FACILITIES & OTHER RESOURCES

Introduction

Hawai‘i’s cultural diversity and physical setting provide a unique forum for research. According to newly released data from the US Census Bureau, Hawai‘i has the highest racial and ethnic diversity among all states with an index of 76.0%, followed by California at 69.7% and Nevada at 68.8%. Racial/ethnic groups (race alone or in combination) in Hawai‘i include White (25%), Native Hawaiian (22%), Filipino (15%), Japanese (12%), and Pacific Islander (2%).2 Also important is the State's geography. Hawai‘i, an island state, is the only state in the nation located in the tropics. The state of Hawai‘i is made up of eight major islands: Oahu (with the capital and urban center of Honolulu), and the neighbor islands which includes Hawai‘i Island, Kauai, Maui, Molokai, Lanai, Niihau, and Kahoolawe (uninhabited). The state is remote - it is over 2,300 miles from the nearest landmass. These cultural and geographical features provide investigators with unique research opportunities that cannot be found anywhere else in the world.

Founded in 1907, University of Hawai‘i (UH) is now a 10-campus, statewide system of public higher education with a single Board of Regents and President. Classified by the Carnegie Foundation as a Category 1 research university, the University of Hawai‘i at Mānoa (UHM) is the flagship campus and is one of a dozen universities or consortia in the U.S. designated as a Land, Sea and Space grant college. The UHM is ranked in the world’s top 2% for academic and research excellence out of more than 26,000 worldwide colleges and universities, according to the 2022 Quacquarelli Symonds (QS) World University Rankings released on June 2021. UHM has ranked perennially among the top 100 educational institutions in the Nation for producing underrepresented minority graduates with advanced degrees. The UHM student body represents a total enrollment of 13,700 undergraduate students and 3,900 graduate students, with an ethnic distribution reflective of the state population. Approximately 25% of the students reported Hawaiian ancestry, and 14% reported Other Pacific Islander ancestry.

University of Hawai‘i at Mānoa John A. Burns School of Medicine (UHM JABSOM) Overall Description

The John A. Burns School of Medicine (JABSOM) was completed at the end of 2005 and include a Medical Education Building (MEB) (left side of photo), a modern vivarium as well as a Biosciences Building (BSB) with reconfigurable lab space (right side of photo).

The BSB has 213,000 gross square feet of space, including 184,142 square feet of state-of-the-art wet laboratories and gross anatomy facilities. The facility houses researchers from JABSOM. It consists of laboratories, laboratory-support functions (including BSL-3 suites for animals and microbes), offices and conference areas for researchers, and a vivarium for small laboratory animals.

The adjacent MEB is approximately 114,546 square feet and houses the Dean and his administrative support staff, the Fiscal Office, and the Human Resources Office. The MEB also features a clinical skills center, access-grid 3D room, patient simulators, and a 150-seat auditorium. Housed on the second floor of the MEB is the access-grid 3D conference facility that is capable of high definition, 3-dimensional imaging simulations and is capable of connecting to Internet2 for high bandwidth communication and supports virtual reality simulations using virtual reality software developed at JABSOM. While high-end video-conferencing resources are available, lower end videoconferencing tools are also available through desktop iChat and Zoom.

Located in the BSB on the 2nd floor, the Pre-Award Office in the Office of the Associate Dean for Research provides pre-award assistance. Services provided include researching funding opportunity announcements and sponsor requirements; assisting with the preparation of biosketches, budget and associated justification, proposal development, submission, and approval through the UH myGRANT electronic submission system; and assistance with electronic submission through sponsor portals such as NIH ASSIST, Grants.gov Workspace, and others. JABSOM Fiscal and Human Resources, located on the 4th floor of the adjacent MEB building, provides post-award support for all JABSOM investigators.

The JABSOM campus routinely finds itself among the top five in surveys of the "most beautiful medical schools" in America. JABSOM's $150 million complex is located on 9.9 acres at the center of the Kakaako Waterfront. The Medical Education Building features modern classrooms, a clinical skills center, and a human patient simulator facility.

LIBRARIES

UHM faculty, staff and students have access to the Health Sciences Library at JABSOM. Emphasis is on Web-accessible materials. Collections include a wide variety of print and electronic resources, primarily in the clinical sciences. The electronic collection is greatly enhanced by cooperative purchasing arrangements with University of Hawai'i's Hamilton Library and with the Medical Libraries Consortium of Hawai'i. Services include Reference assistance for all, including the following: telephone service, assistance with literature searches, help and advice with in-depth inquiries, assistance with interlibrary loan requests and document delivery, as well as individual and classroom instruction in the use of library resources.

UHM faculty, staff and students have access to the UH Mānoa Library. The library has a staff of 45 FTE library faculty, 2 part-time library faculty and 31 other professional support staff, 31 FTE support staff, and 175 student assistants. The collections contain more than 3.4 million volumes, 2.3 million microfilm units, about 5,000 computer files, 15,000 linear feet of manuscripts and archives, more than 73,000 audiovisual items, and nearly 95,000 maps and aerial photographs. Approximately 70,000 serial and journal titles are currently received in paper and/or electronic formats. The library manages its primary business operations using the Ex Libris Voyager integrated library system and are fully searchable online.

COMPUTER RESOURCES

JABSOM has computer systems and software with both wired and wireless network access, e-mail, and high-speed Internet capability. All faculty and staff have desktop and lap top computers. The computer systems support video teleconferencing, and an extensive on-line library through the Health Sciences Library on the JABSOM campus. Computer labs are available in the Medical Education Building at JABSOM, and are linked to the simulation lab and the Access Grid Room. The Access Grid Room has high definition 3-dimensional imaging simulations, virtual reality simulations and high bandwidth Internet2 communication. A Polycom two-way interactive video system, telephone land lines, and Integrated Services Digital Network (ISDN) are available for teleconferencing.

INFORMATION TECHNOLOGY AND TELECOMMUNICATIONS RESOURCES

UH's new $41 million Information Technology Center in the Mānoa campus provides state-of-the-art information technology services to advance research and innovation. The Information Technology Center is a 4-floor structure with a floor area of 70,000 square feet. The Center accommodates the UH's main data center, system-wide data infrastructure, public information technology services, and houses a divisible emergency operations center ("war room") and the university's main data center.

ANIMAL HOUSING AND CARE RESOURCES

The JABSOM Vivarium, operated by the Animal Veterinary Services (AVS), is accredited by the Association of Assessment and Accreditation of Laboratory Animal Care (AAALAC) and operates according to the PHS NIH Office of Laboratory Animal Welfare (OLAW), US Department of Agriculture (USDA), and Animal and Plant

Health Inspection Service (APHIS) guidelines. The AVS employs 14 animal care staff, a staff veterinarian and two veterinarian technicians who provide daily care. Two fiscal staff and three students also support the AVS business office. The Vivarium consists of 18,119 square feet and supports the majority of animal-model studies conducted by investigators from JABSOM, the UH Cancer Center, and local biotechnology firms. It has a holding capacity of 6,111 cages, has 12 animal holding rooms, six procedure rooms including an Animal Biosafety Level 3 (ABSL3) suite, and a sound isolation room for neuro-behavioral and electrophysiological animal testing. There are also necropsy, diagnostic lab, pharmacy, and various storage rooms. The facility uses a building automated system (Edstrom Watchdog®) that controls and monitors temperature, humidity, air-differential pressures, and security. It is also equipped with a state-of-the-art cage wash facility, including a pass-through rack washer, tunnel washer, and autoclave for racks and equipment, an alkaline hydrolysis digester, reverse-osmosis water, and a vacuum bedding supply and disposal system.

The Mānoa Vivarium on the main Mānoa campus is housed in the Biosciences Building and has 8 active animal holding rooms, 4 procedure rooms, a behavioral room, rodent surgery suite, cage wash, and a secured service elevator.

Mice, and a few rats, are the predominant species used at both vivaria, and occasional rabbits at the Mānoa vivarium. Techniplast ® individually ventilated cages (IVCs) are used at both vivaria. Cages are opened under animal transfer stations or Biosafety Cabinets, if the latter is required for containment. Personal protective equipment (PPE) is required to enter the vivaria (shoe covers, laboratory coat). Additional PPE is required to work with sterile or potential chemical or biological hazards in animals. The temperature is set at 72 degrees +/- 2 degrees F, while humidity is set between 30-70% +/- 10%. The Mānoa vivarium's environmental conditions are monitored by a building automated system with remote alarm. At the room level, hygrometers are used to measure temperature and humidity, and mechanical light timers to control light-dark cycles. Cages and accessories are sanitized at 180 degrees F; these are autoclaved when sterile housing or decontamination is required. Autoclavable bedding and irradiated chow is used. Reverse osmosis-derived drinking water (JABSOM vivarium) and municipal drinking water (Mānoa vivarium) are provided to the rodents via water bottles. Chlorine dioxide is used as a disinfectant at both facilities. The Mānoa vivarium's rack washer has dual use capabilities as a chlorine dioxide gas decontamination chamber. Environmental monitoring is performed quarterly and as needed at both vivaria to ensure proper disinfection of cages and accessories.

Animals are sourced from commercial vendors, in-house breeding programs, and other institutions. Sentinel testing is done on a quarterly basis at both sites. The rats and mice in the vivaria are specific pathogen free. Mice from non-commercial sources (outside institutions) must come from institutions with equivalent or higher microbiological status and husbandry practices. All imports from non-commercial sources are quarantined for a minimum of 2-3 weeks. Rodents are tested for specific viral agents via PCR testing while in quarantine. In addition, fecal samples are taken from quarantined animals one week after arrival and are tested using fecal PCR, skin scrape, or fecal float/tape. Results are verified to be negative before animals are released into the vivaria.

CORES AT JABSOM

Bioinformatics Core: The Bioinformatics Core is housed in about 800 square feet of office space in the BSB at JABSOM and the Director is Dr. Youping Deng. The Bioinformatics component has internet-connected desktop PC's running Windows and/or Linux, with access to tresearch computer servers described below. The computers are equipped with proprietary and open source software packages, such as GeneSpring, Partek Genomics Suite and Ingenuity Pathway analysis software, MatLab, SAS, PASS, R, PLINK, and MPlus, for high-throughput data analysis. Array Studio and many open source software tools for microarray, DNA-Seq, RNA-Seq, and CHiP-Seq data analyses are available on the research server. Data storage and exchange is carried out through dedicated Illumina MySpace, MySQL, Oracle, and FTP servers. The SR has 2 high-performance computer servers, each having 28 cores, 256 GB RAM, and 300TB hard drive disk to handle the large volume of data.

Major Equipment: Two high-performance computer servers with 28 cores, 256 GB RAM, and 120 TB hard drive disk are available for use by the Bioinformatics Core: (1) the Cloud Computing for Cancer Research (3CR) Scientific Computing Cluster; and (2) the Cray CS300 Supercomputer consisting of 178 standard compute nodes and six large memory nodes at the UH Information Technology Center.

The Bioinformatics Core serves as a centralized resource for providing expert and timely bioinformatics consulting, analysis, collaborative research, management, and training solutions for high-throughput data. With the advancement of high throughput technologies, biological experiments now generate immense amounts of data, ranging from genomic sequences to gene expression profiles to protein structures, and require sophisticated data mining tools, database systems and well-trained bioinformaticians to manage and analyze the data. The data include different types of "omics" data (e.g., genomics, transcriptomics, epigenomes, proteomics, metabolomics, metagenomics data), which are generated from a variety of platforms such as polymerase chain reaction (PCR), microarray, next generation sequencing (NGS), mass-spectrometers, etc. The facility features high-level expertise in bioinformatics ensuring the support needed to design, conduct, analyze, interpret, and manage results requiring or facilitated by informatics applications. Bioinformatics support will be integrated into all phases of basic biomedical, clinical and translational research through a coordinated program of quantitative health sciences consultation and analysis. Analyst will provide bioinformatics support to include data management, information-technology support, data analyses, interpretative support, and related education and training to DRC supported faculty.

Biorepository Core: The University of Hawai'i Biorepository is a non-commercial, NIH-sponsored, core facility that provides biomedical researchers restricted access to human biological samples and clinical data. The Biorepository has three major resources: Human Reproductive Biospecimen Repository, Comprehensive Human Organ and Tissue Bank, and an *in vivo* Model Resource. The ability to move research into human tissues increases the direct human relevance and applicability of that research. The Biorepository core is the only fully inclusive human tissue biorepository in the State of Hawai'i, providing a wide range of fresh-frozen human tissues or subcellular tissue fractions. The tissue and extracts in the Core are derived from our unique population of Hawaiian/part-Hawaiian, Pacific Islander, Japanese, Chinese, Filipino, Korean, Vietnamese, Hispanic, Caucasian and African-Americans. This core is able to collect comparatively large numbers of samples from minority donors that allow for appropriate powering of studies in minority health.

Biostatistics Core: The Biostatistics Core is located on the 4th floor of the JABSOM medical education building. All offices are equipped with teleconference capabilities and multi-line speakerphones. The facility also has a conference room, office space, and storage space in the building. The core provides comprehensive research design, data management and analysis collaborations and services to biomedical, clinical and translational researchers at UH and its affiliated institutes. It currently has five Ph.D.-level biostatisticians, two M.S.-level data analysts, and one clinical database programmer. The faculty and staff have extensive experience with large database analysis, epidemiologic studies, bench science and clinical research, clinical trials, and community-based investigations. The technical staff has experience in database design, data management, database programming, and web application development.

The Biostatistics Core is led by John J. Chen, PhD, Professor of Biostatistics in the Department of Quantitative Health Sciences. Dr. Chen has expertise in healthcare data analytics, longitudinal data analysis, clinical trial methodology, and statistical genetics. He has broad biostatistical collaborative research and mentoring experience, and brings extensive leadership experience in biostatistical resources development and management. He oversees faculty and staff with expertise and extensive experience with large database analysis, epidemiologic studies, bench science and clinical research, clinical trials, and community-based investigations. The technical staff has experience in database design, data management, database programming, web application development, structured query language (SQL) and REDCap databases.

All faculty and staff are equipped with desktop workstations which operate in a Windows environment PC-based LAN. There is a single 96 GB memory running Ubuntu Linux. All workstations are connected to the JABSOM secure network that is protected with firewalls. All computers are equipped with various statistical software packages (e.g., SAS, SPSS, R) and other specialty packages for study design (e.g., PASS), database design (e.g., ACCESS, REDCap, SQL Server), web development, geographic information system (GIS), and missing data analysis (SUDAAN). UH JABSOM holds site licenses for EXCEL, ACCESS, SAS, SPSS, SQL Server, Matlab, Maple, Mathematica, LaTex, CLC Genomic Workbench, and CLC Drug Discovery Workbench. Each workstation is equipped with a laser printer and has access to high capacity network printer and scanner and network color printers.

Major Equipment: The facility has four high-performance computing servers. There are two HP Z840

workstations each with Intel Xeon 14 core processors and 256 GB of RAM, and a ThinkStation with Intel Xeon 4 core processors and 8 GB of RAM. These are clustered together to form the Facility's Beowulf cluster to support high performance computing needs. The computing servers run Ubuntu Linux and open source software, and are predominantly used for bioinformatics data analysis.

UH provides a secure file drop service that allows for transfer of large files (up to 800MB) between the UH systems and academic centers outside of the UH system. Both uploading and downloading in this system is secure – files are encrypted using "SSL" for transfer over the Internet. For users exchanging files containing sensitive information, an additional level of protection is provided to ensure secure transfer of files.

Genomics and Bioinformatics Shared Resource (GBSR): The GBSR is co-directed by two faculty with complementing expertise, Dr. Maarit Tiirikainen (UH Cancer Center) and Dr. Youping Deng (JABSOM). Dr. Tiirikainen, who has over 25 years of experience in Cancer Genomics leads the Genomics Laboratory. Dr. Deng, with over 20 years of experience in bioinformatics data analysis, leads the Bioinformatics component of GBSR. The facility occupies 1,300 square feet laboratory space in four separate laboratory spaces and office space for the co-director and a cubicle area for staff members. The laboratory rooms are split into pre- and post-amplification rooms to avoid PCR contamination. In addition, one room is dedicated for RNA work. The genomics shared resource laboratory (1400 sq. ft.) offers cutting edge, high-throughput genomic technologies. Services include DNA/RNA isolation and quantitative/quality analysis, custom genotyping, coding and non-coding gene expression analysis, methylation analysis, DNA copy number analysis and gene mutation analysis. Genotyping platforms include the TaqMan OpenArray system, the Affymetrix GeneChip system, and the Illumina iScan or NextSeq 500 system. Whole genome and individual gene expression profiling is offered on the Affymetrix, the Illumina NGS or by real-time PCR including digital PCR, respectively. Methylation analysis is offered on the Illumina systems or by real-time PCR or pyrosequencing. The Bioinformatics team provides expert and timely consulting, analysis, collaborative research, data management, and training services.

Major Instruments: 11 ABI 9700 PCR thermocyclers, 2 ABI Veriti Gradient PCR thermocyclers, ABI 7900 HT Fast Real-Time PCR System, ABI QuantStudio 12K Flex Real-Time PCR System, Qiagen Rapidplate 96 liquid handler, Plate Replicator TomTec Quadra 384, SpectraMax GEMINI XPS microplate reader, Affymetrix GeneChip Instrumentation (w.TG Plus Scanner), Illumina iScan System, Illumina NextSeq 500 NGS System, Illumina iSeq 100 NGS System, two NanoDrop ND-1000/2000 Spectrophotometers, Qubit Fluorophotometer, Agilent 2100 Bioanalyzer, PyroMark Q24 Sequencer, Savant ISS110 SpeedVac Concentrator.

High Biocontainment BSL3 Core: The Pacific Center for Emerging Infectious Diseases Research provides an ABSL-3/BSL-3 Biocontainment Core. Research on microbial agents, which cause lethal diseases in humans and for which effective drugs or preventive vaccines are not available, must be conducted by well-trained investigators in specially built, well-maintained laboratories. The BSL-3/ABSL-3 Biocontainment Core provides the triad of customized service, research and development, and education and training to investigators at the university and the wider research community. The Core assists faculty working with Category A, B and C agents. Core personnel develop pathogen-specific standard operating procedures, provide routine maintenance of A/BSL-3 equipment, develop and conduct project-specific assays (e.g., production of virus stocks, virus titrations, plaque-reduction neutralization tests), animal inoculation and collection of biological fluids and tissues in a manner that complies with State and Federal regulations. Core personnel also assist in obtaining State and Federal permits for importing infectious agents, and in shipping infectious agents to national and international collaborators. Finally, the Core develops training modules and develops improved methods for working with A/BSL-3 and A/BSL-2 agents.

Equipment: The facility is fully equipped to support 'containment research' which involves working safely with infected samples, ensuring no release of infective agents outside the laboratory. Dedicated suites for working with level 3 viruses in the BSL3 laboratory have HEPA-filtered Class II biological safety cabinets (BSCs); CO2 incubators; freezers; standard and inverted microscopes; and centrifuges. HEPA-filtered Class II biological safety cabinets provide outstanding functionality and safety, protecting both the users and the environment. All work with infectious materials is conducted within the BSCs, which are then routinely decontaminated.

Histopathology Core: The Histopathology Core at JABSOM, located on the second floor of the Biosciences Building in room 206B, is supported by the Ola HAWAII grant (U54MD007601), and is led by Associate Dean for

Research Mariana Gerschenson. It provides routine histology processing, specialized histochemical and immunohistological techniques. The core also provides technical assistance, training, and consultation in histological techniques to investigators, students and staff throughout the University on a cost-recovery basis.

Major Equipment: Zeiss LSM 5 Pascal with inverted microscope, Z-Drive, Scan Module, Laser Module, electronic control and controlling computer; Fluorescent microscope with digital imaging system, Zeiss Axioskop 2 Plus; Inverted microscope, Zeiss Axiovert 25-C; Axioscope microscope for dual viewing; Stereomicroscope, Leica MZ16; Tissue embedding center/histoembedder, Leica EG1160; Sliding microtome, Leica, SM2000R; Microtome, Leica RM2135.

Metabolic and Analytic Core: The Metabolic and Analytic Core provides *in-vitro* to *in-vivo* metabolic studies including design, development, optimization and delivery. This core can provide murine echocardiography, blood pressure determinations, surgical procedures and phlebotomy, as well as assistance with mouse husbandry and genotyping. The core has rodent metabolic cages (Panlab OxyletPro Physiocage modular system) and a DSI small animal telemetry system. The core also provides mitochondrial expertise in measuring oximetry using Seahorse Xfe96. Additionally, the core will support the Research Project Leaders for Biostatistics, Bioinformatics, Genomics, Analytical Biochemistry, and Histopathology core usage. This core is led by Dr. Olivier Le Saux, Department of Cell and Molecular Biology and Dr. Noemi Polgar, Department of Anatomy, Biochemistry and Physiology.

Microscopy-Imaging Core: The Microscopy and Imaging Core, supported by JABSOM, offers access to a wide variety of conventional and confocal microscopes, in addition to optical preclinical imaging instrumentation. The staff provides technical assistance, training, and consultation to users of all levels of experience. The core's instrumentation is located in the JABSOM Biosciences Building. It is available for use by investigators throughout the University on a cost-recovery basis.

Major Instrumentation: Leica SP8 confocal microscope, Zeiss Axioskop II Plus with stereology capabilities, Olympus IX81 DSU spinning disk, Olympus IX71 fluorescent microscope, Zeiss Axioimager, Zeiss LSM 5 Pascal confocal microscope, and a Li-Cor Odyssey infrared Imaging System. All are all equipped with attached CCD cameras and desktop computers.

Molecular and Cellular Immunology: The Pacific Center for Emerging Infectious Diseases Research provides a Molecular and Cellular Immunology Core that provides the sole resource for flow cytometry, cell sorting and state-of-the-art immunological services in Hawai‘i. Emphasis has also been applied to developing new or customized immunological methods for core users. In addition, regularly scheduled training sessions are held to enrich the educational and mentoring experience for investigators, faculty and students across the university and broader research community.

Equipment: FACSaria machine for flow cytometry and cell sorting; CellQuest Pro and FlowJo software for analyses. There is also a BD Accuri C6 flow cytometer (CC rm. 132) with 2-laser-4-color analyser, 488 nm and 640 nm laser lines that can accommodate tubes or welled plates. Finally, there is a BD LSR Fortessa flow cytometer (BSB rm. 330) with 4-laser-12-color analyser, 405, 488, 561, and 640 nm laser lines that accommodates tubes or 96 well plates.

Murine Behavioral and Metabolic Research Support Facility: The Behavioral component of this facility provides expertise and equipment for evaluation of learning and memory, emotion and stress-related behaviors in mice, via two multi-purpose modular behavior assessment systems consisting of 9 behavioral assessment paradigms each. The Metabolic components includes four metabolic cage systems for monitoring respiratory metabolism and energy expenditure in animal models of diabetes, metabolic syndrome and other conditions that alter metabolism. Multiple murine temperature probes are available for implantation and use in conjunction with the metabolic cages or separately.

Equipment: The Murine Behavioral facility has a sound isolation room for behavioral testing, and is equipped with a TSE multi conditioning system, a Rotarod, a startle response meter, various mazes, and videotracking equipment/software.

Murine Cardiovascular Phenotyping Core: The Center for Cardiovascular Research provides a Murine Cardiovascular Phenotyping Core for the use of investigators at the University, and by special arrangement, for investigators anywhere in Hawai‘i. This core can provide murine echocardiography, blood pressure determinations, surgical procedures and phlebotomy, as well as assistance with mouse husbandry and genotyping.

Equipment: The Core uses a special procedure room in the vivarium equipped with down-draft tables that produce appropriate ventilation for anesthetic agents. The procedure room contains a surgical dissecting microscope, rodent ventilator, warming apparatus, and oxygen supply.

MRI Core: The Magnetic Resonance Imaging (MRI) Research Center is located at The Queen's Medical Center. Housed there is a 3 Tesla MRI Scanner that is dedicated to basic and clinical research. The MRI Core operates through The Queen's MRI Research Center to provide technical support and training for clinical investigators, in particular those at the junior level, and allow support of pilot studies and studies with new technical approaches to investigate diseases that disproportionately impact minority populations as health disparities. This core is supported by JABSOM.

Transgenics Core: The Transgenic and Embryonic Stem Cell Gene Targeting Core is a state-of-the-art facility with the expertise in the production of genetically altered subjects. Transgenic subjects carrying new or novel genes are created by microinjection of DNA into the pronuclei of fertilized eggs. In this core, highly experienced personnel produce transgenic and knock-out subjects for UH investigators at a very reasonable cost and with very short lead times. The basic services of the Transgenic Core facility are DNA injection, embryonic stem cell injection, and embryo freezing. In addition to these services, the Transgenic Core Facility offers various techniques to the research community including embryo culture, embryo transfer, embryo micromanipulation, mouse in vitro fertilization, and mouse cloning services.

CORES AND RESOURCES AT THE CANCER CENTER

The **University of Hawai‘i Cancer Center** (UHCC), directed by Dr. Naoto Ueno, is the only National Cancer Institute-designated Cancer Center west of California. It serves Hawai‘i and the Pacific through cancer research, education, patient care and community outreach. The building opened in 2012 and provides state-of-the-art office and laboratory facilities strategically located on a 9,898-acre campus that is shared with JABSOM to promote cooperation and synergistic research. The UHCC building has two wings, one dedicated to administration and "dry Lab" offices and a research wing with bench laboratory space; these are connected by a shared elevator and open gathering space. The facility also includes the Sullivan Conference Center on the ground floor. This conference center is used for a variety of functions including seminars, presentations, training sessions, video conferencing, and community events. A 36,000 ft^2 connected expansion annex is available for further development. UHCC maintains freezer farm space (2,925 ft^2 total) on the UH Mānoa campus. All core facilities and shared resources are within easy access of all UHCC faculty. UHCC directly employs approximately 314+ faculty and staff. UHCC supports two research programs, five Shared Resources, and multiple core facilities.

Analytical Biochemistry Shared Resource (ABSR): The ABSR, led by Dr. Adrian Franke, facilitates collaborative cancer research in molecular epidemiology, nutrition, food chemistry, carcinogenesis, and other areas of interest at the Center. The mission of this laboratory continues to be the cost-effective provision of accurate chemical analyses, and provides a base for consultation related to the quantitation of molecules relevant to research interests of Center investigators. The facility occupies approximately 1,000 ft^2 of space on the fourth floor of the UHCC at 701 Ilalo Street. The laboratory is equipped with all basic analytical chemistry instruments in addition to modern, state-of-the-art equipment required for analytical chemistry and handling of biologically and chemically

hazardous materials. Assays established by the ABSR for services include those for micronutrients (carotenoids, vitamins, and others), specific phytochemicals (caffeine and its metabolites, and a wide variety of flavonoids, isoflavonoids, phospholipids, choline analogues, and a wide array of polyphenols), steroids particularly estrogens including their metabolites, an array of phthalates and bisphenol-A, and many other metabolites and small molecules that can be measured using HPLC with photodiode array and mass spectrometry. Various clinically relevant analytes (HDL- and LDL-cholesterol, triglycerides, homocysteine, creatinine, total nitrogen, C-reactive protein, and others) can also be analyzed. Finally, the ABSR can also perform ELISA based assays including those for the detection and measurement of interleukins, adiponectin, 25-hydroxy-vitamin D, and many others using a Versamax tunable microplate reader with Softmax Pro analysis software (Molecular Devices Corp., Sunnyvale, CA). A HTS 7000 Plus Bioassay Reader for fluorescence and absorbance measurements is available as shared equipment at UHCC (Perkin Elmer, Waltham, MA). Multiplex immunoassays can be performed using the newly acquired Luminex 200 instrument (Luminex Corp., Austin, TX) in the ABSR lab. All measurements can be carried out in a variety of matrices including body fluids, tissues, and foods. A full list of available services is continuously updated online.

Resources and Instrumentation:

- 3 fully automated liquid chromatography mass spectrometry (LC/MS) systems including 2 orbitrap (model Q-Exactive, Thermo, Woburn, MA) and 1 triple quadrupole instrument (model TSQ Ultra, Thermo) with the following sources: electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), atmospheric pressure photo ionization (APPI) or direct analysis in real time (DART; model SVP-1000, IonSense, Saugus.MA), all allowing positive and negative ion monitoring. LC models are all Accela (Thermo)
- 3 fully automated high pressure liquid chromatography (HPLC) systems (model Surveyor, Thermo) and 2 ultra high pressure liquid chromatography systems (UHPLC; model Accela, Thermo, attached to the mass spectrometers above), all with quaternary pumps that can all be connected to above MS systems or/and to one of 5 available photo-diode array (PDA) detectors or to fluorescence (FL; model FD100, GTI/SpectroVision, Concord, MA) or electrochemical detectors (Coulochem III with 5021 dual cell or Coularray with 8 cells, ESA, Chelmsford, MA) devices
- 1 Macular Pigment Optical Density (MPOD) reader based on heterochromatic flicker spectrophotometry (Macular Metrix II, Macular Metrics, Rehoboth, MA**)**
- 2 nitrogen generators (Peak Scientific, Billerica, MA)
- 1 post column derivatization system (Timberline Co., Boulder, CO)
- For routine ELISA assays: 2 model 'VersaMax' microplate reader with 'Analyst AD' capabilities for UV/fluorescence readings (Molecular Devices, Sunnyvale, CA) and one Luminex200 instrument (Luminex Corpor., Austin, TX) for multiplexing immunoassays
- 1 spectrophotometer (model BioSpec160I, Shimadzu Co., Columbia, MD)
- 2 clinical autoanalyzers (Roche Cobas Mira Plus CC, Roche Diagnostics Inc., Indianapolis, IN)
- 1 liquid handling robot (model Versa 100, Aurorabiomed, Vancouver, BC)
- 2 rotating evaporators (Büchi, Switzerland)
- 2 centrifuges (IEC Co., Vermont Hill, IL),
- 2 8°C refrigerators
- 1 -4°C freezer
- 1 -20°C freezer

Other equipment include: a solid-phase extraction system, nitrogen gas evaporation system, rotary evaporation system, and a complete Millipore water filter system with ion exchange columns (all from Waters, Milford, MA). Additional shared equipment includes a Beckman L2-65B and a L8-70M ultracentrifuges (SW55 Ti, SW27, 70 Ti, SW41 rotors), Sorvall OTD-50 ultracentrifuge (TV865 rotor), a lyophilizer (Labconco), a Beckman LS 7500 and LS100 liquid scintillation counters, a Beckman Gamma 5500B counter, a model AS 160 speed-vac (Savant, Farmingdale, NY) for evaporation of small multiple samples, five ultra-low temperature freezers (Forma Scientific Co., Queue Systems, Revco Scientific Co., Asheville, NC), a Coulter automatic cell counter, a fluorometer (Perkin-Elmer Co., Cupertino, CA), and several sterilizers including a high pressure vapor sterilizer.

Computer: The following software packages are available: SAS and Epicure statistical packages; MATLAB computing environment and programming language, Visual Studio .Net 2005, Microsoft Office 2010, Paradox, Visual Foxpro, MS Access, and SQL Server 2005 Express database packages. We also have access to multiple

applications for processing genomic data, including Ingenuity, Panther, and CHRCXpress, a web-based data analysis application that was developed in-house.

Chemical Biology Developing Shared Resource (ChemBC): Part of the mission of UHCC is to make scientific discoveries that have significant impact on cancer incidence and mortality in Hawai'i and the larger Pacific. An important component of this goal is to utilize local natural products from the endemic species as chemical probes to study cancer molecular pathways, with the potential for clinical translation. Key to successful chemical biology research is a strong technical infrastructure that allows cutting-edge studies into the underlying cellular, molecular and structural processes and events that are fundamental to the cancer phenotype. The ChemBC provides the infrastructure and capabilities to support structural and chemical biology studies in addition to development of chemical probes and drug leads.

ChemBC services leverage four key resources: a 600 MHz NMR Facility (NMR), a Screening Core Facility (SCF), Natural product Library (NPL), and a Tumor Cell Collection. These resources are integrated into a single operation due to their value in chemical probe development and chemical biology activities. The NPL serves as a source of chemical lead, the SCF is the platform for screening and discovery of probe hits that can then be tested against specific tumor cells from the Tumor Cell Collection. Finally, NMR determines the molecular structure of the new NPL-derived compounds. This fundamental chemical probe discovery pipeline is key to the operations and success of the ChemBC.

Equipment and Resources:
Nuclear Magnetic Resonance (NMR) Facility: To facilitate its basic science and chemical probe discoveries, UHCC has acquired a new 600 MHz NMR instrument. In 2017, the UHCC installed this NMR in the adjacent JABSOM Ancillary Building. This instrument complements, without duplication, the lower-field NMR units that are currently housed in the Mānoa Campus Chemistry Department for structure determination of novel biologically active compounds at sub-milligram levels. The advantage of the higher power 600 MHz instrument is its ability to conduct NMR structural studies of proteins and of small molecule-protein interaction analysis that otherwise could not be achieved with the existing units. As members make discoveries of new chemical "hits" that modulate their respective cancer targets or pathways, studies with the NMR instrumentation will elucidate the possible interactions of the lead compounds with the protein targets for important structural insights that would advance the development of the compounds, while advancing mechanistic understanding relevant to the target of focus. Note that the NMR Facility of the ChemBSR shared resource may also be used by investigators to identify unknown metabolites and determine their structural properties.

Screening Core Facility (SCF): UHCC has an operational SCF, physically located in a 1,500 ft^2 room in the UHCC building. The SCF houses two Beckman Coulter NX^P robotic liquid handlers and a PerkinElmer Envision Multi-label Reader. These instruments allow the medium-to-high throughput screening of chemical libraries, including the UHCC natural product library, for the discovery of chemical "hits". The hits provide leads for medicinal chemistry and structural optimization that can be developed into chemical probes for biological and molecular studies, and as suitable drug candidates.

Natural Product Library (NPL): Currently, the NPL contains 5,500 samples - extracts, fractions, semi-pure fractions, and pure compounds (5,000 fungi/soil bacteria, 200 plant, and 416 marine samples). The natural product library is the result of the research activities of the ChemBC members and natural product chemists: Drs. Shugeng Cao (endophytic fungi/soil bacteria), Leng Chee Chang (terrestrial plants), and Philip Williams (marine organisms). ChemBC activities and the studies that utilize the chemical probes discovered from the screening of NPL provide opportunities for intra-programmatic and inter-institutional collaborations. Presently, this library is continually being screened against targets, including: p53 (PI: Fei), RSK (PI: Ramos), and used for vascular permeability (PI: Matter) and cell viability assays (PIs: Cao, Williams and Chang). Some of the lead compounds identified include withanolides, xanthones, and hirsutinolides (from plants), and puupehenol (from marine sources). The library is physically located in the SCF.

Tumor Cell Collection: The ChemBC also keeps a repository of the entire set of NCI-60 cell lines and 20+ additional validated cancer cell lines, which are made freely available to UHCC members for their research activities, including important biological and mechanistic studies of chemical probes. By making the lines available, investigators have the resource and the opportunity to validate their respective biological observations

across different models as appropriate. Maintaining this tumor cell collection is especially important in Hawai'i because State import controls often take time, leading to delays in obtaining cell lines from NCI, ATCC and other vendors.

The developing ChemBC will promote natural product and small molecule discovery and structural characterization, permit the identification of chemical and molecular leads, and facilitate the studies of protein and other macromolecular structures and protein:ligand interactions at the molecular and atomic levels.

Metabolomics Shared Resource (MeSR): Metabolomics technology provides a unique measure of the global, dynamic response of living organisms to biological stimuli. Using mass spectrometry coupled to chromatographic separations including gas chromatography (GC) and liquid chromatography (LC), high detection sensitivity can be achieved for a broad range of metabolites. This powerful technique provides a chemical snapshot of specific cellular processes that proteomic and RNA expression do not provide.

MSR services offered include metabolite extraction from samples including serum, plasma, urine, and tumor tissues, metabolomic profiling of human or animal samples, metabolomics data processing, analysis and interpretation. These MS systems are operated with most updated software for data acquisition and processing along with suites of both commercial and self-developed software and libraries for multivariate statistical analyses, data reduction, pattern recognition and compound and pathway annotation. MSR typically uses both LC-MS and GC-MS platforms to analyze each sample, broadening the window of metabolite profiling. By utilizing the LC-MS and GC-MS in combination, the major shortcoming of GC-MS (chemical derivatization as an essential prerequisite prior to analysis) becomes an advantage because various chemical derivatization approaches can act as a silencer or an activator for detection of specific groups of metabolites, thus facilitating good variable differentiation in data analysis, interpretation and characterization. Metabolomics SR is located at the UHCC Building, 701 Ilalo Street, Honolulu, occupying ~1,000 ft^2 of laboratory space. The lab space is dedicated to biological sample treatment, mass spectrometry analysis, data processing and analysis and molecular biology for cancer metabolism, metabolomics, drug metabolism, pharmacokinetic, and other bioanalytical studies.

Equipment: The Metabolomics Shared Resource (MSR) Lab at the UHCC, directed by Dr. Wei Jia, is equipped with three new state-of-art mass spectrometry systems:

- Agilent 7890A Gas Chromatography coupled with LECO's Pegasus HT time-of-flight Mass Spectrometry (GC-TOF-MS).
- Waters Aquity I-Class Ultra-performance Liquid Chromatography coupled with Xevo G2-S time-of-flight Mass Spectrometry (UPLC-QTOF-MS).
- Waters Aquity I-Class Ultra-performance Liquid Chromatography coupled with Xevo TQ-S Mass Spectrometry (UPLC-TQ-MS).

The Metabolomics Shared Resource also has the following: BulletBlender Blue tissue homogenizer; Beckman Biosafe Ultracentrifuge System, CenrtiVap Benchtop Centrifugal Concentrators, Millipore Water Purfication System, three Thermo Fisher -80° Ultra Cold Freezers, two Revco -80° Ultra Cold Freezers, refrigerators, two laminar low hoods, two incubators, 2 tissue culture hoods, incubators and cell culture centrifuges, pH meter, top-loading balance, microtiter plate reader, thermal cycler and other miscellaneous equipment.

Microscopy and Imaging Core Facility (MICF): The Microscopy and Imaging Core Facility (MICF) was established to fulfill a critical need for UHCC investigators whose research involves the imaging of biological systems from gross anatomical to subcellular levels. The state-of-the-art instrumentation made available by the MICF enables researchers to analyze or process their samples in a wide variety of ways, including high resolution optical sectioning of fixed cells and tissues, time-lapse imaging of living cell cultures, non-invasive monitoring of tumor formation in whole organisms, and extracting specific cells of interest from tissue sample slides or cell suspensions. The MICF also has two flow cytometers, enabling researchers to analyze suspensions of cells for differences in protein expression, gene expression, or cell morphology. This resource offers technical training to users and is responsible for maintaining the equipment through preventative maintenance services, routine calibrations, upgrades, and repairs. It is also the MICF's continuing mission to pursue the acquisition of new instrumentation in accordance with the needs of UHCC researchers.

The majority of the Microscopy and Imaging Core Facility instrumentation is located on the ground floor of UHCC (rooms 132 and 132A) to minimize vibrations. A 230 ft^2 space in room 132A houses the Leica TCS SP5 confocal system, the Molecular Machines & Industry laser capture micro-dissection system, and the Olympus IX81 Time-lapse microscope with environmental controls for live-cell imaging. A 175 ft^2 space in room 132 houses three epifluorescence microscopes and a Becton Dickinson Accuri C6 flow cytometer. Other equipment, such as the IVIS Lumina imaging system for animal studies is located in the Biosciences Building (BSB) room 146, occupying 35 ft^2 of a 225 ft^2 space within the JABSOM Vivarium. Finally, the Becton Dickinson LSR Fortessa flow cytometer is located in room BSB 330, occupying 30 ft^2 of a 650 ft^2 space. Equipment located within UHCC is available 24 hours per day, 7 days per week for trained Cancer Center members. Access to the IVIS Lumina imager or LSR Fortessa flow cytometer initially requires special clearance but is also accessible 24 hours per day, 7 days per week once access is granted.

All major instrumentation and software are available for reservation via the QReserve website or through communication with core personnel.

Major Microscopy and Imaging Instruments:

- Leica TCS SP5 laser scanning confocal system [automated Leica DMI 6000 microscope with 9 excitation lines, high-efficiency SP detection, and an Acousto-Optical Bream Splitter. Objectives include 2.5x/0.07 pl fl, 10x/0.3 hc pl fl, 40x/1.25 oil hcx pl apo cs, 63x/1.4 oil hcx pl apo cs objectives. Laser lines include 50 mW UV Diode (405 nm), 65 mW Ar (458, 476, 488, 496, 514 nm), 1 mW HeNe (543 nm), 2 mW HeNe (594 nm), and 10 mW HeNe (633 nm)];
- MMI Laser capture microdissection system [automated Olympus IX81 microscope with 4xPhL/0.13 uplfln, 10xPh1/0.3 uplfln, 20xPh1/0.45 lucplfln (0-2), 40xPh2/0.6 lucplfln (0-2), and 60xPh2/0.7 (0.1-1.3) objectives, X-Cite series 120PC fluorescence illumination and 3 color filter set, MMI DXA285CF CellCamera with Super HAD technology, solid state 355 nm UV cutting laser with electronic interface for PC control, MMI CellCut Plus for laser cutting capabilities with mini caplift technology, MMI CellEctor Plus capillary based sorting system for cells in suspension];
- Olympus time-lapse system with environmental chamber [automated Olympus IX81 microscope with 4x/0.13 uplfln, 10x/0.3 uplfln, 20xPh1/0.5 uplfln, 40x/0.95 uplsapo (0.11-0.23) and 60x/1.35 oil uplsapo objectives, X-Cite series 120Q fluorescence illumination and 3 color filter set, Hamamatsu Orca-R2 monochrome camera, Tokai Hit WSK2 stage-top incubation system with GM8000 gas mixer for CO_2 and O_2 control, ZDC laser system for continuous auto focusing capabilities during imaging];
- Xenogen IVIS Lumina [fluorescent and bioluminescent in vivo and in vitro imaging, sensitive detection of low emission light, 5 field of view options, 10 excitation filters (410-760 nm) and 7 red emission filters (720–840 nm), XGI anesthesia system]

Epifluorescence Microscopes:

- Olympus IX71 microscope [inverted microscope with 10xPh1/0.3 uplfln, 20xPh1/0.45 lucplfln (0-2), 40xPh2/0.6 lucplfln (0-2), 60x/1.35 oil uplapo objectives, Olympus U-RFL-T fluorescence illumination and 3 color filter set, Q imaging Retiga 2000R CCD monochrome camera];
- Zeiss Axioplan microscope [upright microscope with 10xPh1/0.3 pl nf, 20xPh2/0.5 pl nf (0.17), 40xPh2/0.75 pl nf (0.17), 63x/1.4 oil pl apo (0.17), and 100x/1.3 oil pl nf (0.17) objectives, DIC imaging capabilities for 20x and 40x objectives, HBO 50 mW mercury lamp fluorescence illumination and 3 color filter set, Coolsnap CCD color camera];
- Nikon Diaphot microscope [with 2.5x, 10xPh1/0.25 pl dl, 20xPh2/0.45 pl dl (0-2), 40xPh3DL/0.85 fluor (0.11-0.23) objectives, HBO 50 mW mercury lamp fluorescence illumination and B-2A filter set, Microfire CCD color camera]

Flow Cytometers:

- Becton Dickinson Accuri C6 flow cytometer [2-laser-4-color analyzer (488 and 640 nm laser lines)] with Csampler for autosampling from 48- and 96-well plates.
- Becton Dickinson LSR Fortessa flow cytometer [4-laser-16-color analyzer (405, 488, 561, and 640 nm laser lines] with HTS for high-throughput sampling from 96-well plates.

Imaging and Data Analysis Software:

- Metamorph (for the analysis of microscopy images), FlowJo (for the analysis of flow cytometry data)

Multiethnic Cohort (MEC) Study: The MEC Study is based in the Epidemiology Program at UHCC, with a subcontract to USC. The MEC includes 215,251 men and women aged 45-75 at recruitment, primarily from five different racial-ethnic groups (African Americans, Japanese Americans, Latinos, Native Hawaiians and whites in Hawai'i and California). The cohort was assembled in 1993-1996 by mailing a self-administered, 26-page questionnaire to persons identified primarily through the driver's license files for the state of Hawai'i and the county of Los Angeles in California. The baseline questionnaire collected extensive information on demographics, medical and reproductive histories, cigarette smoking, medication use, including hormonal replacement therapy (HRT), family history of various cancers, physical activity and an extensive quantitative food frequency questionnaire (FFQ). Every five years, brief follow-up questionnaires were mailed to study participants to obtain updated information. A ten-year re-administration of the full baseline questionnaire was completed in 2003-2008; participants were also asked to measure waist and hip circumferences (with a tape measure that was provided). A 25-year follow-up questionnaire is currently being mailed to study participants. Identification of incident cancer cases is by regular linkage with the Hawai'i Tumor Registry (HTR), the Los Angeles County Cancer Surveillance Program (CSP) and the State of California Cancer Registry (CCR), all of which are NCI-funded Surveillance, Epidemiology, and End Results (SEER) registries. Deaths in the cohort are identified by linkage to the state death-certificate files in CA and HI, and with the National Death Index for deaths occurring in other states. Out-migration in the MEC has been shown to be low (3.7% after 7 years of follow-up).

Multiethnic Cohort (MEC) Study Biorepository: Initially, blood and urine specimens were collected from incident cases of breast, prostate and colorectal cancer, together with a cross-section of the cohort (about 6,000 subjects), for nested case-control studies of genetic susceptibility and cancer. Subsequently, this effort was expanded in 2001-2006 to include the prospective collection of biospecimens (blood, urine, and in a small subset, buccal cells) from all members of the MEC in Hawai'i and Los Angeles, respectively, with a short questionnaire on current medication and dietary supplement use. This biorepository now includes samples from ~74,000 subjects, with multiple 0.5 cc aliquots for each subject of serum, plasma, buffy coat and washed RBCs stored in vapor phase of liquid nitrogen (LN2). Aliquots of urine are stored in mechanical freezers at -80ºC. The biorepository participants are broadly representative of all cohort members.

The Specimen Processing Laboratory handles processing, aliquoting and storage of biospecimens. It is equipped with 3 biosafety cabinets, 2 CO_2 incubators, a direct access de-ionized water tap, 3 refrigerated benchtop centrifuges, 2 -80°C (ULT) freezers, 2 liquid nitrogen dewars, 2 PACE cryobiosystems, and a 23 cu. ft. lab grade refrigerator. Specimens are stored in 2 -80°C mechanical freezers equipped with a 24/7 wireless access temperature monitoring system.

Multiethnic Study Computer Resource: A DELL PowerEdge R930 Server with four Intel Xeon E7-8870 processors yielding 72 cores of processing power is dedicated to MEC data management and analysis. This server is configured with 1024GB (1TB) of system RAM and 120TB of disk space with provisions for expansion. The disk storage is arranged as 3 separate RAID6 drive arrays for fault tolerance and the server and storage units have redundant power supplies. This server is running Windows 2012R2 operating system with Hyper-V for virtualization. MS SQL database server is used for data management.

A DELL PowerEdge R715 Server with 2 AMD Opteron processors yielding 64 cores of processing power is available for Remote Desktop access by USC staff for data sharing and system access. This server is configured with 128GB RAM and 2TB storage space. It is running Windows 2012 operating system with Hyper-V for virtualization and a MS SQL database server for data management.

OTHER RESOURCES AND FACILITIES AVAILABLE

Clinical Research Support Facilities

Kaka'ako Facility

The University of Hawai'i Clinic at Kaka'ako, located on the JABSOM and UH Cancer Center campus, is the first multi-purpose combined research and medical care clinic to open on a UH campus. UH Clinic at Kaka'ako is operated by JABSOM, in collaboration with the University Health Partners of Hawai'i, which is the JABSOM faculty practice plan. The UH Clinic occupies 3,550 square feet and includes a waiting/reception room, office, and charting areas, six exam rooms, and two procedure rooms. An additional room accommodates a dual energy

absorptiometry (DXA) machine. The DXA measures bone density (useful in osteoporosis diagnosis and research) and also can measure the amounts of fat and muscle by body region. This resource is likely to be helpful in the study of metabolic diseases, including therapeutic intervention trials in obesity, diabetes, and heart disease, and in fitness studies examining how to build muscle and strength.

The Clinical Research Support Facility's Processing Lab is located on the 2nd floor of the BSB immediately adjacent to the clinic. This allows for rapid transport and immediate specimen processing, which are important for the aims of many translational research studies. The lab has approximately 780 square ft. of space and is equipped with two bio-safety cabinets, three refrigerated centrifuges, a non-refrigerated centrifuge, five liquid nitrogen dewars, a refrigerator; five ultra-low temperature -80º C freezers; and a -20º C freezer. Processing lab capability include processing of blood into plasma, sera, and viably preserved peripheral blood mononuclear cells (PBMC) and processing of spinal fluid, fat, rectal tissue, and lymph node tissue.


University Clinics at Kaka'ako (clockwise from top left): Entry area, Reception/Waiting Area, Exam Room, and Hallway.

The clinic meets all Americans with Disability (ADA) guidelines, such as wide hallways with hand support rails and large restrooms for individuals on wheelchairs, and infection control guidelines, such as hands-free faucet and paper towel dispensers. All exam rooms are equipped with an exam table, desk, two chairs, mounted ophthalmoscope/otoscope, and a small supply cabinet. One exam room is equipped with a power adjustable exam table and focused light feature for pelvic examinations. A second exam room has a separate entry area, and can serve as an isolation room in cases of suspected flu, tuberculosis (TB), or other airborne communicable risks. A storage room contains common clinic supplies, a small refrigerator used to store a small supply of vaccines and injectable antibiotics, and an autoclave for sterilizing small surgical/colposcopy instruments. The charting area is equipped with four computers allowing multiple researchers to simultaneously chart electronically. The Clinical Research and Regulatory Support Core (CRRS) operational team is comprised of four physician-researchers, including Dr. Dominic Chow; a nurse unit coordinator, Debra Ogata-Arakaki, RN with over 30 years of experience in clinical research at NIH and JABSOM; two clinical research nurses each with over 15-20 years of experience in clinical trials and research work; and a lab technician with three years of experience in processing specimens. The nursing team has worked together under Dr. Chow for over 20 years and maintains full capability to conduct clinical research including Phase I to IV clinical trials ranging from multi-site clinical trials to small locally conceived projects. Clinical trials are registered at ClinicalTrials.gov. As appropriate, applications are filed with the Food and Drug Administration (FDA) for Investigational New Drug (IND). The team maintains certifications to meet the regulatory and ethical needs of clinical research. The CRRS offers support for clinical protocol and case report form development, recruitment, screening, enrollment, randomization, patient and protocol management, phlebotomy, various specimen processing and banking, and data collection. The team has managed studies involving procedures in punch-and-open fat biopsies, lumbar punctures, anoscopies, colposcopies, lymph node biopsies, frequently sampled intravenous glucose tolerance test (FSIVGTT), and leukapheresis. 24-hour research physician coverage is available via the Physician's Exchange Service operating throughout the islands of Hawai'i and admitting privileges are maintained at The Queen's Medical Center, Hawai'i's main tertiary medical center.

Kapiolani Medical Center for Women and Children

The Kapiolani Medical Center for Women and Children (KMCWC) is a nationally recognized, not-for-profit hospital, widely known as Hawai'i's leader in the care of women, infants, and children. Specialty services include adult, pediatric, and neonatal intensive care units, maternal-fetal medicine, and the full range of pediatric subspecialties. The KMCWC is an important clinical research site and resource, providing investigators access to the recruitment of women and children in both the outpatient and inpatient settings. Additionally, the site may provide access to patient databases in obstetrics and gynecology populations, and pediatric populations. Research conducted by the KMCWC site spans the lifecycle, from preconception through adulthood. At KMCWC,

outpatient projects are primarily based within the faculty practice of the Department of Obstetrics, Gynecology and Women's Health. The clinical site is 2,944 square feet and includes a waiting/reception room, office and charting areas, three consultation rooms, four exam rooms and two procedure rooms. The clinic meets all Americans with Disability (ADA) guidelines, such as wide hallways with hand support rails and large restrooms for individuals on wheelchairs, and infection control guidelines such as hands-free faucet and paper towel dispensers. All exam rooms are equipped with an exam table, desk, two chairs, mounted ophthalmoscope/otoscope, and a small supply cabinet. Additional exam rooms are equipped with a power-adjustable exam table and focused light feature for pelvic examinations. A storage room contains common clinic supplies, a small refrigerator used to store a small supply of vaccines and injectable antibiotics, and an autoclave for sterilizing small surgical/colposcopy instruments. Every examination, procedure, and consultation room is equipped with computers with access to electronic medical record system (Epic).

The Queen's Medical Center

The Queen's Medical Center (QMC) is affiliated with JABSOM via an affiliation agreement to expand medical education and research, engage the next generation of healthcare professionals and improve the health and well-being of the people of Hawai'i. Research is managed by Todd Seto, MD, MPH, Director of Clinical Affairs and Research at The Queen's Medical Center (QMC) and Associate Professor of Medicine at UH-JABSOM. Dr. Seto is a practicing non-invasive cardiologist based at QMC, where he cares for a large, underserved, predominantly Native Hawaiian and Pacific Islander population. The QMC is a 505-bed tertiary care hospital that is the primary referral center for the State of Hawai'i and the Pacific Basin. Located in downtown Honolulu, 1.5 miles from UH-JABSOM, the QMC is the major referral center for cancer, heart disease, neuroscience, orthopedics, surgery, emergency medicine, and behavioral health, and has the State's only organ transplantation program and Level I trauma center. A major teaching hospital with a mission to improve the well-being of Native Hawaiians and all of the people of Hawai'i, the QMC serves as the primary clinical training site for UH-JABSOM's Internal Medicine, Surgery, Psychiatry, and Pathology residency programs, as well as fellowships in cardiovascular disease, addiction medicine, and surgical critical care. QMC is the flagship hospital for The Queen's Health Systems (QHS), which is the largest private employer in the State, with nearly 5,000 employees and over 1,500 networked physicians that cover four hospitals on three islands and outpatient centers and other sites across the State. As the largest, most comprehensive medical center in the State of Hawai'i, the QMC includes the essential components for success: a diverse patient population that includes people who have been historically under-represented in research studies; a large patient population with a broad range of disease states and pathology; and an institution with a commitment to clinical care, education, and research that recognizes the value of collaboration and partnership.

The UH-JABSOM Clinical Research Center at QMC provides support for both inpatient and outpatient studies. It is staffed by four research nurses and four research associates, under the direction of Dr. Todd Seto. The Clinical Research Center provides UH-JABSOM and other investigators access to research services, including cardiovascular and pulmonary testing, radiologic imaging, monitored units for infusion and Phase 1 studies, office space and exam rooms for outpatient visits, and data analysts who have access to QMC's enterprise data warehouse. Additional resources include the Hamamatsu/Queen's PET Imaging Center and the High-Throughput Screening Laboratory, a research and development joint venture with Hamamatsu Photonics of Japan that is entering its 20th year. Examples of services provided include markers of pre-clinical atherosclerosis (e.g., carotid intima-media thickness, brachial artery reactivity) for HIV patients on highly active antiretroviral therapy (HAART), cardiopulmonary-exercise testing to assess the impact of a physical activity intervention on oxygen consumption, and FibroScan to assess the impact of medical therapy on liver disease progression.

The Regulatory Knowledge and Support Facility

The Regulatory Knowledge and Support Facility provides services for researchers who need assistance in complying with human subject protection policies. It is led by Venkataraman Balaraman, MD, Professor of Pediatrics, and Kari Kim, MPA. Cumulatively, the staff has over 30 years of experience with clinical research in all environments. Dr. Balaraman and Ms. Kim will provide consultations and training in human subject protection, including Institutional Review Board submissions. In addition, the facility offers independent Data Safety Monitoring Board services to support the needs of research projects, an Advisory Board to review research ethics issues and concerns, and educational sessions throughout the year that focuses on research ethics and regulatory knowledge.

IDeA State Funded Resources at the University of Hawai'i i at Mānoa - Active Grants

INBRE IV- Hawai'i Statewide Research and Education Partnership, (P20GM103466)
PI: Robert Alan Nichols, Ph.D.

The Hawai'i Statewide Research and Education Partnership (HiSREP) comprises a network of nearly all of the institutions of higher learning in the state of Hawai'i, specifically 4 primarily undergraduate institutions (PUIs), 1 University of Hawai'i i (UH) college and 4 UH community colleges under the management of the lead R1 institution, the University of Hawai'i at Mānoa. In the previous grant cycle, INBRE III focused on strengthening the research community and infrastructure at the partner institutions outside of the lead institution. This was accomplished through a tightly coordinated leadership team overseeing an integrated program of support for new laboratory construction under Alterations & Renovation funding, acquisition of new instrumentation, funding for junior investigator research and undergraduate student research experiences paired with outreach and multi-level mentoring. This resulted in substantial expansion of the research base, stronger student engagement leading to a near doubling in student participants, and new initiatives in career advancement. In INBRE IV, HiSREP will continue the development of emerging investigators, but will widen the reach of the network to all levels of biomedical research scientists through a new array of competitive granting mechanisms including teaching-postdoctoral fellowships, pilot projects, new initiatives and team-based collaborative grants through a Developmental Research Project Program (DRPP). Research under HiSREP will be guided by two key themes, Natural Products and Molecular Medicine, which emphasize notable strengths in the biomedical research community in Hawai'i. In addition, HiSREP will support a reorganized Bioinformatics Core as a centralized resource across the state to provide education on bioinformatics, aid with research design, technical expertise including development of new informatics tools, data management and analysis. The Bioinformatics Core will promote community synergy for researchers and students through one-on-one, group, workshop, course and online interactions, the latter through a real-time research community portal. The student research program under the PATHway to Biomedical Careers will look to embrace a wider range of undergraduates by emphasizing collaborative group projects through volunteer, intern, scholar and returning researcher opportunities, including partnerships with complementary undergraduate research programs, while maintaining focus on individual career development through skill training, practical mentoring sessions, extended resources and workforce development. In addition, PATHway will develop proactive advanced training for laboratory supervisors to increase research sophistication as well as opportunity statewide, leading to increased capacity. It will also ultimately enhance undergraduate education through incorporation of research activity into the basic science curriculum. Overall, HiSREP will serve as a catalyst for advancement of the research scientist pipeline with the ultimate goal of elevating the ability of the biomedical research community to make new and important discoveries for improving health and well-being in the state of Hawai'i.

IBR-COBRE Phase 3 (P30GM131944)
PI: William S. Ward, Ph.D.

Overall Component Approximately 70,000 babies born in the U.S. in 2015 were conceived by artificial reproductive technologies (ART), which involves one of two techniques: in vitro fertilization (IVF) in which the sperm fertilizes the egg in vitro, or intracytoplasmic sperm injection (ICSI) in which the sperm is injected into the egg using micromanipulation. The rapid rise in ART world wide, and continued developments of the procedures employed by ART clinics, requires that research keeps pace to ensure the safety of ART and to improve reproductive health. Starting with just three faculty in 2000, with COBRE support starting in 2008, the IBR has grown to 14 full-time faculty in four departments, within the John A. Burns School of Medicine (JABSOM), of the University of Hawai'i at Mānoa (UHM). Of these 14, the COBRE Phases I and II supported 10, and all but two have obtained independent NIH R-series funding. The direct result of COBRE funding is that the IBR has emerged as an internationally recognized center of research excellence for reproductive biology and one of the best centers in the world for mouse gamete manipulation (ICSI and IVF). During Phase I, the IBR recruited five new faculty, establishing it as a reproductive biology research institute and attracting several national and international trainees. During Phase II, the Phase I project leaders became mentors and core directors while maintaining their own labs. Five additional faculty were recruited, bringing expertise in epigenetics, bioinformatics, gene editing and organ development, and we also established a close partnership with the Department of Obstetrics, Gynecology and Women's Health (Ob/Gyn). After ten years of support, the center is now competitive for several grant opportunities that we will pursue in Phase III. Phase III COBRE objective is to

sustain the IBR COBRE as a world-class basic and translational science center of excellence in reproductive biology. This will be accomplished through two Specific Aims. Aim 1: Expand and diversify the expertise of the COBRE research cores. Growing and diversifying the core user base, enhancing and streamlining core operations, and strengthening the core revenue streams will result in the sustainability of the cores and accelerate the pace of scientific discovery, heighten research productivity and increase competitiveness for extramural funding. Aim 2: Develop and implement a Translational Pilot Project Program. We will leverage a strong partnership with the Dept. of Ob/Gyn to develop a new translational arm of research for the IBR. At the end of the Phase III COBRE, we envision that each of the cores will be fully or largely self-sustained, through a coordinated plan of recharge accounts, extramural grants, strategic investments and philanthropy, and that a the IBR will have successfully completed development of translational research arm through a novel implementation of the pilot projects program.

Integrative Center for Environmental Microbiomes and Human Health (P20GM125508)
PI: Anthony Amend, Ph.D.

The goal of the proposed COBRE program is to create an Integrative Center for Environmental Microbiomes and Human Health (ICEMHH) in response to the 2016 announcement of the National Microbiome Initiative (NMI). The NMI was conceived through the recognition that humans are both connected to and reliant upon the microbial communities that constitute the Earth's microbiomes, in the environment as well as the human body. The NIH plays a central role in funding this effort, “with a particular emphasis on multi-ecosystem comparison studies, and investigation into the design of new tools to explore and understand microbiomes” [NIH Human Microbiome Project]. The focus of ICEMHH is the interface between the microbial environment and human health, and spans state-of-the-art `-omics' methods to ecological analyses and predictive models. The University of Hawai‘i brings three compelling strengths to microbiome research: the uniquely tractable and scalable landscape of the Hawaiian Islands, an exceptionally qualified biology faculty, including an integrated cohort of recently hired, microbiome-focused, tenure-track, junior professors, and a dedication to the diversity of people that live on the Islands. As the most diverse biome on Earth, Hawai‘i offers the opportunity to study the effects of ecological gradients on human health, from mountain to sea, and in both urban and rural settings. The proposed projects aim to address two critical and intertwined health problems: the deteriorating environment, and the current spread of insect-vector borne diseases. In this context, proposed research efforts will (i) explore how human health is impacted by exposure to pathogenic microbes in the environment; (ii) examine how the microbiomes of insect vectors affect their transmission of disease within the microcosm of the island of O‘ahu; and, (iii) exploit invertebrate models to provide insight into the underlying cellular, genetic and molecular mechanisms by which microbiomes confer health. In this way, the Center will provide lasting contributions to the State of Hawai‘i, and beyond.

Center for Translational Research on Aging (P20GM125526)
PI: Bradley John Willcox, MD

Kuakini Medical Center (Kuakini) proposes to develop a multidisciplinary Hawai'i-based Center of Biomedical Research Excellence (COBRE) for translational research on aging. This Center will draw on the most promising junior investigators from across the state with cross-institutional and interdisciplinary collaborative efforts between Kuakini, the University of Hawai‘i John A. Burns School of Medicine (JABSOM), and major academic research centers and medical centers. It will cross institutional borders to promote research aimed at improving human healthy lifespan (healthspan) and ameliorating major age-related diseases, including cardiovascular diseases, cancer and dementia, in people of Hawai‘i, the U.S. mainland and around the world. The Center will build upon the strengths of Kuakini's five-decade track record of NIH-funded research, its 420,000-specimen biorepository, and its existing strengths in aging research, notably, the 51-year long Kuakini Honolulu Heart Program (Kuakini HHP) and Kuakini Honolulu-Asia Aging Study (Kuakini HAAS), and Kuakini HHP Offspring Study. This will advance translational aging research and foster meaningful solutions toward the disease and disability associated with the aging process. We will pursue this long-term goal via the following Specific Aims: Aim 1: Create a world class, innovative, interdisciplinary Center for Translational Research on Aging (CTRA) by building on the existing rare and valuable Kuakini Honolulu Heart Program (Kuakini HHP) and its related studies, existing Kuakini HHP Offspring Study, and research infrastructure. Aim 2: Advance the genomic, biological and clinical science of aging, and enhance the world class character of our proposed Center, by enlisting accomplished senior scientists to mentor promising Hawai‘i -based junior investigators in interdisciplinary

research and career development. Aim 3: Elevate the capacity of our Center by: i) creating a state-of-the-art Clinical and Translational Core, and ii) collaborating with other Centers of Biomedical Research Excellence. The Clinical and Translational Core will expand upon the strong epidemiologic, genomic and clinical work of Kuakini HHP and related studies and the Kuakini HHP Offspring Study; benefit investigators in the State of Hawai'i and abroad, and foster translation of basic science and clinical findings into novel applications and therapeutics for healthy aging. COBRE funding will be leveraged with institutional commitments to accelerate the development of research excellence. The Center will collaborate with three other Hawai'i -based COBREs, the COBRE Mouse Phenotyping Core, and the INBRE-funded Bioinformatics and Biostatistics Core at the University of Hawai'i.

Integrative Center for Precision Nutrition and Human Health (P20GM139753)
PI: Marla J. Berry

Precision nutrition is a new and now integral component of precision medicine that exploits differences in how dietary components are absorbed, metabolized and converted to energy, and in how that energy is utilized, resulting in widely varying dietary and nutrient requirements. In Hawai'i, culture and customs influence dietary preferences and economic disparities affect food access, further amplifying differences in nutritional needs and individual responses to dietary components. Recognizing the innovative new opportunities available through precision nutrition approaches, and the transformative potential for impactful nutritional health benefits, particularly to the indigenous and underserved people of Hawai'i, the University of Hawai'i proposes to establish a multicomponent center that enables multidisciplinary research with the thematic focus of Precision Nutrition. The overall goal of this Centers of Biomedical Research Excellence (COBRE) Phase I proposal is the creation of an Integrative Center for Precision Nutrition and Human Health at the University of Hawai'i at Mānoa (UHM), 'integrative' in that it will encompass the interface between precision nutrition research and human health outcomes. Our objectives are to build the foundation needed to grow a cadre of future leaders and mentors in precision nutrition, the fruits of their efforts feeding the attainment of positive impacts on human health, and to broadly disseminate and implement healthful strategies and interventions, nourishing the sustainability of this Precision Nutrition COBRE. The overall goal of creating a Precision Nutrition COBRE that fosters excellence in research, career development, and community health, will be achieved through the following three Specific Aims: Aim 1: To create an Integrative Center for Precision Nutrition and Human Health founded on impactful, scientifically rigorous research, education and training; built around a cadre of promising future scientific leaders; and fostered by outstanding individually-crafted, team-facilitated mentoring and career development activities. Aim 2: To provide research investigators education and training in cutting edge technologies and access to state-of-the-art research Core Facilities, integrating these resources with other research and training programs and facilities at UH, with community-based research in Hawai'i, and with the IDeA network across the nation. Aim 3: To promote development of strong collaborative relationships between academic researchers and the community, based on culturally sensitive approaches, with the goal of achieving tangible health benefits for all. Through the combined efforts of Precision Nutrition COBRE researchers and our community partners, with the guidance of the Community Engagement and Outreach Core, we will collaboratively advance precision nutrition, share and disseminate beneficial and healthful strategies and interventions and positive outcomes throughout the community, the State and beyond. The long-term goal of the Center is to promote health through the advantages of precision nutrition, implemented across the community and beyond, thereby producing lasting, far-reaching positive impacts on human health.

Center for Pacific Innovations, Knowledge, and Opportunities (PIKO) (U54GM138062)
PI: Joseph K. Kaholokula, PhD and Neal Palafox, MD

The Center for Pacific Innovations, Knowledge, and Opportunities (PIKO) will build a statewide clinical and translational research (CTR) infrastructure to improve the health of Indigenous Pacific People (IPP) – defined as Native Hawaiians, Other Pacific Islanders, and Filipinos. IPP comprise 40% of Hawai'i's population and have disproportionately high rates of physical and mental health conditions compared to Whites and Asians. They also make up a majority of Hawai'i's other medically underserved and vulnerable populations. PIKO represents a partnership between the University of Hawai'i (lead), Hawai'i Pacific University, Chaminade University of Honolulu, and a statewide network of practice-based organizations (PBO) and community-based organizations (CBO). PIKO emphasizes the T3 (efficacy studies) to T5 (adoption and institutionalization) domains of CTR where the social determinants of health are strongly operative. PIKO takes a team-science approach to transform current CTR paradigms and to accelerate CTR advances to improve IPP health. PIKO comprises seven Cores:

Administrative; Professional Development; Pilot Projects Program; Biostatistics, Epidemiology, and Research Design; Community Engagement and Outreach; Clinical Research and Regulatory Support; and Tracking and Evaluation. The University of Hawai'i committed $2 million over 5 years to PIKO. The Overall Specific Aims are: Aim 1: Build a robust CTR infrastructure by establishing and implementing CTR activities within and across PIKO partnering institutions; by leveraging resources and expertise of other research infrastructure programs; by creating CTR registries of academic mentors, community leaders, junior investigators, and study participants; and by implementing efficient and effective administrative operations and communication strategies. Aim 2: Strengthen and diversify the CTR workforce by identifying IPP and non-IPP investigators for CTR careers; by enhancing the mentoring and professional development of CTR investigators and community leaders; by supporting culturally responsive and scientifically meritorious CTR pilot projects; and by engaging PBO/CBO to actively participate on all aspects of CTR. Aim 3: Disseminate and implement CTR findings by providing strategic investments in PBO/CBO to strengthen trust-based relationships; by strengthening a statewide network of PBO/CBO to serve as dissemination and implementation partners; by convening an annual conference that brings together CTR investigators and PBO/CBO stakeholders to share best practices, discoveries, and dissemination and implementation strategies; and by leveraging data science strategies to disseminate data and findings that are user-friendly, easy to understand, and accessible. By the end of this 5-year project, PIKO will have promoted high-impact transformative CTR to imprP20GMove the health of IPP and other marginalized communities in Hawai'i.

COBRE-Diabetes (P20GM113134)
PI: Mariana Gerschenson

The John A. Burns School of Medicine (JABSOM) at the University of Hawai'i (UH) proposes to develop a multidisciplinary Hawai'i -based Center of Biomedical Research Excellence (COBRE) in Diabetes Mellitus (DM). This Center will initially span departmental and eventually campus borders to promote the metabolic health of the people of Hawai'i and the Pacific region. The Center will leverage Hawai'i's ability to link basic science mechanisms underlying diabetes through translational research. The overall goals are to: 1) Mentor junior investigators studying DM and insulin resistance (IR), 2) Establish a Mentoring Team, 3) Develop a Resource Core that will facilitate DM and IR research, 4) Develop future investigators using a Pilot Project Program, and 5) Recruit an Associate/Full Professor with expertise in translational DM research. The global prevalence of DM continues to increase in parallel with the expanding presence of obesity and overweight adults and children. In the US, the prevalence of DM now affects 27.9 million children and adults (8.9% of US population) (http://www.diabetes.org/diabetes-basics/statistics/). Among racial and ethnic minorities, DM prevalence exceeds that of the US general population by as much as 3-fold. We have shown that among Native Hawaiians (NHs), the prevalence of DM is 22.4% with an additional 15% diagnosed with impaired glucose tolerance or pre-diabetic status. Indeed, prior epidemiological studies on DM, IR, metabolic syndrome (MetS), and heart disease risk factors among NHs and other high risk ethnic populations in Hawai'i have provided a rich environment to develop this new COBRE dedicated to understanding the molecular biology underpinnings of DM, IR and the MetS. COBRE funding will be leveraged with institutional funds to accelerate the development of research excellence in DM and IR. The research focus of the Center spans the translational spectrum with one clinical study in Native Hawaiians and Pacific Islanders focused on diabetes and immunoepigenetics. While animal and cell models are being employed in three of the four studies aimed at cation channels, glucose transport in skeletal myocytes and adipocytes, and vascular calcification and dyslipidemia in diabetes and chronic kidney deficiency within the context of IR and DM. New resources being supplemented in this proposal include funding support for a Resources Core with Epigenetics, Animal Metabolic Phenotyping and Cellular Metabolism. Pilot projects are also proposed to fund 2-3 new investigators as the initial cohort of junior investigators progress towards research independence. The JABSOM leadership will also recruit an Associate/Full Professor whose research complements and focuses on translational DM and IR.