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| Program Director/Principal Investigator (Last, First, Middle): | Bioinformatics Core (BIC) |
| **RESOURCES** | |
| Follow the 398 application instructions in Part I, 4.7 Resources. |  |
| **OFFICE**  The Bioinformatics Core (BIC) is a computation and data analysis based service unit. The core shares office space with the Institute for Biomedical Informatics (IBI) on the second floor of Richards Building at University of Pennsylvania. This convenient location enables a close collaboration between BIC and the IBI bioinformatics and computational labs.  **HPC**  The high performance computation (HPC) resources are essential for the core to work on large scale biomedical data. BIC is collaborating with Penn Medicine Academic Computing Services (PMACS) to access HPC resources. The PMACS HPC system houses a cluster of 144 IBM iDataPlex nodes, each node configured with 16 physical cores, and 192 or 256 GB of RAM. In addition to the cluster, PMACS also provides two petabytes of IBM SONAS disk storage, in addition to 1.8 petabytes of mirrored archive tape storage. These resources are very competent for computationally intensive data analysis and exponentially increasing data volume for different fields of cutting-edge biomedical research.  **EQUIPMENTS**  In addition to personal workstations and laptops, BIC also has the following computation equipment: two Linux servers with 16 cores, 32 GB RAM and 5TB storage; two high power Dell Precision Tower 7910 with processor E5-2630/E5-2680, 128/256GB RAM, and 2TB/14TB hard drives; and multiple 2TB portable data storage disks.  **SOFTWARE**  BIC has access to a comprehensive list of regular bioinformatics software and databases, both academic and commercial, including annovar, bamtools, bcl2fastq, bedtools, blast, bowtie, bwa, cufflinks, emboss, FastQC, fastx\_toolkit, GATK, geneid, Genome Studio, git, IPA, MEGAN, MongoDB, MUMmer, Mutect, Mysql, ngsutils, picard, plink, R, RepeatMasker, RNAstructure, RSEQtools, rum, samtools, SOAPdenovo, STAR, tophat, Transfac, Trimmomatic, trinity, tRNAscan, vcftools, ViennaRNA, and etc. BIC has the ability and capacity to deploy and utilize all bioinformatics relevant software. | |

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Principal Investigator/Program Director (Last, first, middle): STOUT, Andrea

### RESOURCES

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

**Scientific Environment:** The University of Pennsylvania, Perelman School of Medicine (PSOM) provides a rich environment for collaborative and cross-disciplinary studies in basic biological mechanisms underlying human health and disease. The PSOM has dedicated shared resource facilities open to Penn scientists to support basic and translational research activities.

**Laboratory:** The CDB Microscopy Core occupies roughly 1200 sq. ft. spread across three recently- renovated suites in the Smilow Center for Translational Research, Biomedical Research Building II/III (BRB), and Anatomy-Chemistry. Within each suite are separate rooms for confocal microscopes; offline workstations, incubators, and office areas for staff are nearby each suite.

**Clinical:** N/A.

**Animal:** N/A.

**Computing:** The core maintains two workstations for post-acquisition processing and analysis of large graphics-intensive image data sets. Full versions of the commercial software packages Volocity, Imaris, MetaMorph, and ZEN black are provided for Core users. A 4 TB backup file server is maintained by Penn Medicine Academic Computing Services for users to back up and access their data from anywhere.

**Offices:** Dr. Stout and Dr. Veklich (a Core staff member) each occupy 115 sq. ft. near the BRB microscopy suite. Ms. Jasmine Zhao (the third Core staff member) occupies a 75 sq. ft office in our Smilow Center suite.

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of

each.

### Major equipment:

Laser-scanning Confocal Microscopes:The CDB Microscopy Core maintains four laser-scanning confocal microscopes: a Leica TCS SP8, a Leica TCS SP8 gSTED (super-resolution system), a Zeiss LSM 710, and a Zeiss LSM 510 NLO/META, which also has some multi-photon capability. The two Leica and Zeiss LSM 710 confocals have stagetop incubation chambers for time-lapse imaging of live specimens. The Core also manages a Leica TCS SP8 Multi-photon confocal owned and housed in the Dept. of Genetics.

Spinning Disk Confocal Microscopes: The Core has two Yokogawa spinning disk confocals built around Olympus microscopes and integrated by BioVision Technologies (Exton, PA). Features of both include high-QE EM-CCD cameras, stage-top incubation chambers, multiple laser lines, additional ablation lasers for FRAP/Photoconversion/ablation, and MetaMorph software for acquisition.

Wide field microscopes: For users who don’t require confocal technology, the core maintains five widefield microscopes spread across our various locations. One of them is a GE Healthcare Deltavision deconvolution system whose features include motorized xyz stage, independent filter wheels for customized excitation/emission settings, Photometrics CoolSnap HQ monochrome camera, and an incubation cage surrounding the microscope for live imaging. We also have a Leica DM6000 upright with deconvolution capability, a Zeiss Axioplan for routine epifluorescence, and a Leica DMRBE with high- resolution color camera for histology. Finally, we have a Thermo-Fisher EVOS FL Auto imager with motorized stage, incubation, and two cameras (color and monochrome) suitable for lower-resolution imaging (up to 40x) of a variety of vessels. These features enable it to do tile scanning of entire slides and time-lapse imaging of multi-well plates.

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Principal Investigator/Program Director (Last, first, middle): STOUT, Andrea Zeiss Lightsheet Z.1: Arriving in March 2016, the Zeiss Lightsheet Z.1 will provide capability for fast 3- dimensional imaging in up to 4 fluorescent channels of larger specimens such as zebrafish and Drosophila as well as CLARITY-cleared tissue such as mouse brain or embryos. In addition to speed, the Lightsheet offers the advantage of reduced phototoxicity for live specimens, enabling long-term time-lapse imaging not possible on a conventional confocal microscope.

Incubators: The Core maintains one small incubator in Smilow and two slightly larger incubators in BRB for the convenience of users who transport multiple live specimens which must be kept in a 37 degrees Celsius, 5% CO2 environment when not on the microscope.

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Principal Investigator/Program Director (Last, first, middle): Ganguly, Tapan

### RESOURCES

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

**Scientific Environment:** The University of Pennsylvania, Perelman School of Medicine (PSOM) provides a rich environment for collaborative and cross-disciplinary studies in basic biological mechanisms underlying human health and disease. The PSOM has dedicated shared resource facilities open to Penn scientists to support basic and translational research activities.

**Laboratory:** The Cell Center Service Facility (CCSF) occupies about 1,400 sq. ft. space on the basement of the Anatomy-Chemistry building and the Richards Building. This space provides five tissue culture hoods, several bays for bench work, a cold room, a fume hood, several computers, and office desks for lab personnel. A separate room on Richards basement houses -80 °C and -20 °C freezers, three liq. N2 freezers, and liq. N2 tanks.

**Clinical:** N/A.

**Animal:** N/A.

**Computer:** The laboratory possesses a number of computers to operate laboratory instrumentation. Each lab member has his/her own desktop computer. The computers are connected to a 1GB network with access to shared drives on the Genetics department server for data transfer and data archival.

**Office:** Dr. Ganguly occupies about 140 sq. ft. on the ground floor of adjacent Anatomy-Chemistry building.

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of

each.

## Vertical sterile tissue culture hoods (5) Dual CO2 incubators (4)

Bellco roller bottle apparatus/incubator

Hollow-fiber Bioreactor for producing several mg of antibody or recombinant protein Dry incubators (2)

Inverted microscopes (3) Upright fluorescent microscope

Promega GloMax Luminometer for mycoplasma testing Low speed/general purpose centrifuges (4)

Sorvall RCB5 Plus centrifuge Millipore MilliQ system Autoclave

Miele Lab Glassware Washer

Fly Food Kettle for preparing Drosophila culture medium Liquid nitrogen freezers (3)

Vertical and horizontal electrophoresis apparatus; blotters and power supplies

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| Program Director/Principal Investigator (Last, First, Middle): | Rader, Daniel |
| **RESOURCES** | |
| Follow the 398 application instructions in Part I, 4.7 Resources. |  |
| The [Cell Center Stockroom](http://www.med.upenn.edu/genetics/cellctr/) was established to offer the greatest variety of bioreagents possible while maintaining maximum convenience and savings of time and money to investigators at the Perelman School of Medicine as well as the entire University.  The Stockroom occupies approximately1500 square feet of dedicated space in the basement of Anatomy- Chemistry Building and serves University of Pennsylvania investigators and affiliate institutions by coordinating relations with various suppliers of molecular biological research materials. This involves not only bulk purchasing of these products, but the negotiation of discounts and convenient delivery arrangements.  There are almost 1,200 products on-site for immediate delivery in the Stockroom. Special ordering of non- regularly stocked products is available from 32 bioreagent vendors with discounted pricing and overnight delivery.  The Stockroom possesses eight -20˚ freezers, three refrigerators, and one -80˚ freezer. The Stockroom also has eight computers, two printers and office equipment, including a photocopier and fax machine. | |

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| **RESOURCES** |
| FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Under “Other,” identify support services such as machine shop, electronics shop, and  specify the extent to which they will be available to the project. Use continuation pages if necessary. |

# Clinical Research Computing Unit (CRCU)

### Background

The Clinical Research Computing Unit (CRCU) was established on April 1, 1997 within the Center for Clinical Epidemiology and Biostatistics (CCEB). The CCEB was established in 1993 as a multi-disciplinary unit within PSOM. It is the primary home for epidemiology and biostatistics at Penn. Through its predecessor, the Clinical Epidemiology Unit (CEU), now subsumed within the CCEB, the CCEB has been involved in epidemiologic and biostatistical teaching and research since 1978.

The CCEB’s mission is to improve public health by linking epidemiology, biostatistics, clinical medicine, and the health sciences, bringing epidemiologic and biostatistical research methodology to the health sciences. CCEB faculty have advanced degrees in various disciplines, including applied and pure mathematics, biostatistics and statistics, clinical pharmacy, decision science, economics, epidemiology, genetic counseling, genetics, health service and administration, health policy, history and sociology of science, information science, pharmacology and toxicology, public health, sociology, and social work.

The CCEB has a large, diverse, and active research program. CCEB faculty is engaged in hundreds of different active clinical research projects, both hospital-based and community-based. The culture within the CCEB is one that supports collaboration on research projects with many other divisions within the PSOM and the University of Pennsylvania. In particular, the CCEB has substantial resources that are particularly germane to the conduct of the proposed research in the areas of laboratory, office, computer and major equipment, and service centers. These resources along with the CCEB’s strong and sustained commitment to conducting research will greatly promote the success of the proposed project.

The Clinical Research Computing Unit (CRCU) is a service center and core research facility and was established to develop and implement a technology base and hire professional staff within the Biostatistics Unit of the CCEB to conduct clinical and patient-oriented research at Penn Medicine. These resources allowed CCEB faculty to compete successfully for Data Coordinating Centers (DCCs) of federally funded, large-scale, multicenter clinical trials, and epidemiological studies. These technology resources also permitted CCEB faculty and staff to provide essential collaborative clinical research support for University investigators throughout the wide array of basic science and clinical departments, Centers and Institutes, thus enhancing their likelihood of funding success.

### Overview

CRCU personnel are directly responsible for the clinical data management systems (DMS) and research coordination activities associated with multiple National Institutes of Health-sponsored multicenter multi-study registry and clinical trial networks. The CRCU is fully capable of conducting studies in accordance with FDA Bioresearch Monitoring Program and International Conference on Harmonization (ICH) guidelines. The necessity for compliance with these guidelines is determined in collaboration with PIs according to the scientific goals, sponsorship, and content of the study.

### Development and Implementation of Clinical Research

The professional technical divisions within the CRCU promote infrastructure development such as Standard Operating Procedures that are applied across all projects, as appropriate. This allows standardization of work across projects, and perhaps more importantly, ensures that professional activities are consistent with sponsor and professional standards. Technical division infrastructure and personnel involvement also serve to lower costs through sharing of project experience, resources, and methodologies. From each technical division, the personnel most suited to and experienced with the type of clinical trial being developed are selected and formed into a project team. Discipline representatives lend their specialized, professional knowledge to the

development and implementation of a clinical trial. This team of computing and data management professionals interacts with the scientific team, comprised of the biostatisticians, epidemiologists, and clinicians, to actually implement the scientific concepts and protocols contained within the trial research plan. **Project Operations and Compliance (POCO)** personnel serve to coordinate activities between the technical implementation team, the scientific team and other organizational bodies, and ensure that appropriate compliance measures are followed. **Clinical Data Management (CDM)** personnel examine the scientific protocol and develop the data management processes most appropriate for conducting the study. **Research Technologies (RT)** consisting of Software Systems and Database Services personnel design and develop the underlying database and administrate the use and security of the database as well as utilize specialized methodologies to develop software. They also develop the electronic DMS, which allows Clinical Center and Data Management personnel to accomplish the tasks associated with conducting the project.

### Leadership within the CRCU

The leadership of the CRCU consists of a faculty director and a team of three staff directors. Each managing director leads a discipline-specific sub-unit within the CRCU.

### Faculty Director:

**J. Richard Landis, Ph.D.**, **Professor of Biostatistics**, was recruited to the University of Pennsylvania in 1997 to provide overall leadership for academic and collaborative research programs in biostatistics. In order to facilitate the conduct of data coordinating centers (DCCs) for multi-center clinical trials and clinical research networks (CRNs), he founded the CRCU in 1997, and successfully obtained funding for two large- scale DCCs in 1997-98. Currently, he serves as PI or Co-PI of the DCC for three multi-center clinical research networks, all coordinated within the CRCU, in addition to being Core Director for the Center for Biomedical Informatics in Translation (BIIT) within the CTSA award to Penn Medicine, as well as the Director for the Biomedical Data Coordinating Center (BDCC) for the Abramson Center Core grant. Dr Landis is Director of the Division of Biostatistics within the Department of Biostatistics and Epidemiology, as well as the Biostatistics Unit within the CCEB. He also holds a secondary appointment as Professor of Statistics in the Wharton School. Previously, Dr. Landis was Professor of Biostatistics and Statistics at The Pennsylvania State University for nine years (1988-97), where he founded and directed the Center for Biostatistics and Epidemiology (CBE) within the M.S. Hershey Medical Center. Prior to that, he served on the Biostatistics faculty at the University of Michigan for thirteen years (1975-88).

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### Managing Directors:

**Denise Cifelli, M.S.**, Director for Project Operations and Compliance (POCO), is responsible for the overall leadership of POCO within the CRCU. In this role, she provides senior leadership for the Project Management staff in their conduct of activities across all CRCU projects. Ms. Cifelli has more than 12 years of experience in managing large multicenter clinical research networks and data coordinating center projects across many domains, She is also a teacher, licensed in Pennsylvania.

**Stephen B. Durborow, B.S.**, Director for Research Technologies (RT), is responsible for the overall leadership for the Software Systems Division (SSD) and the Database Services Division (DSD). He provides direct leadership for two divisional technical directors, who lead the software and database design and development activities across all CRCU projects. Mr. Durborow has over 25 years of experience performing and managing software development, database design, and database administration, focusing the last 15 on clinical research. He is responsible for the implementation of technologies new to the CRCU, like Oracle Clinical, in support of the *NIH CTSA* and other CRCU projects. Mr. Durborow is also responsible for the overall leadership of Research Development and Internal Operations Quality Assurance.

**Christopher P. Helker, M.S.P.H.**, Director for Clinical Data Management (CDM), is responsible for the overall leadership of Clinical Data Management within the CRCU. In this role, he provides senior leadership for the CDM staff in their conduct of data management and quality assurance procedures across the broad array of funded projects within the CRCU. Prior to joining the CRCU in 2000, he served as Coordinator for Penn's AIDS Clinical Trials Unit. Mr. Helker is a Certified Clinical Data Manager (CCDM) and a registered nurse, licensed within Pennsylvania.

### Financial Management of the CRCU

**Glen Lafferty**, Director of Fiscal and Administrative Operations for the CCEB, provides oversight for the business operations of the CRCU. Denise Tremblay, CCEB Financial Manager, provides financial reporting and detailed analyses. All business transactions for the CRCU flow through the CCEB's business office.

### CRCU Personnel Organization, Roles, and Activities

The CRCU provides a comprehensive array of technical and non-technical services in Project Operations and Compliance, Clinical Data Management and Research Technologies. A technical implementation team supports each clinical research project. CRCU personnel totals 29 and is distributed as follows: Senior Research Investigator (1), Directors of Operations (3), POCO (9), CDM (8), RT (7), RDQA (1).

These teams of personnel have the following responsibilities:

**Project Operations & Compliance (POCO)** personnel plan, develop and coordinate all quality assurance and regulatory compliance activities of the CRCU technical implementation team, the scientific investigator team and other organizational bodies associated with the project.

**Clinical Data Management (CDM)** personnel develop and implement data management processes, including CRF design and quality assurance activities, consistent with the scientific protocol. CDM personnel work closely with the clinical investigators and sites to facilitate proper collection and processing of research data

**Research Technologies (RT)** personnel design and develop the underlying database and administrate the use and security of the database as well as utilize specialized methodologies to develop electronic data management systems (DMS), which allows clinical center and data management personnel to accomplish data management and quality assurance tasks.

**Research Development and Internal Operations Quality Assurance (RDQA)** personnel perform risk management, project tracking, and proposal development activities across all the projects within the CRCU. RDQA personnel are also responsible for quality assurance of CRCU Standard Operating Procedures.

# Research Computing Environment:

### Overview

The CRCU’s research computing environment employs a number of current technologies that are available and suitable for its research mission. These technologies are acquired through open-source venues and commercial vendor sources and are maintained in “production quality” configurations. The computing technologies and resources, categorized and described below, are identified with one of several major functional information technology (IT) environments.

* IT Responsibilities/Staffing
* Physical IT Environment
* Network Environments - The data communication networks that support the secure transfer and movement of all the data, application logic, and computer programs and project information developed and supported within the CCEB.
  + Physical Networks
  + Logical Networks
  + Security within the Networks
* Computing Hardware Environments - The hardware configurations on which all applications and software are built, run, and supported within the CCEB.
  + Infrastructure Services Platform
  + Data Storage Platform
  + High Performance Computing Platform
  + Database Services Platform
  + Business Continuity/Recovery Platform
* Software/Application Environments - The applications and research software used to develop, maintain, process, and analyze the data within the CCEB.
  + Operating Systems
  + Statistical Applications
  + Database Applications
  + Printing/Scanning

### IT Responsibilities/Staffing

The CRCU’s computing environments are the responsibility of the Penn Medicine Academic Computing Services group. This group focuses on providing hardware and software services, systems administration, business continuity, and security services to research projects within the CCEB, CRCU and other departments in Penn Medicine. The various certifications held by staff members include ORACLE® certified database administration, Juniper Networking certifications, VMware certifications, SUN Microsystems Solaris® certified systems administration, A+ hardware certifications, various security certifications, various Unix certifications, and Microsoft Windows MSCE® certifications.

### Physical IT Environments

The physical building environment for supporting the computing environments required by the CRCU is co- located within a formal data center facility that is managed by University of Pennsylvania; Penn Medicine and Information Systems and Computing personnel. This data center has controlled heating, ventilation, and air conditioning (HVAC) subsystems to maintain the temperature and humidity at a constant level appropriate for computer systems. The data center also has uninterrupted power supply (UPS)/diesel subsystems to ensure that adequate and constant electrical power requirements are met at all times, even during prolonged power outages. The data center has secured and limited physical access and is constructed with walls and doors to prevent break-through efforts and/or illegal entry.

### Network Environments

The data network environment consists of several physical TCP/IP Ethernet networks layered and linked together through a variety of standard networking protocols. These discrete physical networks are layered on

top of the University of Pennsylvania’s University-wide network and are joined in a secure fashion to create a single logical data network.

### Physical Networks

The physical University networks used by the CRCU, each consist of multiple network segments connected via switched hubs and routers that provide a minimum of 10 Megabits per second (Mb/s) to a connected device within the CCEB defined network. The switched hubs will also support the higher bandwidth connections commonly used for many of the servers and data storage devices. The entire physical University network domain is monitored by the University within a centralized Network Operations Center (NOC). Bandwidth and performance monitoring of the physical networks are performed at the NOC. The NOC provides bandwidth and performance monitoring, network technical support, and management reporting to the physical networks used by the CRCU.

### Logical Networks

To provide a viable research network and computing environment for the CRCU and CCEB researchers, a single logical CCEB network is created from the multiple physical University network segments. The physical network segments for the CCEB are linked through various layer 2/3 networking hubs providing the CCEB the ability to define and create a single logical virtual local area network (VLAN). The VLAN provides the ability for all CCEB resources (computer client systems, servers, and users) to be configured within a single network domain. This provides the CCEB the flexibility in the placement of servers, use of available data center room space, and consistency in server configurations and systems management across multiple buildings occupied by the CCEB faculty and staff (currently 5 different physical locations). Utilizing the VLAN technologies, the CCEB has the ability to respond and adapt to new research computing projects, programs, and security/access agendas without incurring substantial new costs in network reconfigurations.

### Security within the Networks

The research computing environment has a security component required due to HIPAA; federal, state, and research compliance regulations; and CCEB best practices for safeguarding research data. Utilizing the VLAN, the CCEB secures its logical network using virtual private network (VPN) protocols and network address translation (NAT) protocols layered on top of the single logical VLAN. The VPN protocols provide encrypted “data in motion” protections and “fire-walled” connections between each of the physical network segments of the logical network. Applying VPN/VLAN encrypted connections allow all internal CCEB data to “tunnel through” and traverse the University’s physical networks as needed, while maintaining security at the logical CCEB network level, thus ensuring the privacy of the CCEB data and the availability of the data to only CCEB managed resources and users.

In addition to the VLAN and VPN technologies, the network utilizes the NAT protocols to provide private network addressing within the logical CCEB network. This additional precaution ensures that all network protocols running into or out of the logical CCEB network are essentially “proxy” connections that are only passed through one of several CCEB firewall devices. Providing a proxy service allows the CCEB to monitor, log and control all data and network protocols coming into and going out of its logical network.

This precaution also allows the internal network to remain effective regardless of external connectivity issues, sometimes outside the control of the CCEB network administrators. Because the NAT protocols use non-routable IP addresses, an additional level of control is provided within the network, as private IP addresses can only exist within the CCEB logical network. These addresses are managed locally within the CCEB, also ensuring that only appropriate connections are identified and permitted within the CCEB data network.

Connections from the CCEB network to the world is provided through the overall University data network, which is then connected to the Internet through a set of redundant connections to major Internet Points of Presences (POP), as well as being connected through the vBNS and I2 high-speed educational networks. This ensures essential high bandwidth connectivity to the various external entities desired by the CCEB research programs. This N+1 type design is critical when developing many of the distributed collaborative programs for the CCEB.

### Computing Hardware Environments

The CRCU computing environment consists of several highly interconnected yet functionally distinct configurations or “platforms” of computer servers. These different configuration platforms provide the necessary research computing services to accomplish the various research objectives for the CRCU.

### Infrastructure Services Platform

There is a centralized set of computer servers within the CCEB that provide the necessary infrastructure services essential to all research being performed within the CRCU. This set of servers consists of multiple UNIX based servers and MS Windows servers of various capacities that provide the following services: User logging, user and system level authentication, email, calendar, print services, general user account file storage, administrative web site hosting, system management, application software deployment, remote file access, and IT audit and reporting functions. Monitoring and logging systems are also in place to track the activities of servers, storage, and users throughout the network, recording critical events.

### Data Storage Platform

The CRCU is supported by a “state-of-the-art” data and document storage environment for its enterprise storage platform. The storage platform currently consists of ~60 Terabyte (TB) of primary data storage targeted for research program and project use. The data storage platform also has several connections to a variety of multi-tape robotic tape devices for business continuity services, providing tape recovery and removable media storage options. All research computer servers in the various platform configurations connect to this enterprise storage platform through use of either multiple High Bandwidth Adapters (HBA), 2/4-Gigabit/second (Gb/s) fibre-channel (FC) direct connections or indirectly through high speed (100Mb/s) Ethernet network connections. The HBA-FC connections are routed through multiple storage-specific SAN switches creating a redundant and physically isolated internal data storage network allowing access to research data.

The current configuration is currently able to scale dynamically beyond the petabyte range for storage to continue to address the ever growing data requirements of research programs within the CCEB. Adding new storage environments, host server connections, and managing these devices within the entire NAS/SAN platform is accomplished through centralized storage management consoles of the current XIV storage system.

### Database Computing Services

The CCEB has substantial database computing requirements for its research programs and projects. The database hardware computing platform currently consists of multiple Intel based servers running Linux, UNIX, and Microsoft-based operating systems..

The database hardware is configured into sets of servers that make up a Production database platform, a Development database platform and a Testing database platform. Each database platform consists of one or more Linix servers that provide the “backend” database services and one or more MS Windows servers which provide the “middle-tier” developed and deployed application services used by the projects, programs, and users/clients.

The application servers connect directly to only the databases servers via a separate network segment. The users/clients connect directly to only the various application servers via web browsers. This overall design provides for a “three-tier” database architecture to provide access to the CRCU database applications for the user/client. Actual databases services are located within tier one, application services are located within tier two, and web browser access on client machines is represented at tier three of this database architecture model.

The multiple (Prod/Dev/Test) database platforms allow a continuous software development lifecycle to be maintained. New database software is tested and configured within the Test environment until it is in full compliance with the programs and operations of the CRCU. This environment can then be installed on both the Development and Production environments. All development efforts can then proceed within a Development environment and when completed can be migrated and implemented on the Production environment for use by the research programs. The Production and Development environments are maintained, in sync, to ensure portability of the developed programs.

### Client Computing Platforms

The CRCU has a heterogeneous server and client system environment. The server platforms thus provide Linux, UNIX, and Microsoft-based operating system processes. The client workstations within the CRCU must be able to support these protocols. The CRCU has desktop systems, laptop systems and remotely connected systems residing outside the managed protection of the CCEB data network.

Client systems within the network will vary in capacities, based on the specific needs of the users, but at a minimum, consist of the following:

The Intel/Sun/Linux/Mac-based client workstations will minimally consist of a 17” monitor, 2-4 GB of memory, 100+ GB disk and Ethernet TCP/IP network connections capable of 10/100/1000 Mb/sec bandwidth. The system, to be added to the network, must be three years or less in age, so the processor within the system is fairly current with the latest releases for the various vendors.

All clients within the CRCU have the ability to store critical data centrally through network connections and file services with the data storage platform previously described.

### Business Continuity/Recovery Platforms

With the research data storage utilizing a centralized storage environment, the business continuity operations are also centralized. The SAN/NAS configuration allows the backup window for all data to be 24 hours and provides the ability for backups to occur on predetermined timestamps of the data.

A "jukebox" tape device containing multiple tape drives and 32 AIT-4/5 tape cartridges provides daily protection against data loss, and allows the ability to create duplicate tapes of weekly/monthly tape archives for storage off-site as part of an ongoing disaster recovery plan. Individual tape drives accommodating tape formats for 3490 IBM tapes, 4mm, 8mm, & ¼ tape cartridges are also available to facilitate the transfer of research data to and from the central CCEB data stores.

### Software/Application Environments

The software and applications that are supported within the CCEB can be identified within the following categories.

### Operating Systems (OS)

The operating systems for the Intel-based servers is Redhat Linux and Microsoft Windows Server 2008. The OS for the Intel-based clients is Microsoft Windows 7.

### Business/Productivity Applications

Key productivity tools are available to most members associated with a project team consist of an IMAP enabled e-mail client, a center-wide calendar & scheduling software, various word processing software in the form of Word Perfect, Adobe Acrobat, the Microsoft Office Suite of products (Access, Excel, Powerpoint, Publisher, and Word), the TeX/LaTeX document processing language, DBMS/Copy, Endnote, Reference Manger, and various public domain software products vetted by the IT staff. These tools support the broad spectrum of tasks on a project. Diagrams and flowcharts are produced within the Microsoft Visio Graphics software package, PowerPoint, or several other graphical products currently on the market.

### Database Applications

The database management and development software that has been standardized for use within the CRCU for major research projects is ORACLE™. Along with the ORACLE database management software, there are several developmental tool kits from ORACLE to provide World-Wide-Web Based Development and Data Repository software development. These tool kits allow development of modular and reusable code segments to enhance and expedite the applications developed within the CRCU. Oracle Portal and Oracle Clinical are also products being used within the CRCU to manage its research programs and projects.

### Printing/Scanning

Printing and scanning are accomplished within the CRCU as both local and networked activities. Local printing and scanning is via user-selectable devices connected directly to user/client workstations.

Networked printing is accomplished using a variety of color copier/printers and smaller projects using Hewlett Packard and/or Dell black & white laser printers and Xerox color laser printers connected directly to the CCEB network. Multiple networked printers are available throughout the various facilities. Networked scanning is accomplished via network connected Copiers/scanners, thus allowing users to produce multiple copies, scans, and even send faxes directly from their desktop machines, in an electronic format.

### Office:

The CRCU currently resides on the “Avenue of Technology” in Philadelphia, at the corner of Market and 36th street.

The Unit is located in Suite 560, 5th floor of the 3535 Market Street building. The building has a guarded lobby and limited access. Entrance to the CRCU suite is by electronic passkey. This suite of office space has a total

area of 8,700 square foot. This space has been allocated to the CRCU for staff offices, machine room space and operational/project function’s area in support of major new initiatives in large-scale, multi-center clinical trials, clinical and patient oriented research projects, and multi-institutional health services research projects. Within the area, there is office space configured to seat at least 50 staff members in a variety of open, semi- private and private offices. There are currently 7 private office areas, 4 semi-private offices, and additional group seating areas. The 5th floor area also provides two conference rooms (seating up to 8 and 16 persons respectively) and is equipped with mobile A/V technologies supporting computerized demonstration and presentation techniques.

Large central-file areas have also been strategically located and designed to accommodate the movement and storage of case report forms, manuals of operations, clinical data management materials and documents; and a special document handling work area for processing large volume copying, scanning, and document mailing and postage activities normally associated with large-scale, multi-center clinical trial projects, has also been provided. In addition, the suite has a kitchen.

CVPF Facility and Equipment

The CVPF is a unit within the Division of Transfusion Medicine and Therapeutic Pathology in the Department of Pathology and Laboratory Medicine at the University of Pennsylvania. The CVPF is accredited by the Foundation for the Accreditation of Cellular Therapy (FACT). The CVPF is a university shared-core resource that supports cellular therapy clinical trials which include manufacture of activated and expanded T lymphocytes, dendritic cells, mesenchymal stem cells, and lentiviral vector and RNA gene-modified T lymphocytes, among others to support investigators at UPenn and collaborating institutions.

CVPF consists of three manufacturing facilities: Maloney, Ravdin, and the Center for Advanced Cellular Therapies (CACT). The three manufacturing spaces share the same Quality Control Laboratory unit, and the Quality Assurance unit, who leads the CVPF Quality Management System and releases all manufactured products at CVPF. The CVPF manufacturing facilities are designed to maximize isolation of the cell and vaccine processing from other building areas, utilities, and activities. Access to the CVPF cleanroom areas is restricted via card-access and/or key lock access leading to a dedicated gown-in entrance. The Air Handler Units (AHU) serving each facility provide 100% outdoor air filtered by high efficiency particulate air (HEPA) filters. They operate as constant supply air-volume systems to maintain constant airflow to the spaces in the manufacturing suites, and to maintain cleanroom classifications.

**CVPF-Maloney**

The Maloney Facility of CVPF is located on the sixth floor of the Maloney Building of the Hospital of the University of Pennsylvania (HUP). CVPF-Maloney opened in 2005 and consists of 1,880 square feet (ft2). As of July 1, 2016, the facility has six active processing rooms and a media preparation room, along with dedicated gown-in and gown-out entrances. Two of the six processing rooms are prioritized for HIV processing. The Maloney manufacturing suite is class 100,000 (ISO 8) and processing is performed in class 100 (ISO 5) Biological Safety Cabinets (BSCs).

**CVPF-Ravdin**

The Ravdin Facility of CVPF is located in approximately 2,000ft2of space on the third floor of the Ravdin Pavilion at HUP. CVPF-Ravdin is in direct proximity to the apheresis cell collection and infusion unit, the autologous and allogeneic blood donor center, the blood bank, and the stem cell processing facility that supports the clinical transplantation service. The facility consists of seven processing rooms, a gown- in/gown-out room, a media preparation and storage room. The interior hallway and common areas are class 100,000 (ISO 8) and the individual cell processing rooms are class 10,000 (ISO 7). Processing is performed in class 100 (ISO 5) BSCs.

**CVPF-CACT**

The CACT Facility of CVPF is the newest manufacturing facility, opened in July 2016 and located on the ninth floor in the newly built South Tower building, adjacent to the Smilow Translational Research Center on the University of Pennsylvania’s campus. The CVPF-CACT cleanroom manufacturing space consists of eight processing cleanrooms, an automation room, a media prep room, and gown-in/gown-out rooms. The interior hallway and common areas are class 100,000 (ISO 8) and the individual cell processing rooms are class 10,000 (ISO 7). The CVPF-CACT footprint of the clean room manufacturing area is approximately 4,500 ft2. Processing is performed in class 100 (ISO 5) BSCs.

**Quality Control Laboratory**

The CVPF-CACT facility also contains the Quality Control (QC) laboratory space that also serves Maloney and Ravdin. The QC lab supports investigational product scale up, validation, and clinical manufacturing by qualifiying critical reagents including media to release for use in clinical manufacturing and performs analytical testing for in process and product release requirements that include sample characterization via FACS analysis, testing for mycoplasma and endotoxin, and sterility testing.

**Critical Equipment Monitoring and Maintenance**

Critical equipment in the CVPF is monitored continuously by the Rees Centron Environmental Monitoring System that is password protected and can be accessed remotely to provide information on the status of

## CVPF Facility and Equipment

critical equipment, for example, incubators and freezers. The Rees sensors record parameters once every 15 minutes and will alarm if these parameters reach conditions outside of the pre-established acceptance criteria. All three facilities are cleaned at predetermined frequencies by trained staff, according to approved internal procedures. Critical cell processing equipment, such as Biological Safety Cabinets, is disinfected before and after each use, and ancillary equipment is cleaned after use, such as scales, and water baths. Common processing equipment is stored in a cleanroom central area and brought into culture rooms as needed. Single use disposable tubing sets are utilized to process the cells to reduce the risk of cross-contamination. Closed system processing steps are used whenever technically feasible. Finally, viable and non-viable Environmental Monitoring is performed at all three facilities.

|  |  |
| --- | --- |
| **Name of equipment** | **Combined total as of July 2016** |
| 20/50 EHT Bioreactor | 2 |
| 4' laminar flow hood | 4 |
| 5' laminar flow hood | 11 |
| 6' laminar flow hood | 13 |
| BACTEC© 9050 Blood Culturing System | 2 |
| BACTEC© FX Blood Culture System | 1 |
| Baxter MaxSep Magnetic Separator | 5 |
| Centrifuge, Microcentrifuge | 20 |
| Centrifuge, Sorvall Bifuge Primo R | 1 |
| Centrifuge, Sorvall Legend RT | 14 |
| Centrifuge, Sorvall Legend XTR | 5 |
| Centrifuge, Sorvall RC3B-plus | 3 |
| Coulter M3 Cell Counter/Sizer | 2 |
| Coulter M4 Cell Counter/Sizer | 4 |
| Counterflow Centrifugation Elutriator | 4 |
| Digital balance | 24 |
| Flow cytometer, BD LSRFortessa | 1 |
| Flow cytometer, FACS Calibur with Cellquest software | 1 |
| Freezer, (-)30 °C | 2 |
| Freezer, (-)40 °C | 1 |
| Freezer, (-)80 °C | 9 |
| Freezer, Controlled Rate | 8 |

## CVPF Facility and Equipment

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| Haemonetics Cell Saver 5 Autologous Blood Recovery System | 11 |
| HEPA filtered CO2 incubator | 32 |
| LN2 Freezer | 20 |
| LN2 Manifold Changeover | 5 |
| Luminometer | 0 |
| Microscope | 21 |
| Miltenyi CliniMACS Magnetic Separator | 4 |
| Plate Washer | 1 |
| REES monitoring system, server based  *(number of points monitored is indicated in parentheses)*\*\* | 4 (433) |
| Refrigerator | 33 |
| Sebra Heat Sealer | 23 |
| Spectrophotometer | 1 |
| Table top CO2 incubators | 2 |
| Terumo Sterile Connect Device | 23 |
| Total Air Particle Counter | 3 |
| Viable Air Particle Sampler | 3 |
| Waterbath | 28 |
| WAVE 2/10 Bioreactor | 25 |

**CVPF Quality Management Plan**

The CVPF Quality Management Plan is modeled in accordance with the standards and practices jointly developed by the International Society for Cellular Therapy (ISCT), the American Association of Blood Banks (AABB), and FACT. The CVPF Quality Management Plan is an integrated program of quality assessment, quality assurance & control, and continuous improvement that governs all areas of operations in the CVPF, such as personnel, equipment, facilities maintenance, and processing procedures. The main purpose of the Quality Management Plan is to provide a consistent manufacturing pathway to reduce variability in product purity and quality, resulting in cellular products of predictable composition. The eleven Quality System essentials which enable the CVPF to function efficiently and effectively include organization, personnel management and training, equipment management, materials management, change management, process control, final inspection and handling, documents and records, incidents and deviations, internal inspections and assessments, continuous improvement, and facilities, safety and environmental monitoring.

Principal Investigator/Program Director (Last, first, middle): Ganguly, Tapan

### RESOURCES

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

**Scientific Environment:** The University of Pennsylvania, Perelman School of Medicine (PSOM) provides a rich environment for collaborative and cross-disciplinary studies in basic biological mechanisms underlying human health and disease. The PSOM has dedicated shared resource facilities open to Penn scientists to support basic and translational research activities.

**Laboratory:** The DNA Sequencing Facility (DSF) occupies about 2,500 sq. ft. space on the basement of the Richards Building. This space provides seven bays for bench work, a cold room, a fume hood, several computers, and office desks for lab personnel. There is an adjacent but separate room for housing -80 °C and -20 °C freezers, a floor centrifuge and storage racks.

**Clinical:** N/A.

**Animal:** N/A.

**Computer:** The laboratory possesses a number of servers (on-site and off-site) and workstations, and numerous computers to operate laboratory instrumentation. PMACS’s (Penn Medicine Academic Computing Services) high performance computing cluster (HPCC) is used for high volume computational work. Each lab member has his/her own desktop computer. The computers are connected to a 1GB network with access to shared drives for routine preservation and archival of scientific data.

**Office:** Dr. Ganguly occupies about 140 sq. ft. on the ground floor of adjacent Anatomy-Chemistry building.

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of

each.

### Major equipment:

Sanger Sequencers: The facility has one ABI 96-capillary 3730 and one 16-capillary 3130XL sequencer. The 3730 sequencer can sequence 96 samples at a time with a capacity of sequencing 12 96-well plates in a 24 hr period with1000 b read length. The 3130XL is used for microsatellite-based genotyping and fragment analysis. It can run a 96-well plate in about 7 hrs.

Ion Torrent PGM and Proton Next-Generation Sequencers: The facility has one Ion Torrent PGM and one Proton sequencer offering multiple read length and throughput options. The PGM supports 200 and 400 b sequencing with a throughput range of 50 Mb to 2 Gb, the run time varies between 2.5 and 8 hrs The Proton currently offers 200 b read length and can sequence 12 giga bases in a 2.5 hr run. The core has a full NGS setup with a number of OneTouch units for library amplification, Agilent bioanalyzer, PCR workstation, Pippin Prep for size selection, NanoDrop spectrophotometer and Qubit fluorometer, and Dell servers for NGS data storage and analysis.

Equipment for molecular biology: The DSF is fully equipped with 8 thermo cyclers, Qiagen Qiacube for DNA extraction, several tabletop centrifuges, one floor centrifuge, Kodak gel imaging system, and Savant Speed Vac.

Liquid Handling System: A Beckman NX robot is used for Sanger sequencing reaction assembly and other pipetting jobs.

Refrigerators and freezers: The core has 3 refrigerators with attached -20 °C freezers, 2 x -20 oC freezers and 1 x -80 °C freezer to store DNA, RNA, enzymes and other reagents.

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|  |  |
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| Program Director/Principal Investigator (Last, First, Middle): | Williams, Dewight R. Ph.D. |
| **RESOURCES** | |
| Follow the 398 application instructions in Part I, 4.7 Resources. |  |
| The Electron Microscopy Resource Laboratory at the University of Pennsylvania Perelman School of Medicine provides access to electron microscopy technologies and services to all researchers in the Southeastern Pennsylvania and Southern New Jersey region. We provide training, material, experimental design, technical staff, assistance in manuscript and grant preparation in addition to all preparatory equipment for sample preparation and a suite of electron microscopes for TEM and SEM. The EM resource laboratory shares laboratory space with portions of the Cell Biology Departmentand the Penn Muscle Institute's light microscopy facilities. These two entities house an array of optical instruments including a light sheet, STED, laser confocal, numerous single molecule optical trapping, and total internal reflectance microscopes along the same corridor. This juxtaposes a significant amount of the campus imaging capabilities in the west wing of the Anatomy and Chemistry basement.  **Laboratory:** The jointly shared laboratory space consists of approximately 900 square feet. This space houses a numerous pieces of ancillary equipment: a Denton 502B evaporator, an SPI sputter coater, Tousimis model 810 critical point drier, three ultramicrotomes, one cryogenic ultramicrotome, Pellco mcrowave tissue processor, Leica CPC100 plunge freezer, Abra HPM 010 high pressure freezer, two automated Leica freeze substitution systems, three ovens, glow discharge unit, Fischione plasma cleaner, centrifuges, scales, dessicators, two fume hoods, laminar flow hood for BSL2 pathogen containment, cell incubators for cell culture, multiple compound and dissecting microscopes. The electron microscopy suite houses four microscopes: an FEI Quanta 250 eSEM with wet STEM and environmental stages, a JEOL JEM1010 TEM with a 1 K x 1 K AMT side entry video rate CCD, an FEI Tecnai-12 S/TEM with BF/DF detector, EDAX eds detector, 2K x 2K Gatan Ultrascan1000 CCD, and an FEI Tecnai F20 S/TEM with a Fischione HAADF STEM detector, 2K x x 2K Gatan Orius CCD for electron diffraction, and a 4K x 4K FEI Falcon II CMOS detector. The FEI S/TEM microscopes are equiped with software for automated data collection using both Serial EM from the Boulder 3DEM facility, FEI tomography for both TEM and STEM, and EPU single particle automated data collection. Holders for the FEI S/TEM microscopes are interchangable and consist of 3 cryogenic TEM holders, 2 high tilt dual axis tomography holder, a high tile single axis tomography holder, 5 specimen sample holder, a Be tipped tilt rotate holder, and a single axis Be tipped holder, in addition to standard single tilt holders. The Falcon II camera is capable of 18 frames a second image output with additional custom hardware that was added.  **Clinical: N/A. Animal: N/A.**  **Computer**: Six workstation computers are available in the facility. Three 64bit windows 7 based computers and three 64 bit Cent OS 7.0 linux based computers. Software on the linux based workstation computers consists of a full range of single particle image reconstruction software: EMAN 1, EMAN2, Sparx, Relion 1.4, Frealign, Bsoft, Chimera, O, Situs, VMD, MDFF, Imagic, Xmipp 3.0, IMOD, Amira 6.0, Spider 15-21, and IHRSR in addition to numerous other small packages related to the CCP4/MRC software suite. The windows system has Tecnai Imaging and Analysis, Amira, Gatan Digital Micrograph, Photoshop, IMOD, and EM2EM available for image processing and analysis. In addition FEI inspect3D and IMOD are available on these systems for tomographic image reconstruction. 58 TB of disk storage is present on the six workstations with five of the six workstation CUDA enabled for GPU processing. The three linux workstation can operate as a HPC cluster consisting of three nodes of 12, 16, and 24 CPUs, each with 64 GB of addressable RAM and 12 TB of RAID 5 storage.  **Office:** EMRL office/conference room is 100 sq feet. It houses a color laser printer dry erase board and  meeting table for four. It also houses an extensive library of EM relate books and atlases for research purposes. | |

### Major Equipment:

FEI Tecnai F20: This microscope possesses a high coherent Schottky electron emitter that allows it to attain a point resolution of 1.9 Angstroms. This microscope operates bright field, dark field, TEM and STEM modes. It is equipped with a cryogenic sample box that allows longer term cryogenic imaging. It has three detectors a high angle anular dark field detector for STEM atomic resolution imaging, a 2048 x 2048 pixel CCD camera for diffraction and video rate imaging, and a second generation CMOS direct electron detector for imaging at low electron dose cryogenically preserved macromolecular complexes. Software on this system consists of Serial EM, FEI EPU, STEM tomography 4.0, TEM tomography 4.0, Digital Micrograph, and TIA. The fiber optic stream from the Falcon II is split between the camera controller and the camera allowing collection of the native camera frame rate of 0.055 frames/sec to be captured on a linux workstation. These frames are automatically collected and motion corrected with dosefgpu\_corr from the Cheng Lab at UCSF or Unblur from the Grigorieff lab at Janelia Farms HHMI.

FEI Tecnai 12: This microscope is dedicated to single particle negative stain and cryogenic sample preparation screening. It is automated with Serial EM but also runs Digital Micrograph, TIA, FEI tomo 3.1 TEM and STEM. This microscope also has a electron dispersive spectrometer for elemental composition mapping in samples. The FEI bright field dark field STEM detector and Gatan US1000 2048 x2048 pixel CCD camera are excellent for imaging at moderate to high resolution. This instrument is equipped with a LaB6 filament that allows point resolutions of 4-5 Angstroms.

JEOL JEM1010: This microscope is a solid pathology TEM with a 1024 x1024 CCD side entry video rate camera. It has a tungsten filament and robust performance with simple operation for biological TEM of thin sections of tissues and cells. It robustness and simplicity of operation makes it our workhorse instrument for cell biology.

Quanta250 eSEM: This SEM is equipped with a Schottky field emitter for high resolution SEM at high, low, and near atmospheric pressures. It as multiple detectors: a standard ETH, circular backscatter, STEM, large field backscatter, gaseous secondary electron detector, and annular dark field detector.

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| Program Director/Principal Investigator (Last, First, Middle): |
| **RESOURCES** |
| Follow the 398 application instructions in Part I, 4.7 Resources. |
| **Flow Cytometry and Cell Sorting Facility**  The Flow Cytometry and Cell Sorting Resource Laboratory is currently recognized as one of the largest and most comprehensive flow cytometry laboratories in the US. In 2014 it was designated a laboratory of exceptional merit by the National Cancer Institute. The resource provides a broad array of instrumentation, support, education and consultation. A wide variety of cell sorting and analytical applications are supported (up to 20 parameters) are offered. Currently the facility offers 6 cell sorters (4 BD Biosciences FACS Aria II, 1 BD Biosciences Influx, 1 BD Biosciences FACS Jazz) and 15 analytical cytometers capable of up to 20 parameter analysis (BD LSRFortessa, BD LSR II, BD FACSCanto, BDFACSCalibur, BD Accuri, Amnis ImageStream Imaging Flow Cytometer). These instruments are located in satellite facilities throughout the University to enhance access to user groups and are available for use, both sorters and analyzers, 24 hours per day, 7 days a week. A very active training and consultation program is in place to support these implementation of the technology in research programs. The Scientific Director, Dr. Jonni Moore (Co-I), and the Technical Director, each have over 25 years of experience in the field of cytomics.  The Path Bioresource Computational Biology and Research IT facility, a division of the Flow Cytometry Shared Resource, provides additional computer and database resources for advanced computational analysis of flow cytometric data. The facility maintains a dedicated high-end Linux compute server with 8 Intel cores, 32 GBytes of memory and a 12 TByte redundant RAID-5 storage area network. The compute server is used to perform automated analysis of flow cytometric data, including cytometric fingerprinting. It houses a MySQL database instance, where the raw cytometry data are indexed with sample and patient metadata to facilitate database-driven computational analysis. All of above resources are housed in a Tier 3 secure datacenter facility located at 3401 Market St, Philadelphia and operated by the University of Pennsylvania. In addition to the compute server and related equipment the facility possesses several Linux, Mac and PC workstations. Raw data and analysis results at Path Bioresource are backed up nightly. Laptop computers that connect to the servers are password protected and their hard drives are encrypted.  . |

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Page **Resources Format Page**

Principal Investigator/Program Director (Last, first, middle): SCHULTZ, David

### RESOURCES

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

**Scientific Environment:** The University of Pennsylvania, Perelman School of Medicine (PSOM) provides a rich environment for collaborative and cross-disciplinary studies in basic biological mechanisms underlying human health and disease. The PSOM has dedicated shared resource facilities open to Penn scientists to support basic and translational research activities.

**Laboratory:** The High-throughput Screening Core (HTSC) occupies roughly 750 sq. ft. of newly renovated space on the ground floor of the John Morgan Building. This space provides separate wet laboratory for laboratory automation and BSL2 tissue culture, -80oC freezer storage, computer, and office areas.

**Clinical:** N/A.

**Animal:** N/A.

**Computer:** The laboratory possesses personal, community workstations, numerous computers to operate laboratory instrumentation. All the computers are connected to a 1GB network with access to shared drives for routine preservation and archival of scientific data.

**Office:** Dr. Schultz occupies roughly 150 sq. ft. adjacent to the main laboratory. Word-processing and graphics are handled with desktop and laptop computers interfaced to networked laser printers.

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of

each.

### Major equipment:

Automated pipetting:The HTSC is equipped with a Perkin Elmer Janus with 96/384 Modular Dispensing Tool (MDT) and Verispan 8-tip for automated liquid pipetting, which was purchased with a NIH Shared Instrumentation equipment grant (S10). The Janus MDT arm is equipped with a 96 well disposable tip head with capabilities of transferring volumes from 5-200 µl, a 384 well disposable tip head for transferring volumes between 0.5- 25 µl, a 50 nl slotted pin tool, and a 200 nl slotted pin tool for transfer of organic small molecules from library plates to assay plates. The MDT workstation is integrated with two plate stack units with capacity for up to 50 microplates each. The Verispan 8-tip independent pipetting arm is used to prepare custom formats (e.g. dilution series) and is designed for use with disposable tips in 20 µl, 200 µl, and 1 ml sizes.

Bulk Reagent Dispensing: The facility has two Matrix Wellmates with integrated stackers and a ThermoFisher Multidrop combi for bulk reagent dispensing. These instruments can be programmed to fill specific plate columns as desired by the user, and is capable of dispensing 0.5-2500 µl per well. The core also has a Biotek ELX405 plate washer for automatted washing of plates.

Multi-mode plate reader: The PerkinElmer EnVision Xcite is a multi-mode plate reader capable of measuring standard detection labels in 96-, 384-, and 1536-well plates, including absorbance, fluorescence intensity, luminescence, ultra-luminescence, time-resolved fluorescence, fluorescence polarization, and AlphaScreen (Amplified Luminescence Proximity Homogeneous Assay).

High-content screening reader: The ImageXpress Micro XLS is an inverted, widefield microscope that utilizes laser-based auto-focus to efficiently image phenotypes of fixed- or live-cells in 96- and 384-well microtiter plates. The IXpress Micro is equipped with a solid state excitation source, a motorized objective bar with PLAN Apo objectives (4X, 10X, 20X, 40X), interchangeable filter cubes for the flexibility to detect the most common flourophores, and a 4.6 megapixel scientific CMOS camera for large field-of-view

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Principal Investigator/Program Director (Last, first, middle): SCHULTZ, David imaging. The MetaXpress® Software, built based on the well-established MetaMorph software, drives the IXpress system to acquire high-resolution images, recognize and segment objects, extract and quantify features, and convert this information into numerical data. Image data is stored in a database on servers maintained by UPENN’s Medicine Academic Computing Services. MetaXpress provides users a flexible platform to analyze their data.

FLIPR: The *Fluorescence Imaging Plate Reader* (FLIPRTetra) Cellular Screening system integrates liquid handling with rapid whole plate imaging of fluorescent and luminescent channels for kinetic cell-based GPCR assays (e.g., calcium, cGMP, cAMP) and ion channel assays (e.g., membrane potential). Our system is equipped with excitation LEDs 335-345 nm, 380-390 nm, 470-495 nm and emission filters 475- 535 nm and 515-575 nm.

Tissue Culture: The core is equipped with BSL2 level tissue culture capabilities, including a 6 ft. tissue culture hood, which can house bulk reagent dispensers (e.g. Wellmate) to dispense cells into assay plates; 2 CO2 regulated tissue culture incubators; a benchtop centrifuge fitted with microtiter plate holders, and; a Leica DMIL LED inverted phase-contrast microscope for use while passaging and preparing cells for assays.

Freezer Storage: Freezer Storage. The core has 4 x-80oC freezers to store siRNA, shRNA, and cDNA libraries, a 1 x -40oC freezer for storage of chemical libraries, and one liquid nitrogen Isothermal freezer (Cryosafe) with a capacity to store >10,000 2 ml sample tubes for storage and archival of cell lines for HTS.

Plate sealer: The core has an Agilent/Velocity 11 PlateLoc heat sealer.

### Libraries:

*Chemical libraries:*

*FDAapproved and known bioactives:* The core manages a library of ~2100 small molecules enriched for FDA approved drugs, FDA like drugs, and pharmacologically active compounds from Selleckchem. The core also has the Library of Pharmacologically Active Compounds (LOPAC 1280) from Sigma.

*Natural Products:* The Core has a library of ~800 purified Natural Products (Microsource) with annotated biological activity.

*Diversity Collections:* With the assistance of medicinal and computational chemists, the core has assembled a library of 44,000 compounds that have been vetted for early stage lead-like characteristics (i.e. MW<660 Da, elimination of known PAINS, etc.) required for high-throughput screening. This library is comprised of 12,000 compounds from ChemDiv’s SMART library, 20,000 compounds from Chembridge’s Core set, and 12,000 compounds from Chembridge’s Express Pick set.

*Genetic libraries:*

*siRNA:* The HTSC has a whole genome siRNA library from Ambion, Life Technologies, which can be screened as custom libraries of siRNAs, including gene ontology categories or user defined gene sets, the human druggable genome (~10,000 targets), or the whole genome siRNA library (21,585 gene targets).

This library is arrayed in 384 well plates with 3 siRNAs pooled against a single target in one well.

Non-coding RNA: Scientists can also screen a library of siRNAs against long non-coding RNAs (2220 targets), and libraries of miRNA mimics and inhibitors (2555 targets each).

shRNA: The core also maintains the complete human (V1.0, V1.5, and V2.0) and mouse (V1.0) TRC shRNA library. The human library contains 129,695 shRNAs, targeting ~20,000 gene targets, precloned into pLKO.1, which can be packaged into lentivirus for delivery. The mouse library contains ~78,000 clones against 16,000 gene targets. The core routinely provides investigators clones to individual genes

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Principal Investigator/Program Director (Last, first, middle): SCHULTZ, David or cherry-picks user-defined sets of clones to create custom libraries of shRNAs that investigators can use to validate high-dimensional genomic data in non-arrayed screens.

cDNA: Investigators can screen 18,000 arrayed, full-length, fully sequenced human and mouse cDNAs from the MGC collection or custom designed genes sets from this library.

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| Program Director/Principal Investigator (Last, First, Middle): | Rockwell, Kenneth A (Investigational Drug Service) |
| **RESOURCES** | |
| Follow the 398 application instructions in Part I, 4.7 Resources. |  |
| **Facilities:**  The Investigational Drug Service (IDS) at the University of Pennsylvania is a research-focused pharmacy service providing medication-related services to the entire Penn research community. Operating out of a primary location at 3600 Spruce St, Maloney Building, Ground Floor, Philadelphia, PA 19104; and a satellite at 51 N. 39th St, 103 Mutch Building, Philadelphia, PA 19104, the IDS provides storage, accountability and dispensing services for clinical trials and drug procurement for pre-clinical trials, as well as consultation on study design, assistance with IND submissions or protocol language, as well as formulation of new products or matching placebos for use in clinical trials. Both locations include a medication storage area with controlled room temperature (20-25c) which is monitored and highly secured, as well as refrigerated (2-8c) and frozen storage (-20c and -80c). The primary facility (Maloney) also accommodates liquid nitrogen storage (< -180c). There is prescription filling and checking space in each location and patient and study- specific records are maintained electronically, in compliance with 21CFR11.  The primary facility also includes a quarantine area for used, damaged or expired materials; a patient counseling area; dedicated auditing/monitoring space; and two rooms dedicated to drug manufacturing and repackaging of clinical trial materials. Both facilities are equipped for the compounding of sterile products, using pharmaceutical glovebox isolators in compliance with USP<797>.  **Major Equipment:**  *Sterile Compounding*: Nuaire NTE797-TE isolators (2), GermFree VersaFlow VSF4 isolator (1), Baxa Repeater Pump (1)  *Refrigeration*: Norlake Cold Room (1), LabRepCo Futura 48ft3 (1), Continental 49ft3 (1), Arctic Air 25ft3 (2), Summit 5.5ft3 (1)  *Freezers*: Sanyo VIP-Series 17ft3 (1), Fisher IsoTemp 24ft3 (1), VWR 8ft3 (1), VWR 5.5ft3 (1), CBS Cryosystems 4001 (1)  *Major Laboratory Equipment*: BD Bactec 9050 (1), Thermo TruScanRM™ Spectrophotometer (1), BD FACS MicroCount (1), Charles River EndoSafePTS (1), Hygeina ENSURE™ Luminometer (1), Nikon Inverted Microscope (1), Motic BA210 Microscope (1), RevSci Saniclave-200P (1), LabConCo SteamScrubber (1), Sorvall Legend XTR Centrifuge (1); various balances, hot plates, stirrers, oscillators and water baths.  *Manufacturing Equipment*: Profill-324™ Capsule Filler (1), Profill-DB™ Capsule Fillers (3), Dott. Bonapace IN-CAP™ (1), Mettler Quantos QS30 Autosampler/Filler (1), Waring Commercial Blender (1)  *Packaging Equipment*: Kirby KL50ic High-Speed Counter (1), Kirby KLX Counter (1), SafeSealRx™ Card Sealer (1)  PHS 398 (Rev. 08/12 Approved Through 8/31/2015) OMB No. 0925-000  Page 1 of 1 **Resources Format Page** | |

Principal Investigator/Program Director (Last, first, middle): Ganguly, Tapan

### RESOURCES

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

**Scientific Environment:** The University of Pennsylvania, Perelman School of Medicine (PSOM) provides a rich environment for collaborative and cross-disciplinary studies in basic biological mechanisms underlying human health and disease. The PSOM has dedicated shared resource facilities open to Penn scientists to support basic and translational research activities.

**Laboratory:** The Molecular Profiling Facility (MPF) occupies about 2,250 sq. ft. space on the basement of John Morgan ground floor and the Smilow Center (SCTR) 9th Floor. This space provides several bays for bench work, two fume hoods, several computers, and office desks for lab personnel. The bioinformatician has his office in Smilow Center.

**Clinical:** N/A.

**Animal:** N/A.

**Computer:** The laboratory possesses numerous computers to operate laboratory instrumentation. Each lab member has his/her own desktop computer. The computers are connected to a 1GB network with access to shared drives for routine preservation and archival of scientific data.

**Office:** Dr. Ganguly occupies about 140 sq. ft. on the ground floor of adjacent Anatomy-Chemistry building.

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of

each.

**Major equipment**: The molecular profiling services are performed on multiple platforms.

### Affymetrix microarray system

GeneTitan Multi-Channel (MC) instrument for automated processing of 16, 24 or 96 samples per batch Four-place FS450 Fluidics Stations (8)

GeneChip Hybridization Ovens (2)

GCS 3000 7G laser scanners with autoloaders and computer workstations (2)

**Agilent microarray system** Agilent Scanner C Hybridization Oven

### Medium throughput profiling instruments

Fluidigm BioMark HD with 2 IFC controllers

Fluidigm Access Arrays with 2 IFC controllers for making NGS amplicon libraries Luminex FlexMap 3D for multiplexed Panomics assay for gene expression

### Low throughput profiling instrument

ABI QS 12 K Flex real-time PCR instrument

### General Laboratory Equipment

Chemagen Magnetic Separation Module I for DNA extraction Qiagen QiaCube for RNA extraction

Agilent 2100 BioAnalyzer(2)

Beckman Biomek FX for automated sample processing Tetrad thermocyclers from MJ Reaserch (6)

Savant Speed Vac system

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Resources Format Page

Principal Investigator/Program Director (Last, first, middle): Ganguly, Tapan

& Standard Molecular biology Lab equipment

**Refrigerators and freezers**: The core has 6 x -4°C refrigerators, 2 x -4°C refrigerators with attached -20 °C freezers, 5 x -20°C freezers and 1 x -80 °C freezer to store DNA, RNA, enzymes and other reagents.

**Computer Workstations:** For data storage and archival, the facility maintains three multi-core, high RAM desktop workstations, which are used for analysis of user data. User data and the associated analyses are stored on a 3 TB fault-tolerant RAID. Sample submission tracking and end-user data download services are provided via two linux servers running customized web services and Oracle databases. Daily incremental backups of all production data are maintained on redundant hard-drives. For analytical tasks requiring increased computing and/or storage, the Perelman School of Medicine’s high performance computing cluster (HPCC) is used.

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|  |  |
| --- | --- |
| Program Director/Principal Investigator (Last, First, Middle): | The Neurobehavior Testing Core |
| **RESOURCES** | |
| Follow the 398 application instructions in Part I, 4.7 Resources. |  |
| The administrative office and wet lab bench space of the core are located on the 10th floor of the Smilow Center for Translational Research. The core behavioral testing suites are located within the sixth floor animal facility. There is >3,000 square feet dedicated to behavior and behavior-related procedures maintained to exacting environmental conditions required for such procedures. These rooms are used as special housing vivarium, small animal surgery suites as well as behavioral testing rooms for investigators on this proposal. The core works closely with faculty and researchers in these facilities and faculty members from these facilities serve on the Core Steering Committee.  Behavior Testing Equipment: The Neurobehavior Testing Core has the following equipment in its mouse facility: Avisoft Ultrasonic Vocalization microphone in a sound attenuating chamber, EEG/EMG acquisition equipment for 18 mice, 16 activity monitoring light and sound proof chambers with individual lights/ventilation, 8 fear conditioning chambers, 2 open field arenas and 8 object recognition setups, 4 marble burying chambers, 4 novelty suppressed feeding boxes, 4 social interaction arenas, 2 olfactory habituation/dishabituation cages, 2 Morris water mazes, 1 cross maze, 1 radial arm maze, 1 passive avoidance chamber, 3 forced swim cylinders, 2 elevated zero mazes, 2 Rotarods (40rpm and 80 rpm), 2 light/dark arenas, VonFrey fibers/testing platform, incremental hot and cold plate, grip strength meters, Randall–Selitto pressure meter, Plantar Test (Hargreaves Apparatus), dry Y-maze, swimming Y maze, 4 righting response brackets, 6 conditioned place preference chambers and a cliff avoidance platform. In addition, the core has a fully operational small animal surgery suite with 2 stereotaxic frames, dissection microscope, isoflurane vaporizer and gas scavenger and micro infusion pumps. This equipment is readily available and could be applied to assess physical and neurological health, arousal, anxiety, social interaction, communication, behavioral inflexibility and cognition in models of human disorders.  Computers: The Neurobehavior Testing Core uses 7 Dell Optiplex (model 9000 series) computers with 17  (20-, 21-, and 24-inch) displays for data analysis, word processing and literature searches and two printers (HP Laserjet 3600, 4600). Software includes Microsoft Office, Prism Graphpad and SPSS for statistical analysis, Sleepsign 2.0 for EEG trace analysis and Avisoft-SASlabPro for USV analysis. Matlab, Freezescan, Topscan and HVS Image video tracking systems are used for analysis of observational based behaviors. Five Dell Precision T3400 PCs, equipped with webcams (Microsoft Lifecam and iSpy64) are used for data acquisition for object recognition, Morris water maze/Barnes mazes novelty suppressed feeding, marble burying and open field activity monitoring systems. Two Dell Optiplex 755 PCs are used for electrophysiological data acquisition. A Dell Optiplex computer is used for Classical Conditioning data acquisition and analysis. A Dell Optiplex runs SD Instruments Most computers are connected to PennNet, and/or AIRSAS, the computer network at the University of Pennsylvania. A Dell computer runs Columbus Instruments mutlidevice activity software for homecage activity monitoring. For acquisition of image for analysis 3 Sony high definition cameras, 2 Infrared capable cameras and webcams with adjustable tripods and mounting brackets are used to record footage of observation based behavior. The core also has a recently acquired two 2TB My Passport WD portable hard drives and Synology 2413 External Storage Array with 5 4TB 7.2K RPM Universal SATA 3Gbps hard drives plus 5 Single Blank Hard Drive Filler Panels (allowing for expansion of storage). | |

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Program Director/Principal Investigator (Last, First, Middle): Next Generation Sequencing Core

### RESOURCES

Follow the 398 application instructions in Part I, 4.7 Resources.

### Location:

The NGSC is located largely in the 12th floor of the Smilow Center for Translational Research, where it occupies about 600 square feet. It also occupies about one hundred square feet in BRB-II/III where two pieces of equipment were placed due to lack of space and logistical convenience. Room 12-253 SCTR was modified to increase the cooling capacity to support the sequencers.

### Equipment:

The NGSC maintains the following equipment.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Group** | **Manufacturer** | **Model** | **Serial Number** | **Status** | **Location** | **Acquisition Date** | **Source** |
| *Sequencers* | Illumina | HiSeq 2500 |  | Active | 12-253 SCTR |  | PSOM |
|  | Illumina | HiSeq 2500 | 431 | Active | 12-253 SCTR |  | PGFI |
|  | Illumina | NextSeq 500 |  | Active | 12-160 SCTR |  | PSOM |
|  | Illumina | MiSeq | 590 | Active | 12-160 SCTR |  | PSOM |
|  | Illumina | HiSeq 2000 | 1160 | Functional | 12-253 SCTR |  | PSOM |
|  | Illumina | HiSeq 2000 | 965 | Not in use | 12-253 SCTR |  | PSOM |
|  | Illumina | HiSeq 2000 | 969 | Not in use | 12-253 SCTR |  | HHMI, owner |
| *Other* | Fluidigm | C1 |  | Active | 12-160 SCTR |  | PSOM |
|  | Beckman-Coulter | BioMek XFP |  | Active | 12-160 SCTR |  | PSOM |
|  | Agilent | Bravo |  | Active | 3-xxx BRB II/III |  | PSOM |
|  | Covaris | LE220 |  | Active | 3-xxx BRB II/III |  | PSOM |

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### Macintosh HD:Users:ninaprak:Dropbox (Personal):HIC:HIC Outreach:HIC Logo:HIC Logo (Vector Graphic).pngFacilities and Major Equipment for Human Immunology Core Lab (HIC)

**Location.** The HIC is located in Stellar Chance Labs, rooms 410-412, where it occupies 1,100 square feet of wet bench space for sample processing, cellular immunology and molecular immunology work. The lab has 14 workstations and one dedicated tissue culture room. The core also has a satellite laboratory

on the 8th floor of the Smilow Translational Research Building, Bay 178 for processing samples from apheresis donors.

**General Description.** The Human Immunology Core (HIC) laboratory is based in the Perelman School of Medicine and funded in part by the NIH, by the Center for AIDS Research (CFAR) at Penn, the Department of Pathology and Laboratory Medicine, the Institute for Immunology (IFI) and the Perelman School of Medicine (PSOM). The core provides cell products, cell processing and state-of-the art immunology assays to investigators who perform immunology studies in humans, including clinical trials. Some assay platforms have also been modified for work in animal models. The Core's leadership has extensive experience in a wide range of immunology assays and in translational medical research. In addition to products and assays, the Core offers scientific consultation and data analysis services. Core assays and services are described below.

**Molecular Immunology Resources.** The molecular immunology laboratory within the HIC performs next generation sequencing of antigen receptor gene repertoires, including human IgH, mouse IgH and human TCR V rearrangements, molecularly indexed human IgH and single cell assays in beta test. The core has separate pre- vs. post-amplification workspaces. The core provides investigators with an easy-to-use service for these complex assays, including advising investigators on which assay platforms are optimal for their studies or interests. The core also performs extensive computational analyses on the immune repertoire data for investigators on a fee-for-service basis.

Instrumentation:

* Illumina MiSeq- for high throughput antigen receptor sequencing
* Four Peltier type thermal cyclers
* Roche LC480 qPCR instrument, which uses 384-well plates and can run up to 5 different colors for multiplex quantitative PCR assays.
* Pippin prep instrument for band purification
* Bio-Rad gel documentation system
* NanoDrop- for nucleic acid quantitation
* Qubit- for nucleic acid quantitation

**Cellular Immunology Resources.** The cellular immunology laboratory within the HIC performs standard immunological assays such as cytokine assessment by luminex, ELISA, digital ELISA (Simoa), ELISPOT and flow cytometry. The HIC performs flow cytometry analysis in collaboration with the Flow Cytometry Core facility, has several panels for T, B and innate cell analysis as well as intracellular staining for cytokines and other analytes. The core also performs flow cytometry and ELISPOT assays on stimulation cultures to analyze responses to specific antigens for cancer, vaccine and infectious disease-based studies. Customized panels can be designed and validated for clinical trial use with the combined expertise of the HIC and the flow cytometry core. Luminex assays utilize antigen or antibody-coated microspheres to measure cytokines or other molecules of interest in a semi-quantitative and rapid fashion.

Instrumentation:

* Simoa HD-1 (digital ELISA)
* Bio-Rad luminex instrument
* FlexMAP 3000 for luminex (co-owned with the Molecular Core)
* CTL ImmunoSpot S3 (ELISPOT reader)
* ELISA plate reader

**Specimen Processing and Storage.** The specimen processing laboratory within the HIC routinely prepares and stores peripheral blood mononuclear cells (PBMCs), plasma and serum as required by experimental protocols. Samples are logged in, processed, stored, and shipped or tested as each protocol dictates. Results are recorded and transmitted electronically to the PI or the appropriate data management center or database. A freezer inventory is maintained to track samples frozen at -80oC or in liquid nitrogen. The Core lab also processes tissue biopsies for use and preservation, depending upon the needs of the study investigator or clinical trial protocol.

Instrumentation:

* + Cryocart
  + Beckman Coulter ViCell XR (cell counting instrument)
  + Zeiss inverted microscope
  + Electronic monitoring of freezers and refrigerators
  + 5 biosafety cabinets

**Cell Product Service**. The Cell Product Service within the HIC provides fresh and cryopreserved cells derived from the peripheral blood of healthy subjects. Cells are obtained by leukapheresis (performed in the Apheresis Unit in the Division of Transfusion Medicine within the Department of Pathology and Laboratory Medicine). Cells are typically available twice a week. The Core has an online scheduling tool for cell product orders and maintains a blanked IRB-approved protocol. Individual investigators receive de-identified cells and do not require their own IRB approval in order to use the service.

Cell products include:

* unfractionated apheresis product
* peripheral blood mononuclear cells
* peripheral blood lymphocytes
* CD3+ T cells
* CD4+ T cells
* CD8+ T cells
* NK cells
* B cells
* monocytes
* cryopreserved cell products

Principal Investigator/Program Director (Last, first, middle): CHOI, Yongwon

### RESOURCES

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

**Scientific Environment:** The University of Pennsylvania, Perelman School of Medicine (PSOM) provides a rich environment for collaborative and cross-disciplinary studies in basic biological mechanisms underlying human health and disease. The PSOM has dedicated shared resource facilities open to Penn scientists to support basic and translational research activities.

**Mouse Facility & Laboratory:** The Penn Gnotobiotic Mouse Facility (PGMF) occupies 3 rooms in Suite 32 of the vivarium space on the ground floor of the Hill Pavilion building. This area provides separate space for centralized germ-free and gnotobiotic mouse services that include access to small experimental isolators for a variety of *in vivo* studies utilizing germ-free mice. Furthermore, the PGMF offers technical support to investigators for numerous experimental procedures. Additionally, the core’s laboratory space is located on the 3rd floor of BRB II/II, room 336. This space provides a separate wet laboratory for microbiology checks, and sample processing from experiments.

**Clinical:** N/A.

**Animal:** The PGMF maintains several common strains of germ-free mice, such as C57BL6, and RAG knockout mice. These strains are available immediately upon request.

**Computer:** Computers are available in both the mouse facility and the laboratory space. A MacBook is available in the mouse facility as well as an iMac in the laboratory.

**Office:** Dr. Choi’s office is located on the 3rd floor of the Biomedical Research Building (BRB II/III).

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of

each.

### Major equipment:

Large Isolators: The large isolators are used to maintain several common strains of germ-free mice, such as C57BL6, and RAG knockout mice. Each isolator is made of either 20-mil vinyl or 20-mil urethane film. They are the standard size of 5' x 2' x 2'. Total cage capacity in each large isolator is 10.These isolators are maintained in room’s 32H, 32G, 32J located in the basement of the Hill Pavilion.

Small Isolators: The small isolators provide space for a variety of *in vivo* studies utilizing germ-free mice. They are also made of either 20-mil vinyl or 20-mil urethane film, and in the standard size of 3' x 2' x 2'. Total cage capacity in each small isolator is 3. All materials to be used experimentally must be autoclavable. These isolators are maintained in room’s 32H, 32G, 32J located in the basement of the Hill Pavilion.

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| Program Director/Principal Investigator (Last, First, Middle): | Garcia, Benjamin A. |
| **RESOURCES** | |
| Follow the 398 application instructions in Part I, 4.7 Resources. |  |
| The Quantitative Proteomics Resource Core (QPRC) is in corporation with the research lab of Dr. Garcia located on 9th floor of the Smilow Center for Translational Research in the University of Pennsylvania, Perelman School of Medicine (PSOM). QPRC has access to the state-of-the-art HPLC systems and mass spectrometry instruments in Garcia lab and processes its own bench space with general lab devices and own designated sample storage space. The Core provides investigators access to the most advanced  high-resolution mass-spectrometry-based proteomics technologies. These approaches are implemented with a broad variety of mass-spectrometry-based experiments to characterize and quantify proteins from complex biological samples. The core staffs are committed to helping address questions regarding protein expression, regulation, interaction, and post-translational modifications, etc.  **Services provided**:   * Protein identification from gel bands or solution samples * Single protein post-translational modification (PTM) analyses using Bottom-Up or Top-Down MS methods * Global proteome expression analyses from cells or tissues using label-free, SILAC or TMT quantification * Protein-protein or RNA-protein interaction experiments * Global histone PTM analysis * Custom analyses based on targets of interest (single target or proteome-wide)   MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of each.  **Major equipment**:  Orbitrap Elite with EASY-nLC 1000 UHPLC: Elite combines the premium dual-pressure linear ion trap (Velos Pro) with a novel high-field Orbitrap mass analyzer to create the ultimate analytical instrument. The superior resolution and spectral quality, as well as the higher scan speed, increase proteome coverage in complex samples even with very low sample amounts. The faster scanning also ensures compatibility with narrow chromatographic peaks from UHPLC separations. And the availability of multiple fragmentation techniques (CID, HCD and optional ETD) offers a new level of versatility for challenging research applications.  Q Exactive with EASY-nLC 1000 UHPLC: QE combines high-performance quadrupole precursor selection with high-resolution, accurate-mass (HR/AM) Orbitrap detection. The superior quality of QE MS/MS data provides ultimate confidence for a wide range of qualitative and quantitative applications. Its high scan speed and spectral multiplexing capabilities make it fully compatible with UHPLC and fast chromatography techniques. QE can easily handle routine applications in proteomics from bottom-up protein ID to semi quantitative isotopic labeling analyses to targeted quantification experiments.  Orbitrap Fusion Tribird with EASY-nLC 1000/1200 UHPLC*:* Fusion mass spectrometer combines the best of quadrupole, Orbitrap, and ion trap mass analysis in a revolutionary Tribrid architecture that delivers unprecedented depth of analysis. It enables analyzing even the most challenging low-abundance, high-complexity, or difficult samples to identify more compounds more quickly, quantify more accurately, and elucidate structures more thoroughly.  Beckman Coutler System Gold HPLC and Agilent 1260 HPLC system with fraction collectors: These off-line HPLC instruments provide high-resolution and robust protein and peptide separation and fractionation for  large-scale proteomics analysis. The systems are equipped with commonly used analytical and | |

semi-preparative columns such as C8, C18, SCX, and HILIC for different application.

Laser-puller P2000 and Capillary Column Packing: The Core packs its own capillary columns in-house using cusmized high-pressure bombs equivalent to commercial ones. A laser puller P2000 facilitates the generation of emitters also comparable to commercial ones at higher outcome and lower cost.

General lab devices: Necessary devices are available to QPRC staff allowing for a wide range of proteomic sample preparations. These include Speed-vacuum evaporator, high-speed centrifuge, and time- and temperature-controlled incubators.

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| Program Director/Principal Investigator (Last, First, Middle): |
| **RESOURCES** |
| Follow the 398 application instructions in Part I, 4.7 Resources. |
| **Other**  The Research Instrumentation Shop, (R.I.S.) is a machine shop facility that supports Perelman School of Medicine faculty to design and construct new laboratory and clinical instrumentation. We accomplish this task using a wide range of machine tools and materials.  **Web link**  <http://www.med.upenn.edu/cores/research_intrumentation_shop.shtml>  **What we do**  We can take a virtual idea that is located only in your mind and turn it into a reality located in your hand!  **Location**  We are located in the John Morgan Building, 3620 Hamilton Walk, room 75, Philadelphia, PA 19104  **Experience**  The staff members, Bill Pennie and Mike Carman have over 40 years of interaction with researchers at the University of Pennsylvania and surrounding institutions.  **Major Equipment**  We have 4 vertical and 2 horizontal milling machines plus 6 lathes and many support machine tools like saws, router table and grinders. We also have sheet metal tools such as shears, brakes, (“benders”) and a notcher.  **Affiliation**  The Research Instrumentation Shop is a core facility administered and supported by the Department of Biochemistry and Biophysics, Perelman School of Medicine. |

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| Program Director/Principal Investigator (Last, First, Middle): |
| **RESOURCES** |
| Follow the 398 application instructions in Part I, 4.7 Resources. |
| **Laboratory and Office**: The Small Animal Imaging Facility (SAIF) is a School of Medicine (SOM) Core resource that provides expertise and instrumentation necessary to apply radiological imaging techniques to small animal models of human disease. The core operates two large laboratories located in the John Morgan basement and the first floor of the Smilow building. The core also operates one satellite facility located behind the barrier on the 6’th floor of the Smilow building. The Smilow lab (suite 1-110) occupies most of the southeastern corner of the first floor of the building. SAIF resources and common areas (hall way, rest rooms and break room) occupy approximately 4,925 sq. ft. of the suite. The John Morgan laboratory includes rooms B100, B95 and B96 for total space occupancy of 2,782 sq. ft. The satellite SAIF resources occupy minimal space of approximately 30 sq ft. Total space occupied by SAIF on Penn campus is 7,737 sq ft.  **Animal**: An extensive amount of research and testing involving animals is performed at the University of Pennsylvania. All protocols that employ animals must be reviewed and approved by the Institutional Animal Care an Use Committee (IACUC) before the study can begin. The IACUC consists of faculty members that actively involved in animal research and is responsible for assuring that all research that employs animals is performed in a safe and humane manor. The university has also created a large, well-equipped University Laboratory Animal Resource (ULAR) in order to support animal research. This facility currently employs a staff of over 40 technicians and professionals, 15 of which have veterinary training. The ULAR is responsible for the procurement, care and use of all University owned animals employed for teaching, research and testing as approved by IACUC and as mandated by federal law and regulations. The ULAR provides professional and technical consultation, assistance and training to researchers and their staff on the humane, proper and efficient use of laboratory animals and interact with the public about issues related to animal use in biomedical research. The ULAR also designs, renovates and maintains animal husbandry resources. It procures all animals used by the university and maintains the legally required records pertaining to the procurement and use for animals. Services provided by ULAR include boarding, routine inspection for disease, treatment, surgical facilities and assistance from veterinarians. This facility is fully accredited by AAALAC and has demonstrated compliance with NIH guidelines. ULAR routinely provides hands on training for administration of anesthesia to the species that are typically used in the SAIF. Other training courses (i.e. surgical procedures) may be arranged upon request. All animals used within the SAIF are purchased from and housed within the ULAR.  The SAIF has constructed limited rodent housing within each of its major laboratories. These resources are Department of Radiology owned, ULAR operated facilities that were created to facilitate longitudinal imaging studies without exposing the larger animal population to potential pathogens. Animals housed in these facilities may be removed, subjected to imaging exams and returned to the housing facility multiple times.  Each of these resources includes Bio-safety level (BSL) 1 and BSL-2 rooms for both rats and mice. Unless directed otherwise, animals in SAIF husbandry resources are fed chow that has been treated with fenben in order to minimize the potential for pin worm outbreaks.  **Computer and Instrumentation:** The SAIF operates numerous pieces of instrumentation used in the generation of small animal images as are summarized in the table below.  In addition, the Department of Radiology maintains a fully equipped electronics laboratory that is available to SAIF users for development and service of components employed in their studies. This facility includes numerous electronic measurement (oscilloscopes, network analyzers, impedance meter, multi meters) and testing (power supplies) devices. The resource also provides materials and supplies employed in the design  and construction of electronic devices (circuit boards, wire, capacitors, resistors, inductors, integrated circuits, soldering iron, solder, etc…). |

SAIF Major Equipment

Sub-Core Equipment Vendor

MRI 4.7T 40cm, 9.4T 8.9cm, 9.4T 31cm

Optical/Bioluminescence IVIS Lumina II, IVIS

Lumina III, IVIS Spectrum (2), Pearl Triology (2)

Nuclear Medicine U-SPECT+, Mosaic PET Scanner, EVS MS-9 CT, eXplore Locus SP microCT

Ultrasound Vevo 770, Vevo 2100, HDI-5000 clinical US

Agilent Inc, Palo Alto, CA

Perkin Elmer, Hopkinton, MA; Li- COR, Lincoln, NE

MiLabs, Utrecht, the Netherlands, Phillips Medical Systems, Cleveland, OH; ImTek, Knoxville, TN, GE Medical Systems, Mickleton, NJ

Visual Sonics, Toronto, Ontario; Phillips Medical Systems, Cleveland, OH

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Principal Investigator/Program Director (Last, first, middle): Stem Cell and Xenograft Core

### RESOURCES

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

**Scientific Environment:** The University of Pennsylvania Perelman School of Medicine (PSOM) provides a rich environment for collaborative and cross-disciplinary studies. The PSOM has dedicated shared resource facilities open to Penn scientists to support basic and translational research activities. The Stem Cell and Xenograft Core (SCXC) provides investigators with a high-quality, cost-effective and comprehensive resource to promote basic and translational research in the areas such as cancer biology, immunotherapy, stem cell biology, infectious diseases and regenerative medicine. Our resource laboratory integrates a large hematologic malignancy tissue bank with extensive xenotransplantation services to support translational research and promote the rapid development of clinically relevant models.

The Core staff has extensive experience with pre-clinical xenograft models to generate human tumors from cell lines or patient-derived specimens, human immune system reconstitution, and transplantation of various tissue-specific stem and ES/iPS cells. The Core staff has extensive expertise in animal husbandry, facility maintenance, and pre-clinical xenograft model development required for these experiments and will work with investigators to optimize xenograft models for achievement of the stated specific aims.

**Laboratory:** The Stem Cell and Xenograft Core has a total of 1,050 square feet of laboratory space divided in general laboratory space, human tissue processing and culture space and mouse tissue harvesting space. The liquid nitrogen freezers (n=4) holding patient specimens are located next to these rooms. This provides separate wet BSL2 laboratory spaces for human specimens, mouse tissues, tissue culture, and -80**°**C / LN2 freezer storage.

**Clinical:** N/A.

**Animal:** Our animal barrier space consists of an entire suite (6 rooms) housing our breeding colonies (2 rooms, 12 glove isolators, 180-cage capacity), a self-service BSL-2 space for users consisting of 2 rooms equipped with individually ventilated racks (900 cages total) and 5 biosafety cabinets. These 2 rooms are each equipped with a dedicated bioluminescence + fluorescence imaging system. One room is used to house weaned pups (140 cages) and for “full-service” experiments (140 cages). An additional room is used as a procedure/euthanasia room accessible only to Core users.

**Computer:** The laboratory possesses personal, community workstations, numerous computers to operate laboratory instrumentation. All the computers are connected to a 1GB network with access to shared drives for routine preservation and archival of scientific data.

**Office:** Dr. Danet-Desnoyers occupies roughly 150 sq. ft. adjacent to the main laboratory. Word-processing and graphics are handled with desktop and laptop computers interfaced to networked laser printers.

### Major equipment:

**Tissue banking equipment**:

Automated cell separator: the AutoMACS (Miltinyi Biotec) allows the automated cell separation of 4 samples in sterile conditions. It is housed in a 4 ft bisosafety cabinet.

Liquid nitrogen and -80C freezers: the Core has a total of 4 LN2 freezers (CryoPlus 3, Forma) to house our collection of hematologic malignancy specimens, and a -80C freezer (Thermo Forma) for reagents and cell lines

Patient specimen processing and cell culture: the Core has 4 biosafety cabinets (4 ft, Forma Scientific), 2 CO2 incubators (Hera Cell, Heraeus), 2 refrigerated centrifuges (Legend RT, Sorvall), an automated cell counter (Cellometer Auto T4, Nexcelom) connected to a PC, and an inverted microscope (CKX41,Olympus)

Database Server: Annotations for each patient specimen in our tissue bank are stored on a secure

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Principal Investigator/Program Director (Last, first, middle): Stem Cell and Xenograft Core

dedicated server (Apple) connected to the hospital (UPHS) network.

### Xenograft equipment:

* Bioluminescence / fluorescence in vivo imaging system (IVIS Spectrum, Perkin Elmer)
* 7 Individually ventilated racks (140 cages/rack PNC, Allentown Caging Co)
* 3 Individually ventilated racks (70 cages/rack PNC, Allentown Caging Co)
* 3 Biosafety cabinet, 6 ft (Baker)
* 3 Biosafety cabinet, 4 ft (Baker)
* 3 Anesthesia machines (VetEquip)
* 12 glove-isolators for breeding colony (6 x 4ft, 6 x 3ft, Park Bioservices)
* 3 supply isolators (Park Bioservices)
* 1 decontamination cabinet (Park Bioservices)
* Chlorine dioxide generator (DRS Laboratories)

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| Program Director/Principal Investigator (Last, First, Middle): | Transgenic & Chimeric Mouse Facility (TCMF) |
| **RESOURCES** | |
| Follow the 398 application instructions in Part I, 4.7 Resources. |  |
| This Core is centrally located on the School of Medicine campus within a few minute walk of users. It is physically housed in the basement of the Clinical Research Building within a microbiological barrier environment. The microinjection laboratory occupies Rooms 38 and 40 (239 and 248 square feet, respectively). The barrier facility in which the core lab is situated was fully renovated in 2013 with major upgrades in air filtration equipment. The core’s mouse cage facility is located in the adjacent Room 36 in the microbiologic barrier area. This room of 237 square feet is dedicated to core use. A core Cryopreservation Storage Facility is located in the Anatomy Chemistry Suite B22. This room (240 square feet) has an overall capacity for 12 cryo storage tanks (dewars), a liquid nitrogen feeder tank and a cryo filling enclosure, with continuously and centrally monitored alarm system. This room has limited access and all cryo-tanks are individually monitored 24 hours a day, 7 days a week.  The core has four fully equipped microinjection stations suitable for DNA injection of embryos and ES injection of blastocysts, each is set up with Nikon or Zeiss inverted scope along with Eppendorf micromanipulator and microinjector. One of these stations is also equipped for Intracytoplasmic Sperm Injection (ICSI) with a piezo drill and a second is used primarily for laser procedures. All microinjection stations are positioned on vibration-stabilization platforms. Other equipment includes: four stereomicroscopes for dissections; two Pipette pullers and microforges; a water bath; pH meter; two iMACs; two Eppendorf microfuges; refrigerator, freezer and liquid N2 dewar; a Nikon Coolpix cameral and a color  monitor; Biocool III apparatus; two CO2 incubators; two dry sterilizers; and an XYClone Laser System. | |

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| Program Director/Principal Investigator (Last, First, Middle): | Vector Core |
| **RESOURCES** | |
| Follow the 398 application instructions in Part I, 4.7 Resources. |  |
| **Location**. The Vector Core is located on the University of Pennsylvania campus (125 South 31st Street, Suite 2000). The facility comprises a total of 16,000 square feet which includes the Vector Core as well as the Quality Control, Immunology and Cell Morphology Groups and the laboratory of Dr. James Wilson. Within the facility, the Vector Core resources are divided in terms of function with two tissue culture rooms dedicated to AAV vector production, one tissue culture room dedicated to adenoviral vector production, and one tissue culture room dedicated to lentiviral vector production. Physical separation of these three production units minimizes the chance of cross-contamination of vector preparations. Separate rooms, which are not used for production work, are provided for working with wild-type or replication-competent viruses and additional precautions taken. The Quality Control Group utilizes three tissue culture rooms, one which houses Taqman and droplet digital PCR equipment for quantitative PCR, another with tissue culture hoods and incubators for cell-based assays and a third for sample preparation and biodistribution analysis. Additional tissue culture rooms are committed to clean cell culture work, process development work and GMP process-comparable AAV vector manufacturing. In addition, separate molecular biology sections for vector construction and recombinant virus analysis as well as dedicated equipment rooms for vector concentration and purification are part of the Core.  **Equipment:** The Vector Core is fully equipped with state-of-the-art instrumentation for the construction, propagation, and purification of viruses and viral-based vectors.  The major resources of the Vector Core production and quality control rooms includes:   * 30 Forma double stack incubators (including 4 double stacks capable of auto-sterilization) * 22 Baker biosafety cabinets * 8 Beckman ultracentrifuges with rotors * 2 Sorvall high speed centrifuges * 6 Sorvall low speed centrifuges * 5 -80°C freezers * 3 Nikon inverted microscopes (with fluorescent capability), * 2 Taqman PCR machines * 1 droplet digital PCR machine * 2 spectrophotometers, 2 gel cameras (one cooled CCD for chemiluminescence) * 1 Biotek Uquant microplate reader * 1 Biotek microplate luminometer * various PCR thermocyclers * 15 Dell Pentium-class computers for data analysis and lab management. | |

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