resource		
12. PROPOSED PROJECT		
Start Date*	Ending Date*	
03/01/2019	02/29/2024	

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 _ 7 _ 8 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
5.a. If yes, please explain: Wistar: National Register (1978), PA Commission (2007)	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename ProjectSummary_Animal.pdf
8. Project Narrative*	
9. Bibliography & References Cited	
10. Facilities & Other Resources	
11. Equipment	
12. Other Attachments	SourcesofSupport_Animal.pdf

PROJECT SUMMARY – ANIMAL SHARED RESOURCE

The Wistar Cancer Center operates an AAALAC--accredited Animal Shared Resource (ASR) serving faculty from all three scientific Programs. Expert management, husbandry, custodial and veterinary staff maintain the ASR, including a modified Biosafety Level 2 (BSL2) barrier, with the following specific aims:

- Provide service in laboratory animal medicine and husbandry, routine animal procurement, animal health surveillance, veterinary care, inventory monitoring, quarantine housing, routine technical support and technical training for all Cancer Center investigators using animals in their research.
- Maintain an NSG (NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wj}/SzJ) breeding colony for the generation of immunodeficient mice.
- Provide access to expertise for the generation of transgenic and genetically modified mice through our inter-institutional collaboration with the transgenic mouse facility at [CONFIDENTIAL INFORMATION.REQUESTER IN AGREEMENT]
- Provide access to the services of a full time veterinary pathologist. [CONFIDENTIAL INFORMATION.REQUESTER IN AGREEMENT]
- Administer Institutional Animal Care and Use Committee (IACUC) mandated new employee orientation and IACUC procedures training as well as aseptic technique training for new researchers.
- House a suite for in vivo imaging, including a PerkinElmer IVIS Spectrum μ CT Imaging System.

Construction was completed, and the new, state-of-the-art vivarium opened in November 2013. Equipped with rack space to house more than 6,000 sterile, disposable, and individually-ventilated mouse cages, the brand new, 13,570 NSF, vivarium employs technologically-advanced, disposable, and individually-ventilated cages supported by a new HVAC system. Since 2013, [CONFIDENTIAL INFORMATION] investment of more than [CONFIDENTIAL INFORMATION] has been allocated to the ASR to fulfill the mission and research objectives of the Cancer Center (CC). This significant capital allocation allowed for the construction and fit-out of the new vivarium, including features which enhance all areas of animal care for Cancer Center investigators. Access controls include ID card swipe, biometric fingerprint scan, and security cameras. Holding rooms are equipped with new ventilated racks. Further investments include isolation cubicles, which are species independent and allow for maximum flexibility while providing the industry standard for containment and isolation. During the project period, the recruitment of 10 new CC members has driven a 47% increase in the use of murine animal models. An additional animal caretaker was hired in 2016 to meet the increasing demand for services. To streamline day-to-day operations of the ASR, a new IACUC protocol and Animal Facility Management system is being incorporated in 2018. Together, the ASR continues to play an essential role to support the scientific portfolio of all three Programs in the Cancer Center, tangibly contributing to key multidisciplinary scientific advances.

CONFIDENTIAL INFORMATION

SOURCES OF SUPPORT – ANIMAL SHARED RESOURCE

The operating budget for the Animal Shared Resource (ASR) is supported by three revenue sources: Cancer Center Support Grant (CCSG) allocations, fee for service/chargebacks, and other (Table 1). "Current support" reflects the actual level for 03/01/18 - 02/28/19. "Proposed support" reflects an estimate for Year 1 of the proposed budget (03/01/19 - 02/28/20).

Table 1. Operating Budget of the Animal Shared Resource

Income Source	03/01/18 - 2/28/19		03/01/19 - 02/29/20	
	Current Support	Percent of Current Total Budget	Proposed Support – Year 1	Percent of Proposed Total Budget
CCSG*	CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT			
Fee for Service/Chargebacks				
Other**				
Total Operating Budget				

*CCSG: allocation from the Cancer Center Support Grant will provide support for FTE described in the Budget Justification.

**Other: CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

The allocations of CCSG and Institute funds in support of ASR staff are summarized in Table 2.

Table 2. Proposed allocation of CCSG and Institute Support for ASR Staff (FTE)

CCSG supported FTE	Institute supported FTE	Total FTE	% CCSG supported FTE	% Institute supported FTE
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/> %	<input type="text"/> %

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator				
Prefix:	First Name*: Andrew	Middle Name J.	Last Name*: Caton	Suffix:
Position/Title*:	Professor			
Organization Name*:	The Wistar Institute			
Department:	Immunol, Microenv & Metastasis			
Division:				
Street1*:	3601 Spruce Street			
Street2:				
City*:	Philadelphia			
County:				
State*:	PA: Pennsylvania			
Province:				
Country*:	USA: UNITED STATES			
Zip / Postal Code*:	19104-4265			
Phone Number*: 215- 898-3871	Fax Number:			
E-Mail*: caton@wistar.org				
Credential, e.g., agency login:	eRA COMMONS USER NAME			
Project Role*: Other (Specify)	Other Project Role Category: Project Lead			
Degree Type:	Degree Year:			
Attach Biographical Sketch*:	File Name:	Biosketch_Caton.pdf		
Attach Current & Pending Support:	File Name:			

PROFILE - Senior/Key Person				
Prefix:	First Name*: Denise	Middle Name	Last Name*: DiFrancesco	Suffix:
Position/Title*:	Managing Director, Animal Shared Resource			
Organization Name*:	The Wistar Institute			
Department:				
Division:				
Street1*:	3601 Spruce Street			
Street2:				
City*:	Philadelphia			
County:				
State*:	PA: Pennsylvania			
Province:				
Country*:	USA: UNITED STATES			
Zip / Postal Code*:	19104-4265			
Phone Number*: 215-898-3782	Fax Number:			
E-Mail*: difrancesco@wistar.org				
Credential, e.g., agency login:				
Project Role*: Other (Specify)		Other Project Role Category: Managing Director		
Degree Type:		Degree Year:		
Attach Biographical Sketch*:	File Name:	Biosketch_DiFrancesco.pdf		
Attach Current & Pending Support:	File Name:			

PROFILE - Senior/Key Person				
Prefix:	First Name*: Richard	Middle Name W.	Last Name*: Boscoe	Suffix:
Position/Title*:	Private Veterinary Consultant			
Organization Name*:	Private Veterinary Consultant			
Department:				
Division:				
Street1*:	150 Ridge Pike A101			
Street2:				
City*:	Lafayette Hill			
County:				
State*:	PA: Pennsylvania			
Province:				
Country*:	USA: UNITED STATES			
Zip / Postal Code*:	19444-1929			
Phone Number*: 484-682-4372	Fax Number:			
E-Mail*: wistarattendingveterinarian@wistar.org				
Credential, e.g., agency login:				
Project Role*: Other (Specify)		Other Project Role Category: Veterinary Consultant		
Degree Type:		Degree Year:		
Attach Biographical Sketch*:	File Name:	Biosketch_Boscoe.pdf		
Attach Current & Pending Support:	File Name:			

PROFILE - Senior/Key Person				
Prefix:	First Name*: Pierre	Middle Name A.	Last Name*: Conti	Suffix:
Position/Title*: Private Veterinary Consultant				
Organization Name*: Private Veterinary Consultant				
Department:				
Division:				
Street1*: 8 West Mill Road				
Street2:				
City*: Flourtown				
County:				
State*: PA: Pennsylvania				
Province:				
Country*: USA: UNITED STATES				
Zip / Postal Code*: 19031-1908				
Phone Number*: 215-380-9252			Fax Number:	
E-Mail*: email-mamlmed@aol.com				
Credential, e.g., agency login:				
Project Role*: Other (Specify)			Other Project Role Category: Veterinary Consultant	
Degree Type:			Degree Year:	
Attach Biographical Sketch*:		File Name:	Biosketch_Conti.pdf	
Attach Current & Pending Support:		File Name:		

PROFILE - Senior/Key Person				
Prefix:	First Name*: David	Middle Name S.	Last Name*: Garlick	Suffix:
Position/Title*: Distinguished Senior Pathologist				
Organization Name*: HSRL, Inc.				
Department:				
Division:				
Street1*: 94 Robinson Road				
Street2:				
City*: Nashua				
County:				
State*: NH: New Hampshire				
Province:				
Country*: USA: UNITED STATES				
Zip / Postal Code*: 03060-5839				
Phone Number*: 508-344-3650			Fax Number:	
E-Mail*: dgarlick@hsrl.org				
Credential, e.g., agency login:				
Project Role*: Other (Specify)			Other Project Role Category: Mouse Pathologist	
Degree Type:			Degree Year:	
Attach Biographical Sketch*:		File Name:	Biosketch_Garlick.pdf	
Attach Current & Pending Support:		File Name:		

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0755245950000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: The Wistar Institute

Start Date*: 03-01-2019

End Date*: 02-29-2020

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Andrew		Caton	Ph.D	Project Lead	CAL. MONTHS	INST.	BASE SALARY		9,459.00	3,538.00	12,997.00
2.	Denise		DiFrancesco		Managing Director					51,390.00	19,220.00	70,610.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

83,607.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Health/Resource Coordinator	3.0			16,684.00	6,240.00	22,924.00
2	Breeding Technician	6.0			22,881.00	8,557.00	31,438.00
3	Total Number Other Personnel					Total Other Personnel	54,362.00
					Total Salary, Wages and Fringe Benefits (A+B)		137,969.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0755245950000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** The Wistar Institute**Start Date*:** 03-01-2019**End Date*:** 02-29-2020**Budget Period:** 1**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item**Funds Requested (\$)*****Total funds requested for all equipment listed in the attached file****Total Equipment** 0.00**Additional Equipment:** File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)

2. Foreign Travel Costs

Total Travel Cost 0.00**E. Participant/Trainee Support Costs****Funds Requested (\$)***

1. Tuition/Fees/Health Insurance

2. Stipends

3. Travel

4. Subsistence

5. Other:

Number of Participants/Trainees**Total Participant Trainee Support Costs** 0.00

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0755245950000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: The Wistar Institute

Start Date*: 03-01-2019

End Date*: 02-29-2020

Budget Period: 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	0.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	137,969.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. Modified Total Direct Costs	78.2	137,969.00	107,892.00
		Total Indirect Costs	107,892.00
Cognizant Federal Agency		DHHS Darryl Mayes 301-492-4855	
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	245,861.00

J. Fee	Funds Requested (\$)*
---------------	------------------------------

K. Total Costs and Fee	Funds Requested (\$)*
	245,861.00

L. Budget Justification*	File Name: BudgetJustification_Animal.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0755245950000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: The Wistar Institute

Start Date*: 03-01-2020

End Date*: 02-28-2021

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Andrew		Caton	Ph.D	Project Lead	CAL. MONTHS INST. BASE SALARY				9,480.00	3,546.00	13,026.00
2.	Denise		DiFrancesco		Managing Director					52,417.00	19,604.00	72,021.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

85,047.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Health/Resource Coordinator	3.0			17,018.00	6,365.00	23,383.00
2	Breeding Technician	6.0			23,337.00	8,728.00	32,065.00
3	Total Number Other Personnel					Total Other Personnel	55,448.00
Total Salary, Wages and Fringe Benefits (A+B)							140,495.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0755245950000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: The Wistar Institute

Start Date*: 03-01-2020

End Date*: 02-28-2021

Budget Period: 2

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item

Funds Requested (\$)*

Total funds requested for all equipment listed in the attached file

Total Equipment

0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)

2. Foreign Travel Costs

Total Travel Cost

0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance

2. Stipends

3. Travel

4. Subsistence

5. Other:

Number of Participants/Trainees

Total Participant Trainee Support Costs

0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0755245950000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: The Wistar Institute

Start Date*: 03-01-2020

End Date*: 02-28-2021

Budget Period: 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	0.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	140,495.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. Modified Total Direct Costs	78.2	140,495.00	109,867.00
		Total Indirect Costs	109,867.00
Cognizant Federal Agency		DHHS Darryl Mayes 301-492-4855	
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	250,362.00

J. Fee	Funds Requested (\$)*
---------------	------------------------------

K. Total Costs and Fee	Funds Requested (\$)*
	250,362.00

L. Budget Justification*	File Name: BudgetJustification_Animal.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0755245950000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: The Wistar Institute

Start Date*: 03-01-2021

End Date*: 02-28-2022

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary(\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Andrew		Caton	Ph.D	Project Lead	CAL. MONTHS, INST. BASE SALARY				9,480.00	3,546.00	13,026.00
2.	Denise		DiFrancesco		Managing Director					53,466.00	19,996.00	73,462.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

86,488.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Health/Resource Coordinator	3.0			17,358.00	6,492.00	23,850.00
2	Breeding Technician	6.0			23,804.00	8,903.00	32,707.00
3	Total Number Other Personnel					Total Other Personnel	56,557.00
Total Salary, Wages and Fringe Benefits (A+B)							143,045.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0755245950000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: The Wistar Institute

Start Date*: 03-01-2021

End Date*: 02-28-2022

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item

Funds Requested (\$)*

Total funds requested for all equipment listed in the attached file

Total Equipment 0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)

2. Foreign Travel Costs

Total Travel Cost 0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance

2. Stipends

3. Travel

4. Subsistence

5. Other:

Number of Participants/Trainees

Total Participant Trainee Support Costs 0.00

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0755245950000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** The Wistar institute**Start Date*:** 03-01-2021**End Date*:** 02-28-2022**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	0.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	143,045.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. Modified Total Direct Costs	78.2	143,045.00	111,861.00
Total Indirect Costs			111,861.00
Cognizant Federal Agency		DHHS Darryl Mayes 301-492-4855	
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	254,906.00

J. Fee	Funds Requested (\$)*

K. Total Costs and Fee	Funds Requested (\$)*
	254,906.00

L. Budget Justification*
File Name: BudgetJustification_Animal.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0755245950000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: The Wistar Institute

Start Date*: 03-01-2022

End Date*: 02-28-2023

Budget Period: 4

A. Senior/Key Person													
Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*	
1.	Andrew		Caplan		Ph.D Project Lead	CAL. MONTHS, INST. BASE SALARY				9,480.00	3,546.00	1 3,06.00	
2.	Denise		DiFrancesco		Managing Director					54,535.00	20,396.00	74,931.00	
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:		File Name:								Total Senior/Key Person		87,957.00	

B. Other Personnel							
Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Health/Resource Coordinator	3.0			17,705.00	6,622.00	24,327.00
2	Breeding Technician	6.0			24,281.00	9,081.00	33,362.00
3	Total Number Other Personnel					Total Other Personnel	57,689.00
Total Salary, Wages and Fringe Benefits (A+B)							145,646.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0755245950000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** The Wistar Institute**Start Date*:** 03-01-2022**End Date*:** 02-28-2023**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item**Funds Requested (\$)*****Total funds requested for all equipment listed in the attached file****Total Equipment****0.00****Additional Equipment:** File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)

2. Foreign Travel Costs

Total Travel Cost**0.00****E. Participant/Trainee Support Costs****Funds Requested (\$)***

1. Tuition/Fees/Health Insurance

2. Stipends

3. Travel

4. Subsistence

5. Other:

Number of Participants/Trainees**Total Participant Trainee Support Costs****0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0755245950000**Budget Type*:** ☒ Project ☐ Subaward /Consortium**Enter name of Organization:** The Wistar Institute**Start Date*:** 03-01-2022**End Date*:** 02-28-2023**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium /Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	0.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	145,646.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. Modified Total Direct Costs	78.2	145,646.00	113,895.00
Total Indirect Costs			113,895.00
Cognizant Federal Agency		DHHS Darryl Mayes 301-492-4855	
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	259,541.00

J. Fee	Funds Requested (\$)*

K. Total Costs and Fee	Funds Requested (\$)*
	259,541.00

L. Budget Justification*
File Name: BudgetJustification_Animal.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0755245950000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: The Wistar Institute

Start Date*: 03-01-2023

End Date*: 02-29-2024

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Andrew		Cabon	Ph.D	Project Lead	CAL. MONTHS, INST. BASE SALARY				9,480.00	3,546.00	13,026.00
2.	Denise		DiFrancesco		Managing Director					55,626.00	20,804.00	76,430.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

89,456.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Health/Resource Coordinator	3.0			18,060.00	6,754.00	24,814.00
2	Breeding Technician	6.0			24,766.00	9,262.00	34,028.00
3	Total Number Other Personnel					Total Other Personnel	58,842.00
Total Salary, Wages and Fringe Benefits (A+B)							148,298.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0755245950000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** The Wistar Institute**Start Date*:** 03-01-2023**End Date*:** 02-29-2024**Budget Period:** 5**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item**Funds Requested (\$)*****Total funds requested for all equipment listed in the attached file****Total Equipment****0.00****Additional Equipment:** File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)

2. Foreign Travel Costs

Total Travel Cost**0.00****E. Participant/Trainee Support Costs****Funds Requested (\$)***

1. Tuition /Fees/Health Insurance

2. Stipends

3. Travel

4. Subsistence

5. Other:

Number of Participants/Trainees**Total Participant Trainee Support Costs****0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0755245950000**Budget Type*:** ☒ Project ☐ Subaward /Consortium**Enter name of Organization:** The Wistar Institute**Start Date*:** 03-01-2023**End Date*:** 02-29-2024**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	0.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	148,298.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. Modified Total Direct Costs	78.2	148,298.00	115,969.00
Total Indirect Costs			115,969.00
Cognizant Federal Agency		DHHS Darryl Mayes 301-492-4855	
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	264,267.00

J. Fee	Funds Requested (\$)*

K. Total Costs and Fee	Funds Requested (\$)*
	264,267.00

L. Budget Justification*	File Name: BudgetJustification_Animal.pdf
(Only attach one file.)	

RESEARCH & RELATED Budget (F-K) (Funds Requested)

BUDGET JUSTIFICATION -- ANIMAL SHARED RESOURCE

The organizational chart and full staff (☐ FTE) of the Animal Shared Resource (ASR), including two attending veterinarians, a mouse pathologist, a transgenic mouse consultant, and the Institutional Official for Wistar's Animal Care and Use Program available to the Shared Resource, are shown in Figure 1.

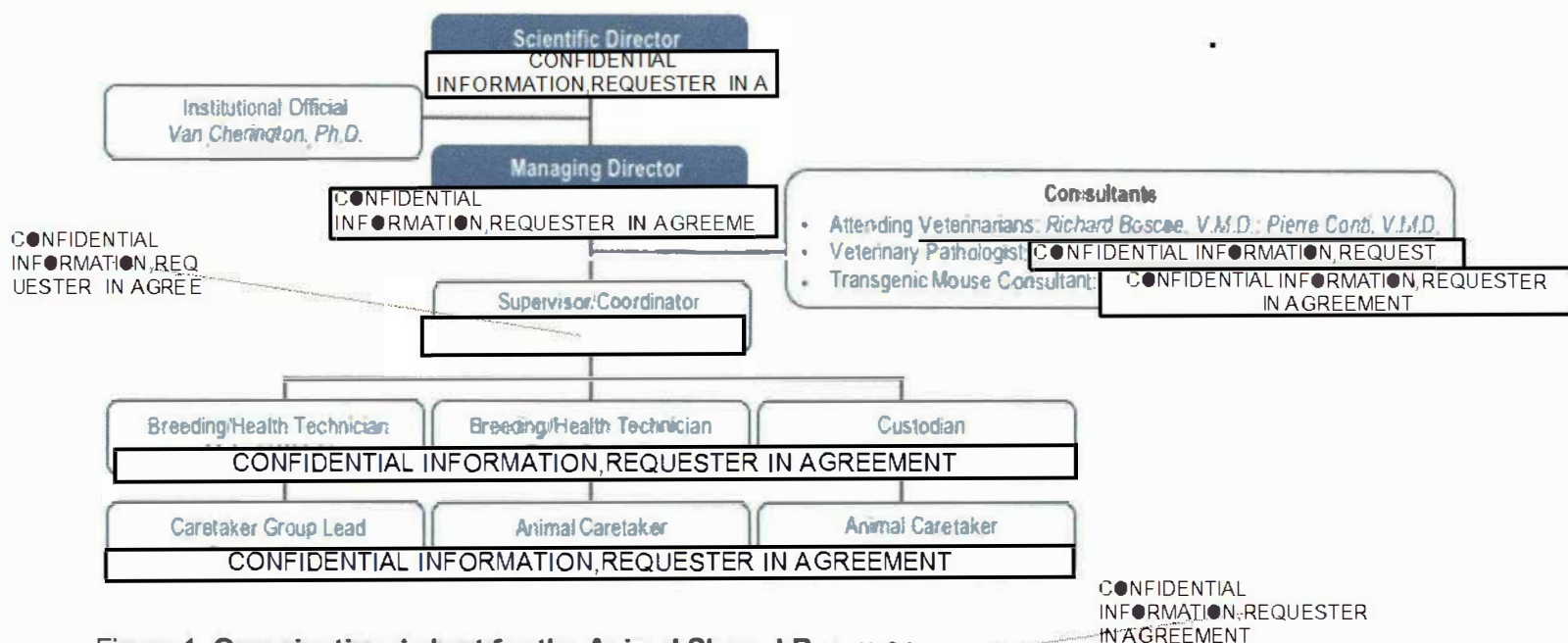


Figure 1. Organizational chart for the Animal Shared Resource

Key Personnel:

☐ Scientific Director, ☐ is a Professor and has been the chair of the Wistar Institutional Animal Care and Use Committee (IACUC) since 2001. His research focuses on mouse models for immune activation, tolerance and inflammation, and he is thus well informed on technological and scientific advances related to experimental rodents. As Scientific Director of the ASR, ☐ provides scientific oversight to ensure that this shared resources meets the scientific needs of Cancer Center members, a role he has held since 2011. ☐ is a member of the Shared Resources Committee of the Cancer Center.

☐ CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

Managing Director

☐ CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

☐ is responsible for the day-to-day management of the ASR. ☐ has a total of 34 years of experience in managing and overseeing the ASR, serving as Director for 13 years and as a supervisor prior to her promotion to Director. Her principal duties include: hiring, training, supervising and evaluating ASR personnel; overseeing husbandry and sanitation; and overseeing all aspects of ASR operations. ☐ is currently pursuing a Bachelor's degree in Business Administration and is a member of the Wistar IACUC. ☐ and Dr. Van Cherington, the Institutional Official for the IACUC and the Wistar Animal Care and Use Program, maintain current knowledge of changes in government regulations and advances in animal husbandry by attending national meetings and webinars sponsored by the Office of Laboratory Animal Welfare (OLAW), Public Responsibility in Medicine and Research (PRIM&R), the American College of Laboratory Animal Medicine (ACLAM), the American Association for Laboratory Animal Science (AALAS), and the Laboratory Animal Management Association (LAMA). ☐ has served as an AALAS Board of Trustees member and liaison, ILAM committee member, an AAALAC member organization delegate for the Association for Independent Research Institutes (AIRI), and AALAS Awards committee member. ☐ is a member of the Shared Resource Committee of the Cancer Center and organizes the ASR User Group meetings.

Other Personnel:

CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

Supervisor/Animal Health Resource Coordinator,

CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT has twelve years of experience in her position, handling major operational duties, including daily ordering of all research animals and supplies. She directs the housing of animals, files protocols, records animal orders to the investigators' protocols and databases, and communicates the status of orders to the scientific staff. She also places weekly orders of feed, bedding, and supplies; records all animal cage counts; and presents the monthly census to the finance office for the animal per-diem billing. She oversees operations, including animal caretaker activities and responsibilities, and holds User Group meetings in CONFIDENTIAL absence. CONFIDENTIAL INFO also serves as CONFIDENTIAL alternate on the IACUC.

CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

CONFIDENTIAL has served in this position for 26 years. He is responsible for ear tagging and collecting serum samples from rodents. CONFIDENTIAL prepares samples for shipment to independent diagnostic labs and conducts bacteriological and endo-and ecto-parasitic testing. He administers prophylactic and therapeutic medication to the research animals when prescribed by the veterinarians. CONFIDENTIAL has been trained by a professional training service company, Animal Care Training Services (ACTs), to train animal users with the handling, restraining, injecting and bleeding procedures they require. He supports the NSG mouse breeding colony and the transgenic mouse services as part of the inter-Institutional service agreement with the CONFIDENTIAL

CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

CONFIDENTIAL Animal Breeding/Health Technician, CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

CONFIDENTIAL has eight years of caretaker experience and devotes % of her effort to the ASR. CONFIDENTIAL Conicello was promoted in 2011 after receiving her Registered Assistant Laboratory Animal Technician (RALAT) certification and being trained by a professional training company (ACTs). CONFIDENTIAL received her AALAS LAT certification in 2013. She supports the NSG mouse breeding colony. In addition, she supports the transgenic mouse services in collaboration with staff from CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

Richard Boscoe, V.M.D., Consultant, Attending Veterinarian, CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

CONFIDENTIAL received his V.M.D. degree from the University of Pennsylvania School of Veterinary Medicine in 1976. He served as Veterinary Medical Officer for the U.S. Department of Agriculture from 1976-1991 and has been an attending veterinarian in laboratory animal medicine since 1993.

Pierre Conti, V.M.D., M.B.A., Consultant, Attending Veterinarian, CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

CONFIDENTIAL received his V.M.D. degree from the University of Pennsylvania School of Veterinary Medicine in 1960 and his M.B.A. with honors from Eastern College. Dr. Conti also received a Certification in Quality Assurance/Regulatory Affairs from Temple University. Dr. Conti has been an associate veterinarian, senior veterinarian, and directing and attending veterinarian in laboratory animal medicine since 1962.

CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT Consultant, Veterinary Pathologist, CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

CONFIDENTIAL earned his D.V.M. from Tufts University School of Veterinary Medicine in 1985 and completed his pathology residency training at Tufts in 1989. Since 2011, CONFIDENTIAL has provided Cancer Center investigators with expert veterinary pathology evaluation and consultation of mouse models of cancer. CONFIDENTIAL coordinates the evaluation, analysis, and reporting of genetic or xenograft models of cancer onset and progression.

CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT Consultant, Director, Transgenic Mouse Facility (TMF) at CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

CONFIDENTIAL, CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT, is a professor at CONFIDENTIAL. He received his Ph.D. from Harvard University and completed his postdoctoral training at Massachusetts Institute of Technology. In 2012, Wistar and CONFIDENTIAL signed an inter-Institutional agreement to provide their investigators mutual access to technologies in shared resources at discounted pricing. Through this agreement, the CONFIDENTIAL TMF provides Wistar Cancer Center members with access to services to introduce, delete or modify endogenous genes to answer questions about gene function. As TMF Director, CONFIDENTIAL provides consultation and oversees delivery of services to Wistar Cancer Center members.

CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT

Obtained by Rise for Animals. Uploaded 08/19/2020

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		432,555.00
Section B, Other Personnel		282,898.00
Total Number Other Personnel	15	
Total Salary, Wages and Fringe Benefits (A+B)		715,453.00
Section C, Equipment		0.00
Section D, Travel		0.00
1. Domestic	0.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		0.00
1. Materials and Supplies	0.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		715,453.00
Section H, Indirect Costs		559,484.00
Section I, Total Direct and Indirect Costs (G + H)		1,274,937.00
Section J, Fee		0.00
Section K, Total Direct and Fee (I + J)		1,274,937.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

Expiration Date: 03/31/2020

1. Vertebrate Animals Section

Are vertebrate animals euthanized? ☒ Yes ☐ No

If "Yes" to euthanasia

Is the method consistent with American Veterinary Medical Association (AVMA) guidelines?

☒ Yes ☐ No

If "No" to AVMA guidelines, describe method and provide scientific justification

2. *Program Income Section

*Is program income anticipated during the periods for which the grant support is requested?

☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period	*Anticipated Amount (\$)	*Source(s)
----------------	--------------------------	------------

PHS 398 Cover Page Supplement

3. Human Embryonic Stem Cells Section

*Does the proposed project involve human embryonic stem cells? ☐ Yes ☒ No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, check the box indicating that one from the registry will be used:

☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

Cell Line(s) (Example: 0004):

4. Inventions and Patents Section (Renewal applications)

*Inventions and Patents: ☒ Yes ☐ No

If the answer is "Yes" then please answer the following:

*Previously Reported: ☒ Yes ☐ No

5. Change of Investigator/Change of Institution Section

☐ Change of Project Director/Principal Investigator

Name of former Project Director/Principal Investigator

Prefix:

*First Name:

Middle Name:

*Last Name:

Suffix:

☐ Change of Grantee Institution

*Name of former institution:

PHS 398 Research Plan

OMB Number: 0925-0001
Expiration Date: 03/31/2020

Introduction	
1. Introduction to Application (for Resubmission and Revision applications)	
Research Plan Section	
2. Specific Aims	SpecificAims_Animal.pdf
3. Research Strategy*	ResearchStrategy_Animal.pdf
4. Progress Report Publication List	
Other Research Plan Section	
5. Vertebrate Animals	VertebrateAnimals_Animal.pdf
6. Select Agent Research	
7. Multiple PD/PI Leadership Plan	
8. Consortium/Contractual Arrangements	
9. Letters of Support	
10. Resource Sharing Plan(s)	
11. Authentication of Key Biological and/or Chemical Resources	
Appendix	
12. Appendix	

SPECIFIC AIMS – ANIMAL SHARED RESOURCE

The Wistar Institute Cancer Center operates an AAALAC International-accredited Animal Shared Resource serving faculty from all three scientific Programs. Expert management, husbandry, custodial and veterinary staff maintain this Resource, including a modified Biosafety Level 2 (BSL2) barrier, with the following Specific Aims:

Specific Aim 1. Provide service in laboratory animal medicine and husbandry, routine animal procurement, animal health surveillance, veterinary care, inventory monitoring, quarantine housing, routine technical support and technical training for all Cancer Center investigators using animals in their research.

Specific Aim 2. Maintain an NSG (NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wjl}/SzJ) breeding colony for the generation of immunodeficient mice.

Specific Aim 3. Provide access to expertise for the generation of transgenic and genetically modified mice through our inter-institutional collaboration with the transgenic mouse facility at

CONFIDENTIAL INFORMATION REQUESTER IN AGREEMENT

Specific Aim 4. Provide access to the services of a full-time veterinary pathologist,

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Specific Aim 5. Administer Institutional Animal Care and Use Committee (IACUC) mandated new employee orientation and IACUC procedures training and orientation tours and aseptic technique training for new researchers.

Specific Aim 6. House a suite and provide custodial support for in vivo imaging using a PerkinElmer IVIS Spectrum CT Imaging System.

RESEARCH STRATEGY – ANIMAL SHARED RESOURCE**1. Technologies, Equipment, Services and Expertise**

The Animal Shared Resource (ASR) is essential to the three research Programs and supports Wistar Cancer Center (CC) research by providing state-of-the-art housing and animal care. The ASR and animal care and use program have been fully accredited by AAALAC International since 1998. Full accreditation was most recently renewed in November 2015, with an upcoming site visit for reaccreditation anticipated for 2018.

Technologies and Equipment

Wistar opened its new, state-of-the-art vivarium in November 2013. Upon its completion, all research animals returned to Wistar from temporary space, providing optimal access for all CC members and facilitating increased usage brought on by 10 new CC faculty recruited during the project period. Since 2013, [REDACTED] invested [REDACTED] for the construction of the new vivarium and equipment listed in Table 1. The new 13,570 NSF vivarium includes 5,009 NSF of procedure and holding rooms equipped with single-use, individually ventilated caging systems. Support areas, 8,561 NSF, include feed and materials storage, staff room and offices, receiving, autoclaves, washer, hydrogen peroxide vapor decontamination equipment, quarantine, and service corridors. Designed for efficiency, the facility utilizes a new caging system to maximize space in holding rooms, and provides remote adjustment of blower operation, air changes/hour, and alert history. Secure access controls include ID card swipe, biometric fingerprint scan, and cameras monitored by on-site security staff 24/7/365 to record personnel entering and leaving the barrier. An Aircuity system was implemented in 2017, providing additional control and real-time air quality results in the vivarium. In 2018, the ASR will implement a new Institutional Animal Care and Use Committee (IACUC) and Animal Facility Management System (eSirius/NTM software) to streamline ASR workflow including: animal procurement, inventory management, services, billing, veterinary care oversight and IACUC protocol management.

Table 1. Equipment purchases and upgrades for the Animal Shared Resource.

Equipment purchases and upgrades	Cost	Source of Funds	Year Acquired
Innovive cage racks, 2 double; 16 single; and blowers	CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT		2013-2017
2 Anesthesia machines, refrigerator, tattoo device			2013, 2017
Isolation cubicles and door sweeps			2016
4 Class II Type A2 vert. laminar hoods, 4'			2016, 2017
Animal Facility & IACUC Management eSirius software			2017
Construction of new vivarium shell and fit-out			2014
TOTAL EQUIPMENT AND IMPROVEMENTS			

Services - The following services are performed by highly trained and experienced ASR staff:

- **Centralized animal purchasing and husbandry.** Staff assign protocols, track animal numbers, report sick animals to veterinarians and treat animals as prescribed, and conduct IACUC-approved procedures.
- **Animal health surveillance program.** Serological testing for common murine viruses, mycoplasma, pinworm and mites is performed periodically on representative samplings of experimental and sentinel animals.
- **Quarantine and infectious agent containment facilities.** Only animals from vendors approved by a veterinarian are accepted into the ASR. Unapproved animals enter quarantine rooms and are only released when proven free of murine virus and pinworm/mite infection and when helicobacter status is known.
- **Veterinary care** is overseen by two highly qualified consulting veterinarians, Richard Boscoe, V.M.D., and Pierre Conti, V.M.D., who serve as attending veterinarians on the Wistar IACUC, assuring veterinary expertise for review of each IACUC protocol. A veterinarian is on call at all times for emergencies.
- **Veterinary pharmacy.** The ASR manages a pharmacy providing agents for treatments, anesthetics and analgesics. Controlled substances are distributed by designated staff under a veterinarian's license.
- **NSG mouse colony.** ASR staff maintain a breeding colony of NSG (NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wjl}/SzJ) immunodeficient mice lacking mature T, B and functional NK cells, and deficient in cytokine signaling.
- **Transgenic and knock-in, knock-out genetically modified mice.** A Memorandum of Understanding for generating transgenic and genetically modified mice between Wistar [REDACTED] was signed in 2012. Through this efficient, cost-effective model for sharing regional resources, CC members have access to [REDACTED] technology and services at the same cost afforded to [REDACTED] members.
- **Mouse Pathology.** [REDACTED] an experienced veterinary pathologist, provides CC members with consultation, histology evaluation, detailed pathology reports, and publication-quality images.

- **Biosafety.** Institutional Environmental Health and Safety staff and Resource leadership instruct investigators on safety techniques. The IACUC protocol review process ensures that safety issues are addressed. Also, **Training** such as orientation, safety, aseptic technique & online testing are provided.
- **Consultation regarding best practices** for investigator protocols and **facilitating collaborative interaction** with CC members, other Shared Resources & outside investigators (e.g. co-managing IVIS with Imaging SR).
- **Quality assurance.** Staff interact promptly with investigators in the event of problems through monthly ASR User Group meetings.

Expertise: The organizational chart and detailed descriptions of credentials for all CCSG supported staff are provided in the Budget Justification section. Briefly, the leadership of ASR has not changed since the last CCSG budget cycle and consists of a Scientific Director [CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT] a Managing Director [CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT] and an Institutional Official, Dr. Van Cherington. Staff [CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT] include a Supervisor [CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT], two Breeding technicians [CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT] and three Caretakers. [CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT] has over 15 years of experience directing animal facilities and has been chair of the IACUC since 2001. [CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT] has over 34 years of experience, serving as director for 13 years. She oversees day-to-day operation, supervises staff, manages maintenance of space and equipment, and consults with users. Dr. Cherington ensures the Institute has a compliant animal care and use program. [CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT] and the three caretakers have 8, 26, and over 30 years of experience respectively in the ASR. Drs. Conti and Boscoe, have been Attending Veterinarians in laboratory animal medicine since 1962 and 1993 respectively. [CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT] is professor and director of the [CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT] transgenic mouse facility. [CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT] Veterinary Pathologist, has provided expert veterinary pathology evaluation and consultation of mouse models of cancer to CC members since 2011.

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2. Importance of the Resource in Relation to the Scientific Objectives of the Cancer Center
Cancer Center (CC) members from all three Programs rely heavily on the ASR. Although no rodent model can faithfully recapitulate the complexity of tumor onset and progression, these models are now indispensable for modern cancer research. Experimental projects related to mechanisms of senescence, cancer experimental therapeutics, tumor metabolic reprogramming and adaptation, and anti-tumor immunity all involve in vivo evaluation of xenograft or genetically modified mice. In this context, the ASR provides a unifying, high-quality vehicle for inter-programmatic collaboration in the CC. During the last CCSG budget cycle period, the ASR supported 110 of the cancer-related publications from all three CC research Programs (Table 2). Examples of pivotal scientific accomplishments supported by the Resource follow below.

Table 2. Cancer-related publications supported by the ASR per Program.

Total WCC publications	GER publications	MCO publications	IMM publications
110*	23	70	57

WCC, Wistar Cancer Center; GER, Gene Expression and Regulation; MCO, Molecular and Cellular Oncogenesis; IMM, Immunology, Microenvironment and Metastasis. *Due to inter-programmatic collaborations the sum of the three Programs does not equal the total publications supported by the ASR.

Key Scientific Accomplishments

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3. Use and Cost Effectiveness of Services

To ensure cost-effectiveness, financial sustainability is considered together with impact of services on research conducted by CC members and an assessment of rates and similar services offered by outside providers. ASR costs are controlled by maximizing operating efficiency and are structured to provide high quality service at the best possible price for CC members. Service of low quality and/or comparably high fees leads to decreased core utilization and impact; therefore, use of ASR services is monitored along with three revenue sources for the operating budget (see Budget Justification): (i) CCSG allocations, (ii) chargebacks for ASR services, and (iii) Institute funds. Both CCSG and Institute funds benefit CC members who pay subsidized rates for services.

Use of Services. The average daily number of mouse cages housed in the vivarium for 2014-2018 is listed in Table 3. During the last CCSG budget cycle, the use of murine animal models by CC members **has increased by 47%**. An increase in the average daily census, from 2,127 to 3,128 mouse cages, has been driven by the recruitment of 10 new CC members.

Table 3. Average daily census of mouse cages (2014–2018).

Year	2014	2015	2016	2017	2018 (Jan-Mar)
Mouse cages	2,127	2,059	2,423	2,889	3,128

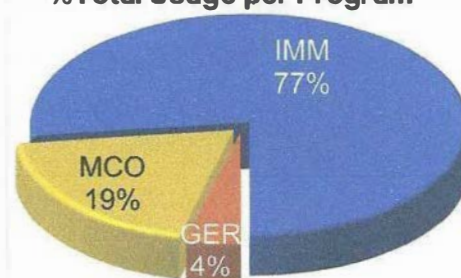
Use of the ASR by CC members assessed per Program is presented in Table 4. 24 CC members, representing all three CC Programs utilized the Resource during the period 3/1/2014 – 3/31/2018. 100% of CC usage (units=cage days) was by peer-reviewed funded CC members. The ASR remains essential to all three Programs, and tangibly advances their scientific goals and thematic objectives (Table 2 and Table 4). Programmatic usage is expected to further increase as a result of recently recruited CC members, [REDACTED]

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Table 4. Current use of the Resource by all three CC Programs.

Usage 3/1/14 - 3/31/18	#Users	# Units	% Total
CC Members, [REDACTED]	24	2,566,451	100
GER Program, [REDACTED]	4	91,366	4
MCO Program, [REDACTED]	6	474,726	19
IMM Program, [REDACTED]	14	2,000,359	77
CC Members, [REDACTED]	0	0	0
TOTAL CC Member Usage	24	2,566,451	100

%Total Usage per Program



Rates for Services and Comparison with Outside Providers

CCSG support for the ASR gives CC members/affiliates access to high quality service at the lowest available rates. Non-affiliated academic users are charged higher rates than CC members to recover direct costs. ASR rates are approved by the CC Director based on total operating costs and are reviewed annually by the ASR Directors and the Assistant Director for Shared Resources. Changes in rates are advertised Cancer Center-wide through memoranda and the Shared Resource web site. ASR fees are based on fixed operating costs and variable costs associated with specific services and remain competitive compared to those in available facilities at neighboring academic Institutions. A comparison of current ASR fees is presented in Table 5, showing rates for Wistar's ASR services vs. comparable rates at a neighboring academic institution.

Table 5. Rates for Animal Shared Resource Major Services.

Description	Wistar CC Member	Comparable Rates
<i>Housing mice</i>	CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT	CONFIDENTIAL INFORMATION, REQUESTER IN AGREEMENT
Mouse cage per diem rate (individually-ventilated cage)		
NSG (NOD.Cg-Prkdc ^{scid} Il2rg ^{tm1Wjl} /SzJ) mouse breeding colony		
Tiered rate per total # NSG mice delivered monthly (1 - >200)		
<i>Transgenic mouse service rates</i>		
Cryopreservation of one mouse line; Re-derivation		
Single-day ES cell microinjection into 50-60 host blastocysts		

Obtained by Rise for Animals. Uploaded 08/19/2020

Transgenic mouse production (pronuclear micro-injections with DNA constructs to provide F1 zygotes)

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4. *Management structure and unique processes.*

The operation and monitoring of the ASR involves a three-tier mechanism ensuring timely response to emerging needs, comprehensive users' feedback, sustained quality of service, and regional competitiveness.

- **Intra-Resource Oversight and Quality Assessment.** Organizational hierarchy: Scientific Director, Managing Director, Staff. The ASR Directors provide oversight and monitor quality of service through user feedback, an annual online questionnaire covering all SR services and an independent yearly assessment of similar services conducted with the Assistant Director for Shared Resources (ADSR). *ASR User Group meetings* are held for all CC scientific staff, convene monthly and provide a formal mechanism for feedback from users on Resource operations, future directions or service improvements. The ADSR also attends User Group meetings to monitor attendance, agenda, and user concerns, and meets with the Managing Director quarterly to review usage, chargebacks, and contributions to publications and grants.
- **Inter-Resource Oversight.** In preparation for the yearly evaluation by the *Steering Committee for Shared Resources*, the ADSR and ASR Managing Director meet to summarize the current and projected operating budget and prioritize any capital requests. Both the Scientific and Managing Directors serve on the *Cancer Center Shared Resource Committee* to discuss operational concerns, potential development opportunities and areas of possible collaboration to further the scientific goals of the CC.
- **Yearly Cancer Center-Shared Resource Evaluation and Budget Modifications.** ASR budget and capital requests are considered together with the annual review conducted by the *Steering Committee for Shared Resources*. As CC Director, Dr. Altieri makes the final determinations on the recommendations made and final approval of the ASR budget is provided by the Institute and the Board of Trustees.

5. *Policies on Use, Operation, and Outreach*

ASR personnel are available Monday through Friday from 8:00 AM to 4:30 PM and outside normal operating hours upon request. Users have access to the ASR 24/7/365. ASR staff communicate with users directly by phone, e-mail or in person, during monthly user meetings, or through the ASR website. ASR Directors are available to provide advice regarding access, colony management issues, and other animal research related matters. An ASR advisory committee (on which the ASR Directors and the Institutional Official are members) assesses user feedback, staff performance, capacity and equipment. CC members/affiliates receive priority access. For all Shared Resources, the percentage of total effort used to serve CC members must be equal to or greater than the percentage of CCSG support for the total direct costs operating budget. ASR receives 11% CCSG allocation for the operating budget with 100% CC usage supported by peer-reviewed funding. If CC member usage allows for unused ASR capacity, requests to house animals from other institutions are considered on a case-by-case basis by the CC Director and the ASR advisory committee to ensure no negative impact on research, capacity or ASR access by CC members. Outreach to users takes place through seminars, distribution of a SR brochure, E-newsletter, and website content to ensure all CC members are informed about the services of the ASR and have opportunities to take advantage of the equipment and expertise offered by the facility.

6. *Development and Future Directions*

For the next CCSG budget cycle, the ASR will focus efforts in several areas to continue the successful trajectory of the past budget cycle and function as an essential service to support the basic and translational mission of the CC. 1) To maximize efficiency and cost-effectiveness through improved automation of CC services, in 2018 the ASR will roll out an automated IACUC and Animal Facility Management System. The system will allow for automated cage census tracking, billing and procurement, and will effectively streamline the IACUC protocol management workflow for new applications, approvals, amendments, annual continuation and *de novo* renewals. ASR staff will train CC researchers who will benefit from the new user-friendly application to submit protocols and faster turnaround time for protocol review and approval. 2) To meet the needs of CC members, the ASR will dedicate effort and add personnel as needed to support recently launched staff services, performing procedures in support of investigators' IACUC-approved animal protocols such as: ear tagging, oral gavage, cervical dislocation, injections (IP, IM, SQ, retro-orbital), bleeding (submandibular, retro-orbital), and tumor caliper measurements. 3) For CC members in need of more technically demanding services, the ASR will explore leveraging its staff experience with animal colony management and breeding to support cutting-edge animal research for CC laboratories.

PHS Human Subjects and Clinical Trials Information

● MB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

Are Human Subjects Involved

☐ Yes ☒ No

Is the Project Exempt from Federal regulations?

☐ Yes ☐ No

Exemption Number

☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8

Does the proposed research involve human specimens and/or data

☐ Yes ☒ No

Other Requested information

VERTEBRATE ANIMALS – ANIMAL SHARED RESOURCE

The Wistar Institute animal care and use program is registered as a research facility with the United States Department of Agriculture, is fully accredited by AAALAC International, and has an Animal Welfare Assurance (A3432-01) on file with the NIH Office of Laboratory Animal Welfare. All aspects of the program operate in compliance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals and the Guide for the Care and Use of Laboratory Animals.

1. Description of Procedures

Cryopreservation and Regeneration of Transgenic and Chimeric Mice: Procedures for cryopreservation and regeneration of mouse strains are performed by personnel from [REDACTED] using the Wistar Animal Facility. Superovulation in female mice (4-6 weeks) of the strain to be cryopreserved is induced by pregnant mare's serum gonadotropin and human chorionic gonadotropin. After 3 days housing with a male, embryos are harvested following CO₂ euthanasia. To regenerate strains, cryopreserved or freshly harvested fertilized embryos are implanted into CD-1 or Swiss Webster females, pseudo-pregnant following housing with a vasectomized male. Embryos from the strain to be rederived are implanted into the pseudo-pregnant CD-1 or Swiss Webster females under ketamine/xylazine anesthesia. Four hundred mice are approved for these procedures. Approximately 20 animals are required for each procedure.

Cell Line Testing: Female mice, 6-8 weeks (CD-1 or other strain if needed to match strain to be used in experiments with cell line) are injected (cell number and route consistent with the Institutional Animal Care and Use Committee (IACUC) approved protocol involving the cell line) with the cell line to be tested. One cell line per mouse. Up to 3 injected mice are housed with two pathogen-free sentinel mice per cage. Blood samples (20-40 microliters – submandibular) are collected pre-exposure and at 28 days post-exposure. Samples are sent to an outside lab for analysis. Mice are monitored for adverse effects, e.g. tumorigenesis, of the injected cells. If injected mice must be euthanized prior to 28 days, un-injected sentinel mice are tested after an extended period (42 days rather than 28 days). One hundred mice are approved for this procedure, and 3-5 mice are required for each test depending upon the number of cell lines to be tested.

NSG Mouse Breeding Program: An NSG (NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wjl}/SzJ) immunodeficient mouse breeding colony is maintained by the Animal Facility to generate mice for research use. Trio breeding is used and the number of breeding cages is determined by projected research requirements. These are based upon periodic updates of standing orders placed by research staff. Pups are weaned by Animal Facility staff at 3 weeks and separated by sex. The mother is placed back into the breeding colony and pups are transferred to experimental protocols according to orders placed. Some pups not used for experiments are returned to the breeding colony at 6 weeks to meet demand and to replace retired breeders. Other mice not required for research or breeding are used for training (see section 4) or are euthanized. Retired breeders (~6 months) are euthanized by CO₂. Approximately 80-240 breeders are required to maintain this colony (variation based upon projected demand).

Animal Facility Training Protocol: The IACUC mandates that all individuals working with animals are properly trained. The animal facility staff ensure that training is provided. Mice on the training protocol are used to train individuals on proper techniques of animal handling, e.g. sex determination, handling and restraint, identification methods (such as tagging, tattoo), injections, oral gavage, blood collection, euthanasia and verification of death. NSG mice from the breeding colony that are not required for research are in some cases transferred to the training protocol at 9-12 weeks for this purpose. Similarly, mice from other research breeding colonies (conducted under investigator's IACUC-approved protocols) that cannot be used for research, e.g. due to incorrect genotype, are in some cases transferred to the training protocol at 3-6 weeks of age. Approximately 300 mice per year are used for the training program.

Sentinel Program: Sentinel mice (female CD-1, 6-8 weeks of age) located on each cage rack in each holding room are exposed to feces and bedding from cages within the same rack. At intervals over 6-12 months blood samples are taken from sentinel mice. Sentinel mice are also shipped to an outside

laboratory for diagnostic testing. NSG immunodeficient mice (6-8 weeks) are also used as sentinels for *C. bovis* in immunodeficient experimental colonies. Approximately 200 mice are used per year for the sentinel program.

2. Justifications

Mice are used for three main purposes. First, they are used for the generation or cryopreservation of genetically-modified mouse strains for use in studies of the interaction of tumors with the microenvironment of intact animals. They are similarly used for expansion and characterization of human tumor cells while preventing the adaption and differentiation of these cells that would otherwise occur in order to allow growth in in vitro culture conditions. Second, they are used for screening of cell lines, tissues, and of the mouse research colony for the presence of pathogens that could potentially infect experimental mice and compromise the data that will be collected. Third, they are used for training of individuals for carrying out procedures on Cancer Center investigators' IACUC-approved protocols. The use of mice is central to the design of the experiments, which rely on the availability of genetically manipulated inbred strains of mice, and no in vitro or computer models exist that can recapitulate the complex and multifaceted processes that are to be studied.

3. Minimization of Pain and Distress

Cryopreservation and Regeneration of Transgenic and Chimeric Mice: Pain during and following surgery (vasectomy or embryo implantation) is managed using Ketamine/Xylazine anesthesia during the surgery and peri-operative extended release buprenorphine for post-surgical analgesia. Mice are kept warm and monitored carefully for signs of distress during their recovery following surgery.

Cell Line Testing: Although they seldom occur, mice are monitored for possible adverse effects, e.g. tumorigenesis, of injected cell lines and euthanized as needed to alleviate pain and distress using criteria defined and approved by the IACUC (e.g. cachexia, immobility).

NSG Mouse Breeding Program: No pain or distress is anticipated. Mice beyond breeding age or that show signs of poor health as determined by a veterinarian are euthanized.

Animal Facility Training Protocol: Although new staff are trained by experienced individuals, adverse outcomes can occasionally occur following training on certain procedures such as blood collection or oral gavage. Mice experiencing adverse outcomes in these cases are euthanized.

Sentinel Programing: Animals are examined daily for health status and euthanized if recommended by the veterinarian.