FACILITIES AND OTHER RESOURCES (OVERALL)

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Institutional Commitment

SEA-TRAC is a multidisciplinary and multi-institutional consortium including the University of Washington (UW), Fred Hutchinson Cancer Center (FHCRC), and Seattle Children's Research Institute (SCRI). These institutions have collectively committed almost $1M funding to SEA-TRAC over the 5 years of this program, representing 29% of SEA-TRAC direct costs, including institutional commitment funds from the UW Provost, as well as financial commitments from the UW School of Medicine, UW Department of Medicine, SCRI and the FHCRC. Specific institutional commitments are as follows:

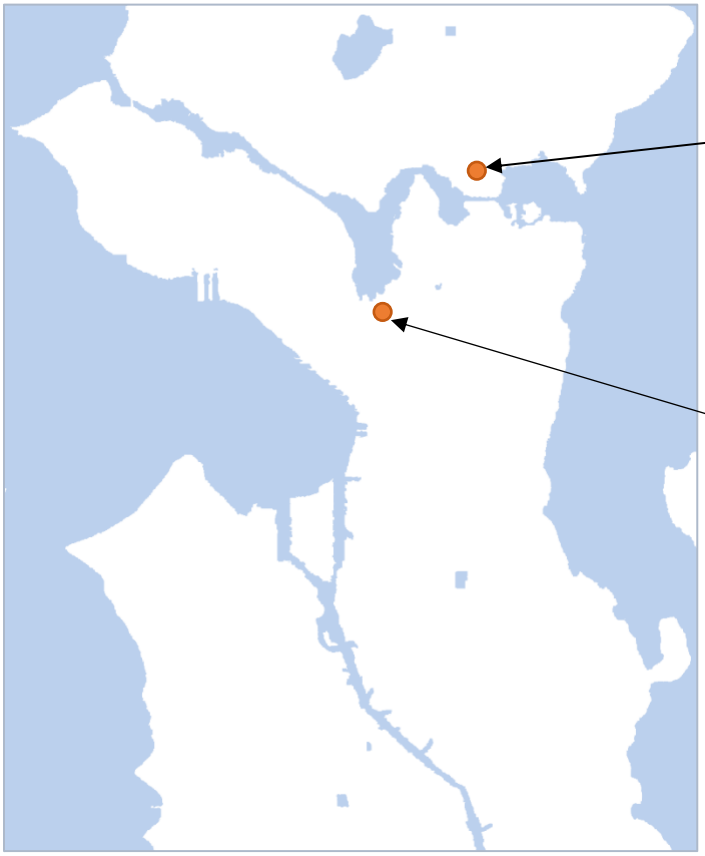
	Annual	5 yr total
School of Medicine	$43,000	$215,000
Dept. of Medicine	$3,000	$15,000
SCRI	$73,248	$366,240
FHCRC	$30,000	$150,000
Provost support	$23,000	$115,000
TOTAL	**$173,000**	**$861,240**

In addition, the two BSL-3 facilities critical to SEA-TRAC researchers are each subsidized by the UW School of Medicine and SCRI, further demonstrating the commitment of these organizations to supporting TB research.

Scientific Environment

The Seattle TB research community is already characterized by a rich collaborative scientific environment. Below we provide descriptions of each significant partner institution, organized by location. A map is provided below that depicts the locations of each Seattle-area partner institution.

Map of SEA-TRAC Locations in Seattle Area



UW Main Campus
- School of Medicine
- School of Public Health
- Department of Medicine
  - Division of Allergy and Infectious Diseases
- Department of Global Health
- Institute for Health Metrics and Evaluation

South Lake Union

UW at South Lake Union
- CERID
- Department of Microbiology
- Department of Immunology

Fred Hutchinson Cancer Research Center

Seattle Children's Research Institute
- Center for Global Infectious Disease Research

UNIVERSITY OF WASHINGTON


Image A: UW Main Campus

The University of Washington (UW) is a world-class institution of higher learning, and as one of the largest institutions of higher education in the West, along with its affiliate institutions, provides an excellent environment for training and research characterized by recent growth, diversity and excellence in all types of health-related research and education. Many of the approximately 3,900 teaching and research faculty are known nationally and internationally for their accomplishments. The UW has been the top public university in federal research funding every year since 1974 and among the top five universities, public and private, in federal funding since 1969. In FY2016, the grant awards at the UW amounted to almost $1.4 billion. Of this, the largest share came from the National Institutes of Health (NIH) and the Department of Health and Human Services (DHHS), indicating the depth and breadth of the University's health research program. The University's research environment also benefits from the diversity at the UW and high-quality facilities located throughout the vibrant and growing city of Seattle.

The UW provides the top Schools of Medicine and Public Health for five states of the Pacific Northwest, with interdisciplinary collaborations facilitated by sharing of a contiguous campus with Schools of Pharmacy, Nursing, Social Work, and Dentistry, adjacent to Colleges of Arts and Sciences, Business, Law, and Public Policy and Governance. The Schools of Medicine and Public Health have jointly established a Department of Global Health providing the focal point for UW international health programs.

The UW research infrastructure offers a wide array of services to support researchers—including technology transfer, human subjects review, and grant and contract services. Faculty and staff have access to the UW library system, which is home to more than seven million volumes and 62,000 current serials. Each UW investigator and staff member has Ethernet access, and the UW mainframe computer is available to investigators and staff, which provides access to online reference services, websites, and databases.

School of Medicine

Founded in 1946, the University of Washington School of Medicine is a regional resource for Washington, Wyoming, Alaska, Montana and Idaho - the WWAMI states. The UW School of Medicine is consistently named one of the nation's top medical training programs; in 2020, U.S. News & World Report ranked UWSOM as No. 2 in the nation for primary care education. Since 1974, the UW School of Medicine has ranked consistently among the top three schools in receipt of National Institutes of Health (NIH) grant funding. UWSOM is currently ranked tenth in the country among research-oriented medical schools. It is recognized for excellence in training primary-care physicians and for advancing medical knowledge through scientific research. The school's students, staff, faculty and alumni demonstrate commitment to community service through volunteer activities.

Research scientists at the UW School of Medicine explore every aspect of health and disease, from the molecular mechanisms of gene action to population studies of global illnesses. UW research scientists' work has contributed to improved understanding of the cause of diseases and to better treatments and prevention of many disorders.

One distinguishing characteristic of the UW School of Medicine is interdisciplinary collaboration. Scientists, educators, and clinicians are dedicated to helping each other reach the common goals of improving people's health and alleviating suffering from disease.

School of Public Health

The UW School of Public Health is ranked among the top ten public health schools in the U.S., and has had over 10,000 graduates in the past 40 years. The School houses the Departments of Epidemiology, Global Health, Biostatistics, Environmental and Occupational Health Sciences, and Health Services, and offers interdisciplinary programs in Health Administration, Maternal and Child Health, Nutritional Sciences, Pathobiology, and Public Health Genetics. More than 30 centers and institutes bring together faculty from

throughout the School to collaborate and do research across disciplines. The School partners with a number of health organizations including the Bill & Melinda Gates Foundation, Fred Hutchinson Cancer Research Center, Group Health Research Institute, Seattle Children's Hospital, U.S. Department of Veterans Affairs, PATH, and local and regional health departments across a five-state region.

Department of Medicine
The University of Washington's Department of Medicine is one of the largest departments at the UW, with 13 subspecialty divisions and over 3500 faculty and staff. It has ranked in the top 10 best-funded departments of medicine in the United States since 2006. The Department has more than 1,000 full-time faculty members who are active in all levels of training—medical school, four residency pathways, and subspecialty fellowship programs. The Department's residencies and fellowships are considered among the best programs in the country. Department of Medicine faculty members are leaders of major multidisciplinary and translational research centers at the University of Washington, including Center for AIDS and STD, Center for Lung Biology, Center for Research in Reproduction and Contraception, Diabetes and Obesity Center of Excellence, Fred Hutchinson Cancer Research Center, Institute for Stem Cell and Regenerative Medicine, Institute of Translational Health Sciences, Kidney Research Institute, and affiliated with a number of research centers and projects including the AIDS Clinical Trials Unit, HIV Vaccine Trials Unit, Center of Excellence in Women's Health, HIV Prevention Trials Unit, and Virology Research Clinic. Research partners include the Fred Hutchinson Cancer Research Center, Puget Sound Blood Center, Group Health Center for Health Studies, and other centers of advanced study, and research takes place in multidisciplinary centers affiliated with the Department, as well as laboratories at UW Medical Center, Harborview Medical Center, VA Puget Sound Health Care System, and Fred Hutchinson Cancer Research Center.

Division of Allergy and Infectious Diseases, Department of Medicine
The Division of Allergy and Infectious Diseases is one of the most prestigious in the country and has over 145 faculty members, including Drs. Seshadri, Hawn, and LaCourse. Faculty have been nationally and internationally recognized for their work in a variety of subspecialties, including phagocyte biology and function, HIV/AIDS and other sexually transmitted diseases and infections, viral diseases, immuno-compromised hosts, bacterial pathogenesis, geographic medicine, urinary tract infections, and the molecular biology of infectious diseases. The Division offers two fellowship training programs which are closely integrated with a number of local hospitals, clinics, and research institutions to provide a wide variety of clinical and research experience. Research training is offered in 9 areas of special emphasis: Clinical Epidemiology of Infectious Diseases, Clinical Trials, Human Immunodeficiency Virus Infection, Immunocompromised Host, Infectious Disease Immunology, Leukocyte Biology and Function, Pathogenesis of Bacterial, Fungal, and Parasitic Diseases, Pathogenesis of Viral Diseases, and Sexually Transmitted Diseases. Affiliations include Fred Hutchinson Cancer Research Center, Harborview Medical Center, Seattle Cancer Care Alliance, Seattle Children's Hospital, University of Washington Medical Center, and VA Puget Sound Health Care System.

Department of Global Health
The Department of Global Health (DGH) was established in 2007 through a generous gift and endowment from the Bill & Melinda Gates Foundation, and complementary Washington State resources. UW DGH bridges the schools of Medicine and Public Health, with a mandate to harness the expertise and interdisciplinary power of all 16 UW schools and colleges. Currently, the department has more than 330 faculty representing 15 of 16 UW schools and colleges and 41 departments. It is the second largest department at the University in terms of funding for research and training programs, and includes more than 30 centers, programs, initiatives, and the Institute for Health Metrics and Evaluation (IHME). The Department offers a wide selection of programs, including MPH and PhD degrees, Health Metrics & Evaluation Fellowships, and Graduate Certificate Programs in Global Health, Global Health of Women, Adolescents, and Children (Global WACh), Global Injury and Violence Prevention, and HIV and STIs. A Global Health Minor is also open to students from across campus. Current and emerging focus areas include: health metrics and evaluation, infectious diseases, workforce development, health system strengthening and implementation science, climate change, global trauma and violence, global medicines safety, women, children and adolescent health, and a strong crosscutting focus on social justice and equity.

Institute for Health Metrics and Evaluation (IHME)
IHME is a UW-affiliated institute dedicated to improving health for everyone worldwide by improving health evidence. IHME provides rigorous and comparable measurement of the world's most important health problems and evaluates the strategies used to address them.

UW High Performance Computing: UW-IT provides a capable cyberinfrastructure (CI) for researchers at the University of Washington, comprising data center, network, data storage, high performance computing (HPC), and consulting resources. The Hyak condominium-style HPC cluster has been in production since July of 2010. Hyak provided dozens of UW research groups with access to more than 40M CPU hours of throughput annually and is anticipated to grow to more than 70M hours from ~10,000 CPU cores. Hyak supports traditional HPC workloads, relying on high-bandwidth, low-latency communication, as well as parameter-parallel, big-data, and interactive use cases. Hyak includes a rich software environment, including optimizing compilers, high-level languages (Matlab, R, Mathematica, etc.), and a wide variety of commercial and open source domain- specific applications. Hyak's execution model allows all users fair access to idle CPU resources throughout the cluster regardless of their level of investment. As a result overall utilization is approximately 80% and individual research groups may achieve (or exceed) 100% utilization of the CPU resources they fund even if their demand is low at times and high at others.

Infrastructure: The UW-IT CI includes a 100Gbs High Speed Research (HSRN) network spanning both campus data centers which connects Hyak, the campus data transfer nodes (DTN), and research data archives to a Science DMZ. The HSRN extends to campus via a new 40Gbs backbone. Hyak resides in a professionally managed, Energy Star certified data center, opened in 2010, providing 9,500 square feet of space and 2.2MW of power.

University Investments: Over the last five years, UW has invested more than $20M in support of research computing. $8M of data center capital costs were funded by indirect cost recovery (IRC) levied on research grants. One third of the new data center space is devoted to research based on this investment. $1.65M in HSRN and Science DMZ costs were funded by grants and UW-IT. Total investment in Hyak and research data storage to date exceeds $11M, of which approximately $6M has come from central sources, while the remaining ~$5M represents direct investments by UW faculty.

Teleconferencing Capabilities: We anticipate that SEA-TRAC will need to host logistically complex international videoconferences, most often utilizing Zoom, Skype, or Microsoft Teams. All UW faculty, students and staff are provided with remote access to these tools. In addition, numerous auditoriums and conference rooms are equipped for remote video conferencing.

Library: The UW Health Sciences Library is available to all faculty, trainees, and staff. The library has been selected by the National Library of Medicine to serve as the Regional Medical Library for a five-state region. The library has extensive computer and informatics capability, with a large number of medical journals available online. All UW support services are available for the use of trainees and faculty. These include computer graphics services, photographic services, and financial management services.

SOUTH LAKE UNION
Many key SEA-TRAC facilities and resources are located in Seattle's expanding biotechnology and medical research hub known as South Lake Union. Here, the UW School of Medicine has five new research buildings that house the Center for Emerging and Re-emerging Diseases (CERID), the Department of Microbiology, the Department of Immunology, and the UW BSL-3 facility where work with live M. tuberculosis is performed. And additional administration building houses the Orin Smith Conference Center and computational laboratory space. Resources within the site include high-end imaging, high-throughput screening, confocal microscopy, flow cytometry, metabolomics, and proteomics.
In addition, the South Lake Union area is home to the Fred Hutchinson Cancer Research Center, Seattle Children's Research Institute, the Institute for Systems Biology, the Institute for Disease Modeling, the Allen Brain Institute, Partners for Appropriate Technology in Health (PATH), and numerous biotechnology companies, including Kineta, ZymoGenetics, Novo Nordisk, and others. Headquarters of the Bill and Melinda Gates Foundation are less than 10 minutes away by foot. This scientific environment, together with the University of

Washington main campus, offers numerous opportunities for collegial support and collaborative research arrangements. The following section describes resources for TB research and training in South Lake Union.

University of Washington at South Lake Union

Center for Emerging and Re-emerging Diseases (CERID)

CERID is located on the University of Washington's South Lake Union campus, very near the UW BSL-3 facility and among other major partners in Seattle's global health hub. The center occupies the entire 6th floor (17,000 sq. ft.) and a portion of the 7th floor (~6,000 sq. ft.) in Building E where the Hawn Lab is located, along with an additional ~5000 sq. ft on the 8th floor of Building F where the Seshadri and Sherman Labs are located. The center is a cooperative facility with an open lab design and many shared resources for the work proposed here.

Drs. Seshadri and Hawn are two of fifteen current principal investigators in CERID. Each has a private office (120 sq. ft.), tech desk areas (4x4 ft.) for each full time staff member, and 48 linear feet of wet lab space. Desktop and laptop personal computers are available to personnel within the lab and are connected by Ethernet to the University of Washington. All computers and files are password protected and computers are HIPAA compliant. There is a network laser printer and system-wide backup services, statistical software, antivirus software, and firewall. Multiple phone lines and website hosting are available through the University. Access to the building and floor level is limited via a security key card system during both business and non-business hours.

Department of Microbiology

The UW Department of Microbiology in the School of Medicine is world renown for research and training in diverse areas of microbiology. Its twenty-four Core faculty, including four members of the National Academy of Sciences, ten American Academy of Microbiology Fellows, four Fellows of AAAS and one Howard Hughes Investigator, are housed in both the Health Sciences Building (main campus) and in new, state-of-the-art facilities on the South Lake Union campus. Dr. Sherman's laboratory is located in South Lake Union, very near his departmental office (~250 sq. ft.), and in close proximity to the UW BSL-3 facility, our collaborators at CERID, the SCRI Center for Global Infectious Disease Research, the UW Immunology Department, Center for Innate Immunity and Immune Disease, as well as the Institute for Systems Biology, the Allen Brain Institute, and the Fred Hutchison Cancer Research Center. The Department offices are fully-equipped with ultra-high-speed internet, phones, security, power back-ups and facilities for hosting both virtual and in-person conferences. The Department is served by a capable administrative staff of nine people.

Department of Immunology

The Department of Immunology was established in 1986 by the University of Washington School of Medicine. The department was created with support from the Howard Hughes Medical Institute (HHMI), which provided initial funds for laboratory and administrative space, and resources for recruiting leading immunologists to complement UW researchers already conducting immunology work. The Department of Immunology is home to 13 core faculty members and 19 adjunct and affiliate faculty, approximately 70 postdoctoral fellows, and 35-40 graduate students, including students from the graduate Molecular and Cellular Biology program and the Medical Student Training program. UW Immunology faculty are internationally recognized for innovative and significant contributions to research in diverse areas of immunology. Faculty have an outstanding record of obtaining research funding; many faculty members are recipients of NIH MERIT Awards and prestigious junior faculty awards from the Cancer Research Institute, Burroughs Wellcome, Pew and Seale Scholars Programs.

Seminar Opportunities: SEA TRAC members will be able to attend and present at two local bi-weekly meetings. The first is the UW Bacterial pathogenesis training grant meeting (Director Ferric Fang) that is attended by labs in Microbiology (Brad Cookson, Joseph Mougous, Michelle Reniere, Pete Greenberg, Ajai Dandekar, Nina Salama, Samuel Miller, Matt Parsek, Pradeep Singh, Jason Smith, Evgeni Sokurenko), Pathobiology (Kevin Hybiske), Pediatrics (Lucas Hoffman), Allergy and Infectious Disease (Rajagapol, Thomas Hawn, David Fredricks), Pathology (Kelly Smith), Genome Sciences (Colin Manoil), and Global Health (Christoph Grundner). Second is the Mycobacteria Interest Group (MIG) meeting that is run by the current TRTC and will be incorporated in to SEA-TRAC. It brings together all local researchers and trainees interested in mycobacteria, including all current and proposed members of SEA-TRAC. Further, the Department of Microbiology, Department of Immunology, CERID, SCRI, FHCRC and ISB all hold seminars that are open to all SEA-TRAC members.

Biohazards: Some SEA-TRAC projects will involve work with live *M. tuberculosis*. Two fully accredited BSL3 facilities are available for in vitro as well as in vivo animal *M. tuberculosis* work.

In the E building of the UW South Lake Union Campus, a 3-minute indoor walk from the Sherman, Seshadri and Hawn labs, the UW BSL-3 facility is 8700 square feet with 12 BSL3 laboratories, 6 ABSL3 animal housing rooms, 6 ABSL3 animal procedure rooms, 2 BSL3/ABSL3 shared equipment rooms. Each laboratory contains 2 biosafety cabinets, a centrifuge, refrigerator, -20°C freezer, -80°C freezer, 2 cell culture incubators, 1 inverted phase microscope, 1 bright field microscope, 1 water bath, 1 mobile liquid nitrogen dewar, and 1 computer and telephone connection. The shared equipment rooms contain 1 micro ultracentrifuge, 1 floor centrifuge, 1 ultracentrifuge, 2 -80°C freezers, an ice flake machine, 1 desktop computer, 1 multifunctional plate reader (Synergy H4 269455), 1 mobile liquid nitrogen dewar, 1 room oxygen monitoring system, 1 mobile rodent anesthesia machine with isoflurane precision vaporizer and computer and telephone connections. In addition, a major equipment upgrade for the BSL-3 facility recently occurred. New shared equipment available to SEA TRAC includes: a fluorescence-activated cell sorter (FACS, Sony MA900); an IVIS imager for live, whole animal imaging of labeled pathogens and host cell types; a high-content cell imaging multi-mode reader (Cytation 5); a widefield inverted microscope with temperature and atmosphere-controlled incubation (Nikon Ti2-E), and a high-throughput plate washer/dispenser (Biotek EL-406). All this equipment is in place and available to the SEA-TRAC program.

Each ABSL3 animal housing room contains 1 biosafety cabinet, 2 sealed negative pressure, rodent ventilated cage racks. Each ABSL3 animal procedure room contains 1 biosafety cabinet, and will contain 1 mobile rodent aerosol chamber for aerosol infection. The BSL3/ABSL3 facility is monitored by 24-hour video surveillance and card reader access. Directional airflow is monitored by pressure monitors and alarms, and controlled by the building automation system. Agents are stored in locked -80°C freezers located within the BSL3 laboratory rooms. Infectious materials are treated with an appropriate disinfectant and/or autoclaved within the facility by trained staff prior to removal. All waste is processed in autoclaves. Researchers and staff are trained on an annual basis by members of the UW Department Environmental Health and Safety (EH&S) and UW Department of Comparative Medicine (DCM). All air passing out of the BSL3/ABSL3 facility is not recirculated and is HEPA filtered prior to being discharged to the roof. Room air is exhausted through a single pass HEPA filter housing. The BSL3/ABSL3 suites have dedicated, ducted exhaust systems. Pressure monitors at the doors display pressure differentials, and thus, airflow direction. The BSL3/ABSL3 suite is controlled by the building management system.

A second BSL-3 facility, owned and operated by SCRI, is described in the SCRI Facilities section below.

Computer: There are numerous PCs in the laboratory and offices, so that all researchers have unimpeded access to computers and the internet. Current software for word processing, spreadsheet analysis, and graphics is available as are ImageJ for image analysis, Prism for statistical analysis, and FlowJo for flow cytometry analysis.

UW Bio-Molecular Imaging Center: The Bio-Molecular Imaging Center (BMIC) develops novel imaging techniques for anatomic, functional, tissue and molecular applications, provides a full range of imaging services, and facilitates research for scientific and biomedical institutions throughout the Pacific Northwest. BMIC aims to be a place where new collaborative research opportunities are established, as well as a primary resource for the international scientific community. In collaboration with Philips Medical Systems, BMIC is equipped with a state-of-the-art Philips Achieva 3T Whole Body Scanner which is geared primarily towards human and translational research.

UW Confocal Facility: A new Zeiss Confocal Microscope; model LSM510Meta is available to South Lake Union labs. The instrument is located in room 423 and its purpose is to support research at the UW Medicine SLU campus; as well as labs from the main campus and even surrounding research facilities. The LSM510 instrument and software provides for conventional multiple fluorescent reporter detection in optically thin sections. Our particular unit also provides the ability to combine the Nomarski (a.k.a. differential interference contrast or DIC) optical image with the fluorescent signal in order to better visualize the cellular or tissue location of a fluorescent reporter. The instrument is additionally capable of Time series capture (for live-cell imaging and physiology studies), Z-stack acquisition with 3D reconstruction (projection and deconvolution), photo-bleaching (permits

FRAP: Fluorescence Recovery after Photo-bleaching), FRET analysis (Fluorescence Resonance Energy Transfer), and a wide variety of image analysis modules.

High Throughput Screening Core: The Quellos High Throughput Screening (HTS) Core specializes in Functional Genomics as well as Drug Discovery and Small-Molecule Optimization through chemical screening. It is located within the UW's Institute for Stem Cell and Regenerative Medicine at the South Lake Union Campus of the University Of Washington School Of Medicine serving Academic Institutions (e.g., Fred Hutchinson Cancer Research Center) as well as BioTech and Pharma organizations in Washington State and nationwide. A team with industrial and academic experience is available to aid investigators in their assay optimization and screening activities. The Quellos HTS Core was created to provide “state of the art” high throughput and lab automation approaches that were once only available in large pharmaceutical organizations.

Histology and Imaging Core: The Histology and Imaging Core (HIC) located at the UW School of Medicine South Lake Union was developed as a collaborative effort between the Center for Lung Biology and the Department of Comparative Medicine (HIC Organization). The HIC provides expertise in a broad range of histology, immunohistochemistry, imaging, image analysis and comparative pathology services. The lab is equipped with state-of-the-art automated, histology, immunohistochemistry, digital microscopy and live-cell imaging instrumentation which allows for high throughput processing and analysis while maintaining excellent quality and reproducibility.

Flow Cytometry Core: Located in the new University of Washington South Lake Union campus, the SLU Flow Facility provides state of the art instrumentation and technical expertise to facilitate investigators in performing quality cell sorting and analysis. They support research investigators affiliated with the Institute for Stem Cell and Regenerative Medicine (ISCRM), as well as those from UW main campus, and investigators from surrounding institutes. Instrumentation includes: BD FACSAria II, a state of the art 4-way cell sorter, equipped with solid state 405, 488, 561, 640-nm lasers. This instrument is housed in an approved BL2 space. BD FACSCanto II, an instrument is capable of detecting 8 parameters (6 colors) simultaneously. NanoPro 1000- The NanaPro 1000 system is a capillary-based nano-immunoassay platform which uses isoelectric focusing to resolve various phosphorylation states in signaling proteins. Additional BL-3 sorting capability is available through our collaborations with the Center for Global Infectious disease Research, located only a 5-minute walk away (see below).

Genotyping Core Facilities: The Genomics Resource core facility at Fred Hutchinson Cancer Research Center provides wide-ranging genotyping services that encompass several unique technology platforms. Instrumentation and expertise are available in the Genetic Analysis lab to perform various assays using ABI's capillary electrophoresis-based 3730 DNA Analyzer. Services are also available using microarray-based SNP mapping employing the Illumina platform. The resource also operates Illumina Genome Analyzer technology for SNP discovery and confirmation. In addition, the resource houses several 7900HT Real-Time PCR instruments that can be independently used by investigators for their genotyping needs.

Genomics Resource Core Facilities: The Genomics Resource has the expertise to perform transcript and small RNA analysis using the latest cutting-edge technologies. Platforms available for expression profiling include both commercial and in-house manufactured microarrays, as well as digital gene expression analysis using ultra high-throughput sequencing. The Genomics Resource offers NextGen Sequencing services for two platforms: Illumina HiSeq 2000 and Roche/454 GS Junior. Services include sample QC, library prep and QC, cluster optimization (HiSeq), and sequencing. Support equipment includes a Covaris LE220 System used in the preparation of sequencing libraries, as well as an Agilent Bioanalyzer 2100 and an ABI StepOne Real-Time PCR System for use in library QC. The facility also provides access to HutchBASE, a customized version of BASE v2.6 (BioArray Software Environment) that was originally developed at Lund University in Sweden. BASE is an open-source, MIAME compliant, comprehensive web-based data storage and handling solution with additional LIMS capabilities. HutchBASE is used for sample submission, order processing, and workflow tracking, as well as data QC, pre-processing, and normalization. The application also allows for data interfacing with a number of downstream analysis applications. Data analysis and annotation tools provided by the Resource include commercial software (e.g., Partek Genomics Suite, Ingenuity Pathway Analysis), as well as open-source software such as SAM, Cluster/TreeView, CyberT, FatiGO, Bioconductor packages (e.g., limma), MeV, etc.

Major Equipment: Shared or readily accessible equipment within UW SLU campus includes everything necessary for modern bioscience: fume hoods, shaking and stationary incubators, refrigerated centrifuges that accommodates swinging bucket and fixed angle rotors, refrigerated microfuges, ultracentrifuges, Covaris ultrasonicator, Nikon TiE fluorescent microscope, numerous thermocyclers, Molecular Devices Spectramax 384 plus UV/Visible microplate readers, multiple Kodak Image Station 4000R for gel imaging (chemiluminescence, UV, and visible light), electroporators, -80°C freezers, -20°C freezers, refrigerators, liquid nitrogen tanks, power supplies, gel boxes, water baths, and mixing devices. Tissue culture equipment includes biosafety cabinets, water-jacketed CO_2 incubators, and inverted microscopes.

Additional equipment and facilities are available with the entire UW Medicine South Lake Union campus which has many core facilities. These cores include: Bio-Molecular Imaging Center, Cell and Tissue Culture Cost Center, Confocal Facility, Genome Sequencer, High Throughput Screening Core, Histology and Imaging Core, and the SLU Flow Cytometry Core. Additional resources available within the larger UW system and Fred Hutchinson Cancer Research Center include Genotyping and Microarray Core Facilities.

Fred Hutchinson Cancer Research Center

Academic / Administrative Environment and Resources

The Fred Hutchinson Cancer Research Center (FHCRC) (Image B) is home to three Nobel Laureates and is one of the largest independent research organizations in the United States. It was formed in 1971 with a mission to pursue "the elimination of cancer and related diseases as causes of human suffering and death. FHCRC conducts research of the highest standards to improve prevention and treatment of cancer and related diseases." FHCRC received its first Cancer Center Support Grant in 1973, and attained Comprehensive Cancer Center status in 1976. Since that time, it has sustained continuous growth in multiple disciplines and now supports more than 2800 employees, over 200 faculty members, and an annual budget of over $480 million (with over $345 million in research grants and contracts). FHCRC is a foremost research and clinical care facility. During the past decade, FHCRC researchers have become leaders in infectious disease research and vaccine development. FHCRC is an international hub for research on HIV/AIDS and the testing of vaccine candidates, boasting some of the world's most respected pandemic researchers. Its combined clinical and research facilities and programs provide an ideal environment for which to pursue the successful completion of this project.

Image B: FHCRC Campus in Seattle, WA, USA.

The Center is organized into five scientific divisions: Basic Sciences; Clinical Research; Public Health Sciences; Human Biology; Vaccine and Infectious Disease. There are also multiple administrative departments (Finance, Human Resources, IT, Legal, Facilities, etc.) that support the work of the scientific divisions.

The Vaccine and Infectious Diseases Division (VIDD)*:* established in 2010, is a recognized leader in translational and "bench-to-bedside" science. VIDD integrates the expertise and creativity of scientists in basic, translational and clinical research to prevent, treat and cure infectious diseases, including known and emerging infections of major global health importance and cancer-related infectious diseases. Applying an innovative multidisciplinary approach, our division houses three formal research programs that systematically pursue explicit goals aimed at eliminating the burden of death and disease from infection. These programs include Biostatistics, Bioinformatics and Epidemiology; Immunology and Vaccine Development; and Infectious Disease Sciences. VIDD also houses major collaborative research networks including the COVID-19 Prevention Network (CoVPN), HIV Vaccine Trials Network (HVTN) and the HIV Prevention Trials Network (HPTN), which engage researchers globally in the development of preventive vaccines for COVID-19 and HIV. Within these programs and networks, VIDD's scientists relentlessly work to develop innovative approaches to preventing and treating HIV, coronavirus and other infectious diseases, improve treatment of serious infections among immunocompromised patients and create novel techniques to reduce the impact of infectious diseases worldwide. Dr. Fiore-Gartland is a member of the **Biostatistics, Bioinformatics, and Epidemiology Program**

(BBE) within the Vaccine and Infectious Disease Division. BBE consists of over 35 faculty members, many of whom hold joint appointments at the University of Washington. The use of quantitative sciences for studying human infectious disease processes and infectious disease prevention agents have had a unifying effect on laboratory and clinical studies and is a fundamental element in the forward progression of rigorous medical research. A hallmark of BBE is the pursuit of simultaneous excellence in methodological and applied science, harnessing the development of novel approaches to answer better scientific questions emerging from ongoing research studies. Members of the program conduct quantitative scientific research employing biostatistics, bioinformatics, computational biology, infectious disease epidemiology and mathematical modeling. VIDD faculty supporting this proposal include Drs. Fiore-Gartland, Julie McElrath, and Jim Kublin.

Data Science Core (DSC) Resources at FHCRC

The SEA-TRAC Data Science Core (DSC) will be co-directed by Dr. Shuyi Ma of the Seattle Children's Research Institute and Dr. Andrew Fiore-Gartland of the FHCRC. Having leadership spread across two institutions will give us the ability to leverage the computing resources of both institutions, which will ultimately provide greater flexibility and capacity to serve TRAC researchers. The following is a brief description of the facilities and resources at FHCRC that will be utilized by the SEA-TRAC DSC.

All resources and services are complementary to grant-funded projects of FHCRC faculty, except for "extended services" which involve charges. In the following, we provide an in-depth introduction to our current computing resources:

Scientific Computing (Center IT): The Scientific Computing group is staffed with 7 FTE and provides the following services to FHCRC research groups and shared resources:

- High-Performance Computing (access to the Gizmo HPC cluster including large memory machines, scratch spaces and web gateways for job submission through web browsers)
- General Linux/Unix support (Linux Desktop Support, managing applications on departmental Linux servers)
- Software Development Support (SCM/Subversion source code management, code evaluation for R,
- Python, shell scripting support, software packaging, performance evaluation)
- HPC and Linux/Unix Training
- File and Data management assistance / Data archiving

Local Computing Resources: The 'Gizmo' cluster is currently equipped with 504 to compute nodes / 2664 CPU cores and more than 24 TB of main memory (RAM) and is connected to a fully redundant Isilon high- performance storage cluster via Cisco Nexus 7000 series 40G networking equipment. Gizmo can directly access a storage capacity of more than 3 Petabyte and has dedicated high-performance scratch space of 500TB with a maximum throughput of 8GB/s. Gizmo consists of:

- 3 Intel Xeon (E5-2697v3, 2.6 GHz) nodes, each with 28 cores / 384 GB RAM / 10G network for a total of 84 cores / 1152 GB RAM (head / development nodes)
- 456 Intel Xeon (E3-1270/1241 v3, 3.5 GHz) nodes, each with 4 cores / 32 GB RAM for a total of 1824 cores / 14592 GB RAM
- 19 Intel (E5-2667v3, 3.2 GHz) nodes, each with 16 cores / 256 GB RAM / 10G network for a total of 304 cores / 4826 GB RAM
- 3 Intel Xeon (E5-2697v3, 2.6 GHz) nodes, each with 28 cores / 786 GB RAM / 10G network for a total of 84 cores / 2304 GB RAM
- 23 Intel Xeon (E5-2670, 2.6 GHz) nodes, each with 16 cores / 64 GB RAM for a total of 368 cores /1472 GB RAM

Each cluster node contains 1-6 TB local disk space which can be used for non-shared temporary data. 25 Nodes are equipped with fast 400GB NVMe flash disks for scratch space. All of the cluster nodes are 64-bit systems running the current version of the Ubuntu LTS Linux operating system. A variety of standard software is installed on the head nodes and on each work node. This includes the current version of R which is updated on a monthly basis as well as several MPI / parallel processing frameworks. A total of 361 nodes or 1816 CPU cores are equally shared by all FHCRC research groups. The Slurm HPC scheduler is used to implement fair sharing of HPC resources and ensures that all research groups can access a minimum number of resources at all times. In this cluster segment, all Principal Investigators are given the same priority. The remainder of the resource is owned by individual PIs and managed in a condominium model. 50% of these "private nodes" in the condominium are lightly used. When systems are not used by their owner's other research groups are permitted to use them

temporarily to maximize the return on the investment.

Cloud Computing Resources: The Center is currently using Amazon Web Services (AWS) for its Infrastructure as a Service (IaaS) cloud platform. Our internal network has been extended into a secure AWS Virtual Private Cloud (VPC) that is covered by a HIPAA Business Associates Agreement (BAA) with AWS. This environment is fully audited and integrated with our Security Information and Event Management (SIEM) system. This environment allows researchers to quickly provision computing, storage and database resources with the ability to scale systems both vertically (scale up) and horizontally (scale out) easily to meet just about any performance or capacity requirement. In AWS the center offers a dedicated HPC cluster using the same software stack and compute power as Gizmo. This allows researchers to run jobs in the cloud at times when local resources are scarce. For workflows using docker containers researchers have access to AWS Batch and Azure Batch, managed high-performance computing platforms. In addition to the secure VPC, we also have a public VPC for external collaborations.

Data Storage Service (Center IT): Storage Services are staffed with 3 FTE (24/7 on-call support). The Fast File storage service provides a high-performance POSIX file system. The Service is based on Isilon X Series scaleout network attached storage technology. The system can be accessed via SMB and NFS protocols. File system snapshots, which are stored on the system for 11 days, provide the first level of data protection. A cloud-based mirror of this file system (using objective and AWS S3) provides backup and disaster recovery capability.

The Economy File storage service: offers a high capacity object storage system that can scale to sizes > 50 Petabyte at low cost. The Service is based on commodity storage hardware, open-source cloud storage technology (OpenStack Swift) and is commercially supported by swiftstack.com. The system can be accessed via Swift or S3 protocols. Three replicas (copies) of the data are stored in 3 different buildings on campus providing high resiliency and data protection. The system is equipped with a recycle bin that protects against accidental deletions of files and currently allows for data restoration within 60 days after deletion. For cloud-based workflows, the center also offers access to AWS S3 storage as part of the Economy File storage service.

Extended storage services: Each principal investigator and member track faculty receives an allocation of 10 TB (5 TB of high-performance storage “Fast File,” 5 TB of slower storage “Economy File”) as complimentary service. Usage beyond that amount will incur a monthly cost per the published storage price list. (Current pricing: $30 per TB/month for “Fast File” and $3 per TB/month for “Economy File”). Investigators are expected to request funds for data storage through their grant applications.

Information Security Office (Center IT): The Information Security Office (ISO) is staffed with 12 FTE. The ISO maintains a highly available Intrusion prevention system and high-performance firewall and offers services such as encryption, forensics and consulting.

Biostatistics Shared Resource is a Center-wide biostatistics resource. This shared resource has two primary functions. The first function is to provide statistical computing supports to computational faculty members who need to have following supports: 1) implementing novel methodologies in R, MATLAB, C/C++, Java, Python, or any computer languages, 2) conducting simulation studies to test new methods, 3) processing various high dimensional data (RNAseq, microbiome, proteomics, metabolomics, etc.), 4) managing processed data (omics and clinical data), 5) performing customized data analyses in R, MATLAB, and SPSS. The second function is to provide biostatistical consultations to faculty members who are affiliated with public health sciences, clinical sciences, cancer biology or basic sciences, and to assist them with statistical analyses with various software packages.

Information Technology (IT) Equipment and Support: Center IT is staffed with nearly 120 FTE and provides support for a complex heterogeneous information technology environment. Center IT manages the FHCRC storage services which consist of a Nimble Storage Area Network (SAN), a NetApp Enterprise storage cluster for enterprise file services and an Isilon Storage cluster to provide high throughput data access for high performance computing. The total networked storage capacity is currently 1 PetaByte. Data protection is implemented by DataDomain appliances in conjunction with Commvault Simpana backup software and IBM Tivoli Storage Manager.
Many of the server services are provided by virtual systems using the advanced VMWare VSphere technology. The virtual systems have the added protection of being recoverable through snapshots which are taken and stored on a daily basis. The vSphere environment is configured as self service Enterprise cloud and currently hosts more than 800 virtual machines.

The network infrastructure consists of multiple Local Area Networks (LANs) connected to the FHCRC network. Intel personal computers, Macintosh systems, and LINUX/UNIX workstations are connected to servers running different operating systems. The FHCRC network is connected to the Internet through the Pacific Northwest GigaPop Network (PNWGP) with 1 Gbit/s. The Network is protected by redundant firewalls and a redunant intrusion prevention system. There are over 5,000 local workstations, printers, and servers connected to the FHCRC Network.

Center IT supports both UNIX/IMAP (Zimbra) and Microsoft Exchange for e-mail services in a highly available configuration. Center IT also provides support for over 60 applications that are made available to the entire Center including an enterprise level SharePoint Collaboration platform.
Special survey research support for computer-assisted telephone interviewing, automated open-ended coding, data entry software and optical scanning is available from the Consortium's Collaborative Data Services shared resource. The CDS Creative Services unit provides support in the preparation of high-quality materials utilizing a variety of graphics packages on both PC and Macintosh platforms. HP Color LaserJet and Epson Stylus Pro printers are available for high quality and large format printing production.

Information Security Office: The Information Security Office (ISO) is staffed with 5 FTE. The ISO maintains a highly available Intrusion prevention system and high performance firewall and offers services such as encryption, forensics and consulting.

***VIDD Network Support**:* The Division is staffed with two FTE and provides services that are specific to programs under the divisional umbrella that would otherwise be duplicated by each research group. They provide IT direction, planning and project management for the Division. Examples of specific services provided include IT program vision and direction, prioritization across IT program(s), basic architecture and technical input, risk assessment and planning, high-level relationship management, IT project management, resource management, etc.

Desktop Support: Desktop Support is staffed with 6 FTE during business hours (8am-5pm, PST) and provides limited after hours support for emergent issues. The main endpoint computer operating systems are Microsoft Windows 7 and 10 Enterprise and Mac OS X. The primary application suite used on all computers is Microsoft Office 2010 and 2016. Remote users can access data servers through the Internet by using a secured Virtual Private Network tunnel. Statistical software used in the program includes R, SAS, SPSS, STATA, SPLUS and MATLAB. Database applications supported in the program include Microsoft SQL Server, PostgreSQL, Oracle, Sybase, and Access.

All physical servers have redundant power and network connections, and use RAID to insure protection against drive failure. These virtual systems are supported by multiple hosts and have a high degree of redundancy. Physical servers are backed-up daily through Center-supported tape backup system

Seattle Children's Research Institute at 307 Westlake

Academic / Administrative Environment and Resources

Seattle Children's Research Institute (SCRI), the research division of Seattle Children's Hospital, is one of the top five pediatric research centers in the nation whose discoveries in bench, clinical, and outcomes research are recognized by scientists worldwide. With a workforce of over 1,800 people and over $200 million in total extramural funding, SCRI fosters a cutting-edge academic environment supporting multidisciplinary research, collaboration, and professional development (Image C).

Image C: SCRI at 307 Westlake in Seattle, WA, USA.

The research campus is in the heart of Seattle's biotechnology community, close to key partners including the University of Washington, the Fred Hutchison Cancer Research Center (FHCRC), the Institute for Systems Biology and several prominent

biotechnology institutions. SCRI and partnering institutions have established a rich, vibrant, collaborative, and well-funded research environment with excellent facilities that facilitate close collaborative relationships between clinical, translational, and basic science researchers with weekly research conferences, seminars and joint projects in a campus-like atmosphere.

SCRI is organized into seven Centers, each of which specialize in specific research areas: the Center for Global Infectious Disease Research (CGIDR), Center for Immunity and Immunotherapies, Center for Integrative Brain Research, Ben Towne Center for Childhood Cancer Research, Center for Child Health, Behavior and Development, Center for Developmental Biology and Regenerative Medicine, and the Center for Clinical and Translational Research.

The Center for Global Infectious Disease Research (CGIDR) is the largest pediatric infectious disease research program in the US. Located at 307 Westlake (Image Y) the center's cross-disciplinary team of researchers are leaders in discovering solutions leading to the prevention and treatment for infectious diseases that can pose risks to our communities, and disproportionately impact children and those in poverty, including: tuberculosis, HIV/AIMDS, malaria, human papillomavirus, group B *streptococcus*, and SARS-CoV-2. CGIDR faculty supporting this proposal include: Drs. Coler, Ma, Parish, Urdahl, and John Aitchison.

SEA-TRAC projects and programs will be conducted within the 86,000 ft^2 laboratory and office complex located at SCRI's 307 Westlake building. The space contains 20 interconnected laboratory areas and centralized facilities. The facility contains tissue culture (including BSL3), shared equipment, chemical preparation and dark rooms, as well as a glass wash and sterilization room. The facility is designed for molecular biological, immunological, and biochemical research.

BSL-3 and A-BSL-3**:** CGIDR has a state-of-the-art *Mycobacterium tuberculosis* (*Mtb*)-dedicated BSL-3 facility with a combined ~4,000 ft^2 laboratory space. The facility has two laboratories with separate entries and exits for microbiological work (BSL-3) and animal work (A-BSL-3) at biosafety level 3. Both laboratories are designed and equipped to ensure biocontainment and biosafety: The labs have negative pressure, dedicated gas lines, ultra-low freezers, Institute computer network access, showers, pass-through autoclaves, and alarms. Equipment includes CO_2 incubators, double-door incubators for controlled growth of *M. tuberculosis*, centrifugation equipment with aerosol containment, spectrophotometers, 96-well luminometer/fluorometers, bead-beaters, refrigerators, freezers, sinks, microscopes, controlled-access anterooms, telephones, and all other equipment needed to conduct work with BSL-3 organisms. Both labs have ample -80 freezer space and procedures in place to safely acquire, process, ship, and store biologically hazardous specimens that contain *M. tuberculosis* and other infectious agents.

The A-BSL-3 laboratory is entered through a key card-controlled anteroom holding personal protective equipment and exited through a decontamination and exit anteroom. The A-BSL-3 laboratory has two rodent BSL-3 animal holding rooms and a type II biosafety cabinet each. One animal holding room contains an infection closet with negative pressure relative to the adjacent room that holds an aerosol infection chamber. The A-BSL-3 has a total of 12 type II biosafety cabinets, eight of which reside in three separate laboratory suites with negative pressure that allow for added flexibility in containment. In addition to general equipment, the lab contains a SeaHorse, an Omnilog, and a fluorescent microscope.

The BSL-3 laboratory is entered through a key card-controlled anteroom holding personal protective equipment and exited through a decontamination and exit anteroom. The lab has 7 type II biosafety cabinets and an ImageExpress robotics and imaging station. A flow cytometry lab is housed in a separate suite within the BSL-3 and allows for analysis and sorting of *M. tuberculosis*-infected cells (see flow cytometry section). The flow lab provides training and technical support, assistance with experimental design, data analysis and interpretation, and assistance in developing novel multicolor flow cytometric techniques.

Each laboratory has a faculty-level director, and the facility is managed by a dedicated manager with >15 years of experience with *M. tuberculosis*.

Data Science Core (DSC) Resources at SCRI

The SEA-TRAC Data Science Core (DSC) will be co-directed by Dr. Shuyi Ma of the Seattle Children's Research Institute and Dr. Andrew Fiore-Gartland of the Fred Hutchinson Cancer Research Institute. Having leadership

spread across two institutions will give us the ability to leverage the computing resources of both institutions, which will ultimately provide greater flexibility and capacity to serve TRAC researchers. The following is a brief description of the facilities and resources at SCRI that will be utilized by the TRAC DSC.

The Bioinformatics and High-Throughput Analytics Center at SCRI provides researchers computational resources on various platforms, each suited to fit different types of computing tasks. SCRI supports a high-performance computing (HPC) cluster to facilitate data processing of large, complex datasets, machine learning, and batch processing of multiple parallel jobs. The SCRI cluster currently consists of 2 head nodes, with 20 worker nodes (560 core, 18.8 TeraFLOPs). Each node contains Intel E5-2690 v4 14-Core processors, 512GB memory, with EDR InfiniBand 100 Gbs interconnects. It also includes two additional "fat" nodes with 2TB RAM and 64 CPU for large jobs that do not distribute well across nodes, as well as 4 GPU nodes, providing an additional 160 CPU cores, and 28,000 GPU cores. A large attached storage array provides 1 petabyte of scratch space. The HPC environment provides a library of common tools used for bioinformatics analysis and the ability to wrap custom workflows in self-contained Singularity containers. We support development in R, python, and have several Matlab licenses and toolboxes available for general use.

In addition to the computing cluster, SCRI maintains several high-performance Linux servers that are procurable by multiple concurrent users through a web interface. Each machine provides 40-48 cores with up to 256GB RAM with 2 TB of scratch space. These machines are intended for brief use, such as for pipeline development on pilot datasets, or running of small serial jobs that can be distributed on multiple cores within a single node.

The Bioinformatics Group provides investigators access to state-of-the-art infrastructure (hardware and software) and personnel to track, store, manipulate, and analyze the biological data needed for hypothesis generation and testing. The facility is equipped with several multiprocessor Linux-based servers for high-capacity (multi-Gigabyte) computation and Windows-based SQL Servers for database management, as well as Terabyte-scale storage capacity on the Storage Area Network. These servers host a variety of genome-scale software, including sequence alignment and assembly, gene prediction and annotation, local BLAST service (using specialized databases), a client/server-based desktop sequence analysis package, microarray data analysis and statistical packages, and a proteomics analysis pipeline, as well as custom-designed project-specific scripts, software and GUIs. This group is overseen by Dr. Peter Myler, Professor, and is staffed by Bioinformatics software specialists and programmers, as well as a Systems Administrator from the Information Technology department. The staff provides support for project-specific data and process management databases, data manipulation and analysis, as well as software training and consultation.

IT Infrastructure: SCRI at 307 Westlake has over 250 server instances (Linux and Windows) running on both "bare metal" hardware and on two VMware ESXi clusters. The VMware clusters are deployed in a highly-available configuration, with load balancing across hosts provided by a distributed resource scheduler. Two Linux compute clusters with a total of 244 processing cores and a 600 terabyte storage area network (SAN) with full "snapshot" rollback capability are available for researchers to use. All servers are connected by a 10 Gigabit Ethernet network linked to the Internet via the Pacific Northwest Gigapop with a 1Gb/s fiber optic connection providing high-speed, secure access to resources at the University of Washington (with which CID Research is affiliated), Institute for Systems Biology and other collaborating sites. The Center makes extensive use of cloud-based computational resources at Amazon Web Services (AWS) and Google Cloud Platform (GCP). Collaborative systems include a SharePoint 2010 server farm with more than 50 externally-facing sites. The scientific desktop network consists of 300 PC and Macintosh computers linked via a 1Gbps Local Area Network with secure wireless capability. Additional shared resources include high-resolution scanners, high speed color laser printers and multi-media production equipment. Centralized software includes packages for DNA sequence analysis, statistics, proteomics analysis, microscopic image management, laboratory information management systems (LIMS), grants management, word processing, reference-citation management, collaborative interchange and technical graphics. Professional IT staff maintains the information technology infrastructure. Secure central SCRI servers provide safe storage and regular data backup protocols. On-site information technology support is available.

The Single Cell Systems Biology Core makes possible the analysis of individual cells, the study of their unique behaviors, the determination of their molecular components, and the integration of data to derive fundamentally new insights into the complexity of cellular function and interactions. The Core provides specialized equipment

for cell isolation, live automated cellular imaging, transcriptomics and Next Gen sequencing. Major equipment includes: The BD FACS Melody is an automated cell sorter with 3 lasers, 9-color capability, and an automated cell dispensing unit for sorting single cells into plates. It is housed in a Baker biosafety cabinet for containment of sorting live cells in a BSL2 environment. This instrument dramatically increases throughput for cell sorting capabilities through instrument access, sorting speed and accuracy, and the ability to sort into 96 or 384 well plates. Two Keyence BZ-X700 fluorescence microscopes provide a fully- automated, easy-to-use system that captures high-resolution widefield images from live and fixed samples on slides, dishes, and well-plates. The systems can image in fluorescence (DAPI, GFP, TRITC, Texas Red and Cy5), brightfield and phase contrast and has a built-in high sensitivity cooled 14-bit CCD camera for accurate measurement of expression levels and precise quantification. The systems feature optical sectioning through structured illumination for capturing clear fluorescence images without blurring from out-of-focus light. It also supports XY stitching, z-stack full focus imaging, multi-point capture, and time-lapse imaging. The Takara iCell8 system provides a MultiSample NanoDispenser (MSND) and imaging station to enable the isolation, selection, and harvesting of single cells for transcriptomics and other downstream analysis. This technology uses imaging to visualize 5,184 nanowells to ensure each well contains only a single cell. The cell samples can be stained with cellular dyes and visualized with fluorescence filters to analyze the viability of the single cells. The technology also uses nanowell-specific barcodes to allow the tracing of sequencing data back to the individual cells that were selected for analysis. The 10X Genomics Chromium with NextGEM technology is a reagent delivery system that partitions cells or nuclei and prepares sequencing libraries in parallel such that all fragments produced within a partition share a common barcode. This is used in single cell gene expression to identify and characterize rare cell types. It is also useful in immune profile studies to look at the complexity of the cellular diversity and immune cell profiling. Other applications include Single Cell ATAC to accelerate biomarker discovery and understand gene regulatory networks for studying disease pathogenesis and cell variability in thousands of single cells. The Illumina MiSeq next gen sequencer enables researchers to perform in-house targeted gene sequencing, metagenomics, small genome sequencing, targeted gene expression, amplicon sequencing, and HLA typing. The Fluidigm BioMark HD system utilizes microfluidics technology for real-time PCR (qPCR), SNP genotyping and digital PCR assays in a high-throughput, low volume fluidics chip (48x48 or 192x24 format). These options give researchers the flexibility to choose the appropriate ratio of assays to samples to meet their project objectives.

The Flow Cytometry Core provides access to state-of-the-art equipment for fluorescent-based cell analysis and sorting, as well as training and technical support, assistance with experimental design, data analysis and interpretation, and assistance in developing novel multicolor flow cytometric techniques. The sorter at the 307 building is housed in a Biosafety Level 3 (BSL3) facility within a biosafety containment hood to allow sorting of BSL2+ and BSL3 infected samples. In addition, Seattle Children's has a second Flow Cytometry core facility in the Center for Immunity and Immunotherapies at the Jack McDonald Building location. They have two flow cytometers and two cell sorters for BSL2 that can be used by all our trained researchers. The facility is equipped with the Becton Dickinson (BD) FACS Aria II cell sorter capable of detecting 17 colors simultaneously with four lasers - Blue (488nm), Violet (405nm), Red (633nm) and Green (532nm). This sorter is housed in a custom biosafety cabinet in a Biosafety Level 3 facility to add another level of containment. The is also a BD Cytopeia Influx high speed cell sorter capable of detecting 8 colors simultaneously with three lasers - Coherent Sapphire (488nm), Red (635nm), and UV (350nm) – and offers flexibility for sorting larger cells at up to 70,000 events per second. The Core also provides two BD LSRII flow analyzers outfitted with four lasers for detecting up to 18 fluorophores simultaneously in a Biosafety Level 2 environment. Both include a high throughput sampler that can rapidly introduce samples directly from 96 and 384 well plates. Seattle Children's has an additional Flow Cytometry Core facility located in the SCRI Center for Immunity and Immunotherapies less than 1 mile away. This facility houses two FACS AriaII cell sorters and two LSRII analyzers for BSL1 and 2 organisms.

The Scientific Imaging Core provides advanced fluorescence instrumentation at a BSL2 level of biocontainment. The imaging equipment and software allows researchers to describe cell changes and function under varying conditions and to characterize molecules following gel separation and image detection. Expert consultation services and instrument training are provided for all Core users. Major equipment includes: The Leica STELLARIS 8 confocal microscope system is a true confocal point scanning system, including a White Light Laser (range from 440 nm up to 790 nm) as excitation light source, an Acousto Optical Beam Splitter and a highly sensitive, prism-based spectral detection design with computer controlled adjustable bandwidth for all internal detection channels. There are 4 laser ports to connect the 405 nm laser and VIS laser excitation light sources on our system. Also included in our system are 5 Power HyD® detectors, which provides enhanced

detection efficiency and photon counting. The extended detection range of up to 850 nm (near infra-red), combined with the excitation range of the White Light Laser, allows the separation of an extended range of spectrally overlapping fluorophores. The STELLARIS 8 also allows researchers to select 8 single excitation wavelengths in an experiment. The enhanced detection efficiency and the optimal match of excitation and detection enable long term gentle live cell imaging. The system includes a conventional and resonance scanner (Tandem) along with Dynamic Signal Enhancement and LIGHTNING software to deliver superb image quality at live-cell dynamic speeds and in super-resolution. STELLARIS 8 comes with a lifetime-based tool set (TauSense software) that provides additional information in a semi-quantitative manner using gate-based technology and mean average arrival time. Tau Modalities provide for functional imaging (Tau-Contrast), removal of undesired signal contribution (Tau-gating) and enables separation of spectrally overlapping fluorophores with varying lifetime differences (ex: Alexa 555 and Alexa 594). The GE DeltaVision Elite optical/digital-sectioning fluorescence microscope is a fully-automated, high resolution microscope system capable of 3D live or fixed cell imaging in real time. It is equipped with DIC optics for acquiring visible light images and up to seven channels for imaging fluorescently labeled cells. This system includes multi-wavelength automated image capture for DAPI, FITC, TRITC, mCherry, CFP, YFP, and Cy-5 dyes. The SoftWorx software package comes with deconvolution capabilities and other image analysis features to create the highest quality images for publication. The Imaging facility also has a Perkin Elmer IVIS Lumina II live animal imaging system. This high-sensitivity, low noise, *in vivo* imaging technology platform enables noninvasive visualization and tracking of cellular and genetic activity within a living organism, in real time. Specialized imaging software suites available to all researchers include Imaris 3D cell imaging package and the Huygens Essential deconvolution program.

The Protein Production Lab provides protein production and purification for bacteria and mammalian expression systems. The facility is fully equipped with multiple ÄKTA PrimePlus and Purifier FPLC systems. This group includes a team of experienced protein technicians that provide services in collaboration with all our scientific programs.

Animal Care Program: The Animal Care Program is centralized with rodents housed in three facilities within the 307 Westlake building. All animal facilities are operated as a Specific Pathogen-Free barrier (i.e. Cages, bedding, feed and water are sterile; controlled limited personal access; PPE requirements; IVCs, BSCs, negative isolated change stations). The main Vivarium (2600 ft^2) is separated into two sections, a barrier (4 rooms) and a non-barrier area (2 rooms). The barrier area is limited access and animals removed from this area may not return. Each room in the Barrier is partitioned with BioBubble Room Enclosure System into Animal Holding and an anteroom with an BSC. Select rooms within the main vivarium may be designated for housing animals infected with ABSL2 pathogens. When this occurs, animals are housed in negative pressure HEPA filtered IVCs and all animal care and use activities are conducted in BSCs using prescribed isolation procedures. Animals in the non-barrier area may leave the main facility and be returned to the non-barrier animal rooms only. An MTB ABSL3 biocontainment facility is part of the MTB BSL3 facilities located on the 2nd floor of the 307 Westlake building (described above). A third facility, consisting of an anteroom and holding room is used for breeding select strains of rodents. Animal health is monitored by a staff veterinarian, animal care staff, and a sentinel program. The animal program is overseen by the SCRI's Institutional Animal Care and Use Committee (IACUC). SCRI has an active Animal Welfare assurance on file with OLAW (A3640-01) and is AAALAC accredited.

Major Equipment: Seattle Children's Research Institute (SCRI) at the 307 Westlake building maintains shared equipment that is available to all laboratories. This includes fluorescence imaging microscopes for fixed and live cells, PCR and Real-Time PCR machines for 96 and 384 well format, UV-VIS spectrophotometers, luminescence and fluorescence plate readers, gel documentation systems, bioanalyzers, cell/particle counters, HPLC purification system, liquid scintillation counter, anaerobic chamber, and an x-ray irradiator. The Center also recently acquired a new Odyssey CLX near-infrared imager for imaging fluorescent-tagged western blots and protein microarrays with a high level of sensitivity, as well as a new CTL Immunospot reader for fluorescent elispot assays. Training is provided by qualified staff on all equipment and overseen by a lab equipment manager. SCRI has a wide variety of standard scientific equipment for general use including fume hoods, biosafety cabinets, cold rooms, water purification system, autoclaves, balances, gel dryers, ovens, pH meters, film processor, speed vacs, incubators, shaking incubators, ultracentrifuges, high-speed refrigerated floor centrifuges, backup -80 freezers and other equipment.

Office: All principal investigators have 140 ft^2 of secure office space near the laboratory. There is also office space for the support staff, and locked filing space is available at each site as needed. Each floor has at least three conference rooms that seat from 6 to 15 people for meetings.

Other Resources: Administrative assistance for grant preparation, HR, purchasing and accounting-related services is provided by several departments that we call "Research Support Services" (RSS). RSS departments assist in the identification, application and management of research activities. RSS departments routinely assess performance on the basis of service metrics. RSS includes: Office of Biostatistical Services, Office of Clinical Research, Institutional Animal Care and Use Committee, Institutional Biosafety Committee, Institutional Review Board, Office of Research Finance, Research Regulatory Affairs, Office of Business Intelligence & Data Integration, and the Office of Sponsored Research.

*Library**:*** Professional library services at CGIDR include mediated literature searching in scholarly research databases, citation analyses, collaboration portal support, and curation of an institutional repository. Librarian consultation topics include bibliographic citation management software, MEDLINE, NIH Public Access Policy compliance, copyright, social media tools, and individual information management. CGIDR scientists have full access to web-based knowledge resources at SCRI and University of Washington including: current journals subscriptions, reference texts, news sources, databases across the biomedical and health research sciences and in relevant areas such as computing, technology, public policy, and business. Documents not available online may be requested for delivery via SCRI document delivery services. SCRI is a full member of the National Network of Libraries of Medicine.