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Training Program in  
Infectious Diseases in the  
Immunocompromised Host

Program Brochure

Fred Hutchinson  
Cancer Research  
Center

# OVERVIEW

## Program Description

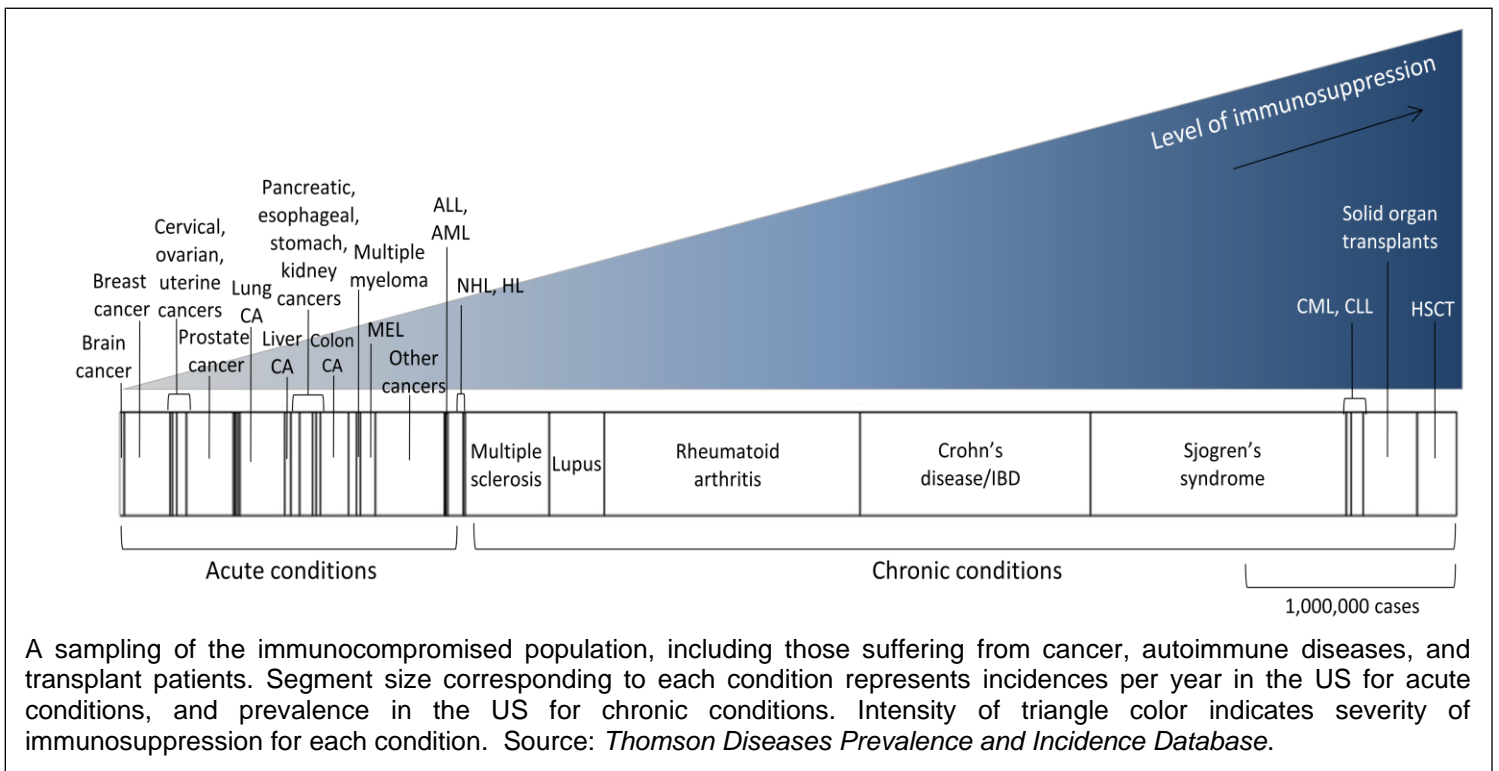
### ABOUT THE TRAINING PROGRAM

The Training Program in Infectious Diseases in the Immunocompromised Host has been established to train MD and PhD students to perform clinically relevant research in infectious diseases within the immunocompromised population.

### THE RATIONALE

The overall burden of infectious diseases is on the rise. A 2007 WHO report warned that infectious diseases are spreading more rapidly than ever before, and new infectious diseases are being discovered at an unprecedented rate.

The proportion of the US population experiencing immunosuppression is also rising, partly attributed to the advancement of solid organ and hematopoietic stem cell transplantation techniques, therapies for autoimmune diseases, and immunosenescence (immunosuppression due to aging). Cancers and numerous immunologic disorders may also be linked to more specific or limited forms of immunocompromise, either by the immunosuppression caused directly by the disease or through the use of additional immunosuppressive treatments. This high-risk population experiences an increased risk of infectious diseases. Moreover, the outcomes of such infections and conditions, even those otherwise considered benign in healthy patients, can cause severe morbidity and mortality in the immunosuppressed.



This is a problem for which society demands effective and innovative solutions, and we aim to address it by providing the next generation of physician and postdoctoral scientists with specialized training in infectious diseases in immunocompromised hosts.

## FRED HUTCHINSON CANCER RESEARCH CENTER AND THE SEATTLE CANCER CARE ALLIANCE

Fred Hutchinson Cancer Research Center (**Fred Hutch**) is a premier research institution in Seattle, Washington. Our interdisciplinary teams of scientists conduct research in the laboratory, at patient bedside, and in communities throughout the world to advance the prevention, early detection, and treatment of cancer and other diseases. Our researchers, including three Nobel laureates, bring a relentless pursuit of, and passion for, health knowledge and hope to their work and the world.

To accelerate the progress of clinical research, we are part of the Fred Hutchinson Cancer Research Center/University of Washington/Seattle Children's Cancer Consortium, or Seattle Cancer Care Alliance, a.k.a. **SCCA**. This research and clinical collaboration enables our scientists to leverage each institution's strengths and develop premier research programs across many types of diseases. Furthermore, this consortium is among 40 National Cancer Institute-designated comprehensive cancer centers in the United States.

Our consortium partners' campuses are located within Seattle city limits and are linked by free shuttle services between campuses to promote interdisciplinary research and full access to consortium resources. The proximity of Fred Hutch, the University of Washington, Seattle Children's, and the SCCA, both physically and institutionally, provides an amazing support system and plethora of resources for researchers.

## A 3-D Map of Fred Hutchinson Cancer Research Center and the Seattle Cancer Care Alliance



# INFECTIOUS DISEASE SCIENCES PROGRAM (IDS) OF THE VACCINE AND INFECTIOUS DISEASE DIVISION (VIDD)

## INFECTIOUS DISEASE SCIENCES PROGRAM (IDS)

The Training Program in Infectious Diseases in the Immunocompromised Host is based in the Infectious Disease Sciences Program (**IDS**) of VIDD with close collaborations and interactions with other divisions as well as various departments and units within the University of Washington and Seattle Children's.

Established in the 1980s at Fred Hutch, IDS has been home to many major innovative programs, including projects to study herpesvirus infections, respiratory viruses, invasive fungal disease, the microbiome and its role in human disease, HIV vaccine research, infection-related cancers, and infection control and hospital epidemiology.

Our researchers conduct interdisciplinary collaborative research and training at the highest level of excellence. The IDS Program has strong and long-standing collaborations and partnerships with multiple stakeholders, including patients and researchers, physicians and medical centers, data scientists and policy makers, industry sponsors, and federal agencies.

IDS's mission is to advance knowledge of host-pathogen interactions and develop innovative management strategies for infectious diseases in immunocompromised and immunocompetent persons.

## VACCINE AND INFECTIOUS DISEASE DIVISION (VIDD)

Fred Hutch comprises of five scientific divisions: Basic Sciences, Clinical Research, Human Biology, Public Health Sciences, and Vaccine and Infectious Disease (**VIDD**). VIDD's mission is to develop treatments and prevention strategies that counter infectious diseases throughout the world. Investigators working in VIDD research the human immune system, pathogens, and vaccines via statistical, clinical, and laboratory science. VIDD comprises several programs: Infectious Disease Sciences; Biostatistics, Bioinformatics and Epidemiology, which includes the Statistical Center for HIV and AIDS Research and Prevention (SCHARP); Immunology and Vaccine Development; and Global Oncology.

VIDD is home to one of the world's largest HIV research units and is the hub of the international HIV Vaccine Trials Network (HVTN), a global effort to develop and test a successful HIV vaccine. We have also been making a global impact with our prevention and treatment work by initiating collaborations with global partners such as the Uganda Cancer Institute, the Cape Town HVTN Immunology Laboratory in South Africa, and the China CDC.

## THE GOAL

The mission of our training program is to develop the next generation of physician and postdoctoral scientists with expertise in infectious diseases in the immunocompromised host. Our goal is to provide rigorous and interdisciplinary training to foster innovative and collaborative research in infectious diseases in the transplant setting and other known and emerging areas of immunosuppression. We aim to train individuals who will use that expertise to advance knowledge and develop innovative strategies to prevent, treat and control these infections. Fred Hutch, with its variety of resources and established training success, is uniquely suited to this goal.

## THE CURRICULUM

The core curriculum for the training program includes formal courses, didactic exercises and conferences that are important for all trainees regardless of their degree or research interests/projects. Some of the training is skills-based and covers key learning objectives, while others involve attendance and interactive research-focused group events.

## **CORE EXPECTATIONS**

- Participation in core curriculum components.
- Development of critical skills in research methodologies relevant to an individual discipline or track.
- Development of skills in presenting research. All trainees are expected to present their research at local, national, and sometimes international meetings.
- Development of skills in scientific writing. A critical goal of this training program is to nurture skills in writing scientific papers, research proposals, and grant applications.

## **CORE CURRICULUM ELEMENTS**

### ***Orientation Course in Infections in Immunocompromised Hosts***

All new trainees attend a one day orientation course in which program faculty and track leaders address research in immunocompromised hosts, in addition to human subjects training. The course also introduces trainees to faculty members and to one another.

### ***Annual Retreat on Infections in Immunocompromised Hosts***

The program hosts an all-day research retreat. All of the training program faculty and trainees are encouraged to attend. MD and PhD scientists supported on the training grant (as well as others receiving training in the field, e.g., international scientists) present their on-going research for discussion. All presenters receive immediate feedback on their presentations from at least two program faculty. The feedback and discussion are meant to further develop individual skills in presentation, data analysis, and interaction with other scientists.

### ***Annual IDS and Virology Symposium***

Physicians, scientists and trainees of Fred Hutch's IDS Program and the UW Virology Division come together for a joint symposium to share and celebrate research progress. Each T32 trainee gives an oral presentation on their research. EAC members also meet to discuss trainee progress and evaluate the training program.

### ***Symposium on Infectious Diseases of the Immunocompromised Host***

This symposium occurs biennially, and we hosted this event for the third time in June 2019. The two-day program features lectures by thought leaders in the field and early-career, rising star investigators. Trainees are encouraged to present their original research through short oral presentations or as part of our lively, interactive poster session. Networking opportunities include small group mentoring dinners.

### ***Allergy and Infectious Disease Orientation Course for MD Fellows***

MD fellows also attend a two-week orientation course covering a broad range of clinical ID topics at the beginning of their clinical years (which precedes the start of the research fellowship covered by this program).

### ***Research in Progress Reporting and Participation***

Each trainee will attend research in progress meetings with their mentors. In addition, trainees are required to present at least once every year their research progress at either an internal or external conference or lecture series that focuses on infections in the immunocompromised host.

### ***Affinity Groups on Infectious Disease in the Immunocompromised Host and Mathematical Modeling***

These groups meet throughout the year, featuring presentations by leading experts in these focus areas. Our T32 trainees and faculty are strongly encouraged to attend, and these events are open to all trainees, faculty, and staff in our scientific community.

### ***Vaccine and Infectious Disease Division Seminar Series***

This weekly seminar series at Fred Hutch features research presentations from faculty, scientists, senior fellows/postdocs, and guest speakers on a broad range of topics including infectious diseases, immunology and biostatistics.

### ***Solid Organ Transplantation (SOT) Grand Rounds***

The weekly seminars cover topics in SOT including infectious disease and immunology topics, featuring both local and external speakers.

### ***Fred Hutch Research Ethics Education Program***

Fred Hutch-based trainees (postdoctoral researchers, clinical fellows, and graduate students) are required, during their tenure at Fred Hutch, to attend six approved events. One of the six events must be a case study discussion group.

### ***ITHS Clinical and Translational Boot Camp***

This two-day course introduces ID fellows to the latest information about clinical and translational research, including observational studies and clinical trials.

### ***Targeted Lectures and Workshops on Key Skills and Methodologies***

Trainees are strongly encouraged to attend these courses, which have been developed to build key skills that will provide a strong foundation for trainees' burgeoning research careers.

- *State-of-the-Art Statistical Methodology*. This newly-developed course will introduce T32 trainees to state-of-the-art methods, technologies, and analyses, with a focus on high-throughput and high-dimensional assays. It will be led by T32 Senior Mentor and Fred Hutch Biostatistics Faculty member Dr. Ollivier Hyrien.
- *Journal Club* on infections in the immunocompromised host. At this monthly forum, T32 faculty guide our T32 trainees in discussing scientific articles relevant to their projects, with a specific focus on methods. Faculty provide supplementary information about rigorous methodology and analysis as needed. All faculty and trainees working in the field are invited. Our journal club takes place at faculty members' homes to foster strong relationships between training program faculty and trainees and also interactions among faculty.
- *Manuscript Writing Boot Camp*. Trainees are invited to this dedicated writing time, to make progress on and receive feedback on manuscripts. Senior program faculty as well as Ashley Sherrid, Technical Editor with the IDS program, will also be available to provide individualized instruction and support.
- *Foundations in Biostatistics and Clinical Trials*. This course introduces Fred Hutch fellows to biostatistics and clinical trials. It is taught by Dr. Ted Gooley, T32 Supporting Mentor and Fred Hutch/UW Biostatistics Faculty.

### ***Joint Opportunities with Related Programs***

Our T32 program has teamed up with complementary UW/Fred Hutch training grant programs to host two, half-day joint retreats that feature research presentations by T32 recipient-trainees, aimed exposing our trainees to key related fields of research. The Annual Oncology Research Training Retreat includes T32 and K12 recipient-trainees in medical oncology, gynecologic oncology, pediatric oncology, and infectious disease. Similarly, the Joint Retreat on Host Defense and Infectious Disease in the Immunocompromised Host (held for the first time in November 2019, with a virtual event planned for November 2020) includes T32 recipient-trainees in immunology, host-pathogen interactions, and infectious disease, as they relate to immunocompromised hosts.

Additionally, several linkages with the pediatric ID fellowship program have been developed to benefit both programs. Due to these linkages, both pediatric and adult ID fellows participate in most elements of the Core Curriculum, including orientation sessions, weekly conferences, an annual research retreat and journal clubs. Two pediatric faculty serve as mentors in this program (Dr. Englund, Dr. Waghmare).

## ***Grant Writing***

We expect and strongly support grant writing at different levels: internal pilot grants, foundation and fellowship grants, loan repayment grants (if applicable), and, ultimately a career development (e.g., K award) project. Grant writing seminars are available at Fred Hutch and the UW, and senior mentors are available for input and grant review.

## ***Didactic or Graduate Courses***

MDs participating in **Tracks 1** will have the opportunity to obtain a master's degree in epidemiology at the UW. The UW-based Institute of Translational Health Sciences (ITHS) offers reduced tuition for Fred Hutch-based program participants. Alternatively, the Harvard School of Public Health offers a summer program in clinical effectiveness. This prestigious and intensive eight-week course focuses on the quantitative and analytical skills needed for a career in clinical research and is a shorter yet valuable alternative to a full degree program. Both options will be available to trainees in the appropriate tracks. Additional UW-based courses are available, and the selection will be individualized during training planning meetings.

## ***Advanced Clinical Training in Immunocompromised Host ID (MD track only)***

Although the main focus of the T32 is training in research, we believe that future medical leaders in immunocompromised ID must have superior clinical training that goes beyond the standard training obtained during the first clinical fellowship year. Therefore, we created the following opportunities to enhance clinical experience and skills. We believe that these limited clinical activities are critical and will be synergistic with the research goals and, ultimately, create both clinically and academically competent leaders. The clinical commitment will be carefully monitored during the regular program review process.

- Basic training part of ID fellowship: focus on inpatient immunocompromised ID.
- Participation in the outpatient clinics in HCT/cancer and SOT in year 2
- Participation in ID attending service as junior attending in year 3 with co-attending of a senior, experienced immunocompromised host physician (two 14-day blocks in the last year of training). This opportunity is aimed at solidifying the training in immunocompromised host ID medicine and continuing the trainee's career trajectory by functioning at the attending level (with primary responsibility and note signing) with concurrent co-attending by experienced program faculty. This provides a unique training experience and allows for increased salary supported by the clinical billing, thereby avoiding a career delay. This innovative model is facilitated by a title of Senior Fellow/Acting Instructor available in our system, which permits functioning in a hybrid fashion of a senior fellow and clinical attending (with billing privileges).
- Clinical transition meetings (bi-weekly): these meetings are case-based and open to all fellows and faculty with interest in the immunocompromised ID; they are also attended by pulmonologists.
- Clinical care conferences: a quarterly meeting that discusses ID management issues, reviews abstracts from national ID conferences, and reviews autopsy findings.
- Participation in infection control and stewardship meetings. We offer representative attendance in infection control meetings; many ID specialists will have to assume partial functions in these areas (even if they are not a dedicated leader in a particular hospital).

## ***Career Development Opportunities***

In addition to the above opportunities for developing skills in manuscript and grant writing, presenting their research, and broadening their scientific knowledge, trainees in our program are encouraged to take advantage of numerous career development resources at Fred Hutch and UW.

- The Fred Hutch Office of Scientific Career Development (OSCD) Director is available to have an informal career conversation with every new trainee.
- OSCD facilitates the Ivory Tower Quest Series (panels and talks on putting together application packets and interviewing for faculty positions), the Exploration Program for Industry Careers (EPIC, featuring half-day site visits to local biotech companies and networking opportunities), and the First Friday Series (seminars featuring scientific career options). They also provide examples of successful faculty applications.
- The Fred Hutch Student-Postdoc Advisory Committee (SPAC) Seminars and Workshops enhance the professional development of trainees so that they master the skills necessary for a successful career and learn

about the types of careers that are available to them in both academia (including grant writing) and non-academic fields.

- UW career development resources include Fellows' Day, with a speaker panel on different career paths. We actively encourage trainees in year 3 to apply for independent positions in a research career pathway.

## Facilities and Resources

The collaboration between the members of the Seattle Cancer Care Alliance provides access to a variety of resources for endeavoring researchers. These resources include, but are not limited to, the following:

### CLINICAL

Clinical space is located at various locations across Seattle. As part of the Cancer Consortium, the SCCA clinic resides in a seven-story, 159,000 square foot facility on the Fred Hutch campus. It houses outpatient clinics, multi-bed clinical trial units, radiation oncology, diagnostic imaging, clinical laboratory, infusion therapy, apheresis, minor procedures, physical therapy, pharmacy, patient support services, and faculty and administrative offices. Additionally, the SCCA inpatient unit at the University of Washington Medical Center (UWMC) has 50 beds on the 7th and 8th floors.

Other affiliated sites and hospitals include UWMC and Seattle Children's Hospital. This unique network of hospitals gives fellows the opportunity to train under world-renowned physicians with diverse patient populations and access to world-class resources. Clinical training takes place at these locations.

The Infectious Disease clinics for HCT/cancer patients will be held at the SCCA building while the SOT ID clinic is located at the UWMC.

### COMPARATIVE MEDICINE

Fred Hutch, along with its Consortium partnership organizations such as the UW, provides a broad variety of animal housing, veterinary, and research support services. The facility is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) and complies with all United States Department of Agriculture (USDA), Public Health Service (PHS), Washington State and local area animal welfare regulations. Comprehensive animal husbandry services are provided for all vertebrate animals used in the Consortium's programs of research. All housing and use of vertebrate animals is done in Comparative Medicine's centralized facilities which occupy approximately 50,000 net square feet.

### COMPUTER

Fred Hutch's IT infrastructure and services are provided by a centralized department (Fred Hutch IT). It is currently staffed by 120 IT professionals that support, maintain and design Fred Hutch's complex heterogeneous research and administrative computing environments across multiple data centers. The services that Fred Hutch IT provides are extensive and they include:

- IT Help Desk support 8am to 5pm and 24/7 emergency IT on-call support
- Desktop, laptop and mobile computing management and support
- Clinical informatics systems/application management and support
- High Performance Computing (HPC), Scientific Computing support, and Software development support
- Messaging services: e-mail and calendar
- Anti-spam and anti-malware services
- Collaboration services: SharePoint



- Data storage services: SAN & NAS and Data protection services: file and database backups, off-site
- Connectivity services: wired networking, wireless, VPN and high-speed Internet access
- Telephone and voicemail services
- Security: encryption, firewalls, intrusion prevention, forensics and consulting

Fred Hutch IT manages the institution's Storage Area Network (SAN) which consists of a 3PAR/NetApp consolidated storage system 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.

In order to accommodate the growing demand for computer resources and mitigate the power demands of physical systems, 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.

Fred Hutch IT supports both UNIX/IMAP (Zimbra) and Microsoft Exchange for e-mail services. Fax and photocopier machines are also available throughout Fred Hutch.

Fred Hutch IT also provides support for over 60 applications that are made available to the entire organization including an enterprise level SharePoint Collaboration platform.

The Information Security Office (ISO) is part of Fred Hutch IT and is staffed with 5 FTEs. The ISO maintains a highly available Intrusion prevention system and high-performance firewall.

## OFFICE

Office space is provided by Fred Hutch to its divisions and programs. Faculty occupies offices, while fellows are provided work-space within close proximity to their mentors. There are 93 conference rooms of varying sizes on campus with video conferencing capabilities in most of the larger conference facilities. Other amenities to campus buildings include secure file rooms and an on-site copy center.

## SHARED RESOURCES AT THE FRED HUTCH

The Shared Resources (<https://sharedresources.fredhutch.org/>) at the Fred Hutch consist of facilities and laboratories that are made available for use to all Fred Hutch investigators as well as our consortium institutions, external academic and biotechnology community. The facilities give investigators the opportunity to augment their research with resources that would not otherwise be convenient or cost effective in each individual laboratory. The Fred Hutch's centralized facilities have proven to improve the feasibility and efficiency of performing clinical trials and permit more rapid translation of laboratory studies into clinical applications. These Shared Resources include:

- Antibody Technology
- Arnold Library
- Biologics Production
- Collaborative Data Services
- Comparative Medicine
- Electron Microscopy
- Experimental Histopathology
- Flow Cytometry
- Genomics
- Glassware Services
- Immune Monitoring

- Nutrition Assessment
- NWBioTrust
- Prevention Center
- Proteomics
- Scientific Computing
- Scientific Imaging

The resources are available to trainees and serve the purpose of providing routine services for a variety of research activities, many of which are also focal points for technology dissemination and collaborative research. All resources are staffed by personnel with expertise specific to that facility.

Fred Hutch has two secured freezer facilities that occupy ~10,000 square feet on the campus. There is dedicated space for liquid nitrogen and scientific freezers for long-term specimen and sample storage. Since our last T32 grant submission, a second on-site secure facility was added to accommodate the specimen storage needs of Fred Hutch faculty. Both facilities and freezers are monitored 24 hours a day, 7 days a week by the Engineering Department.

Within Fred Hutch Shared Resources, the Research Cell Bank maintains the centralized transplant genomics repository of frozen blood cells and DNA derived from hematopoietic cell transplant patients, donors and family members dating back to the 1970s. The cell bank houses blood, cell and DNA material from more than 20,000 HCT recipients and donors.

#### Scientific Computing (recently moved to under Shared Resources)

The Scientific Computing group is staffed with 8 FTEs and provides the following services to Fred Hutch research groups and shared resources:

- High Performance Computing (access to the Gizmo HPC cluster including large memory machines, scratch spaces and web gateways for web job submission)
- High Performance Cloud Computing support for Amazon Web Services
- General Linux/Unix support (Linux Desktop Support, managing applications on departmental Linux servers)
- Software Development Support (Github 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

#### **Other Resources/Services**

Within the IDS Program of VIDC, two IRB-approved biospecimen repositories exist, the Infectious Disease Biorepository and Microbiome Biorepository. The Infectious Disease Repository is open for use by all Fred Hutch investigators and houses over 385,000 specimens. Research utilizing the repository has led to four funded NIH grants and ten funded projects through foundations or institutional funding. For the Microbiome Repository, access is available to over 31,800 samples for Fred Hutch investigators.

An additional resource available to mentees within the IDS Program is centralized data and statistical support. Within the last three years, IDS has hired a statistical research associate and data management analyst. The statistical research associate has over 15 years of experience working in the field of infectious disease research in the immunocompromised host. The statistical research associate provides guidance to trainees on how best to develop the parameters for collection and analyze their research data for abstracts, publications and grant submissions. The data management analyst works with the faculty and statisticians to collect and retrieve data from Amalga (a clinical research platform containing patient data from across our partners at the SCCA, UW and SCH), clean data for statistical analysis, and develop RedCap databases for a variety of clinical research projects. These resources are available for trainees based in the IDS Program.

Fred Hutch has a Clinical Research Support (CRS) Administrative office that supports the center and consortium partners' mission to ensure the conduct of efficient, compliant and high-quality clinical research. CRS oversees the

following resources to support on-going research: clinical trials website management, contracts and fiscal management, partner access, protocol review meeting coordination, quality management, research management data and training. In 2018 in conjunction with the CRS, Fred Hutch IT and our consortium partners at the UW and SCCA, a Clinical Trials Management System (CTMS) called OnCore was developed and rolled out to our organizations. This system allows our organizations the ability to manage clinical trial portfolios more effectively.

The Arnold Library provides high quality, responsive services, and resources in support of Fred Hutch's research, education and patient care programs. The library's physical space houses study carrels with wireless Internet access, patron computers and the Shared Resources Computer Lab. This centralized resource encompasses subscription management for more than 30,000 ebooks and over 37,000 online journals as well as a variety of databases and web services. Librarians curate Fred Hutch researchers' profiles, provide center-wide tracking of scholarly publishing, support Center authors with NIH Public Access Policy compliance, manage the Shared Resources website, provide training and support for citation management tools like EndNote, provide reports and consultation on publication metrics, host a course guides system to support faculty instructors, manage the Fred Hutch history archive and administer several institutional repositories.

Finally, the training program is serviced by a thrice-daily courier service to transport specimens and materials between clinics and laboratories through an affiliation with the Virology Division at the University of Washington. This service has been highly effective and beneficial over the past 2 decades in promoting interdisciplinary research.

## Track Descriptions

Our program training has three different yet finely integrated tracks that represent not only the individual strengths of the training faculty but also areas of innovation and unmet scientific and medical need. Senior faculty mentors with outstanding credentials within the unique area have been selected to be leaders of each track.

### **1) CLINICAL RESEARCH, INFECTION PREVENTION AND STEWARDSHIP EPIDEMIOLOGY, PATHOGEN DYNAMICS AND CLINICAL TRIALS**

#### **Michael Boeckh and Ajit Limaye, Co-Track Leaders**

This track will provide trainees with excellent opportunities to develop skills in a broad range of areas related to the epidemiology of infections in HCT and SOT patients as well as moderately immunosuppressed patients, e.g., after a new diagnosis of cancer or those with autoimmune or chronic diseases requiring immunosuppressive treatment. The transplant ID programs at the Fred Hutch and UW have multiple and diverse ongoing projects that focus on the spectrum, risk factors, biomarkers/diagnostics, and outcomes of bacterial, viral, and fungal pathogens in HCT and SOT recipients. Through collaborations with faculty with expertise in mathematical modeling and biostatistics, this track will also provide trainees within depth experience in the relationship between pathogen and clinical outcomes and host determinants of pathogen dynamics, an area with important implications for defining the pathogenesis of infections in immunosuppressed hosts and in the design of interventional studies. Studies will be facilitated by a state-of-the-art molecular diagnostic laboratory directed by Keith Jerome and an unparalleled sample biorepository. This track will also provide trainees with excellent opportunities to develop skills in all aspects of observational and interventional trials. Trainees will obtain experience in trial design, patient recruitment and retention, implementation, monitoring, regulatory aspects, funding, and data analysis. This track also provides trainees with opportunities to study the epidemiology of healthcare associated infections as well as potential interventions aimed at reducing the risk of such infections in the immunocompromised host. This training program is one of the few existing programs aimed at expanding knowledge in the nascent field of infection control in these vulnerable patient populations for decades. Potential projects for trainees may focus on targeted organisms (e.g., multidrug-resistant organisms, respiratory viruses, etc.), targeted conditions (e.g., central line associated bloodstream infections), targeted interventions (e.g., chlorhexidine gluconate bathing, environmental decontamination, etc.), or addressing antimicrobial stewardship in these high-risk patients. Training will be obtained through attendance at weekly clinical trial meetings for ongoing trials, coursework in

biostatistics and epidemiology, and attendance at scientific meetings. The breadth of faculty expertise and the long and distinguished past track record of successful clinical investigator trainees will ensure that future trainees are well prepared for independent careers as translational investigators. Trainees in this track are encouraged to pursue a Master in Epidemiology/Public Health degree.

## 2) IMMUNOLOGY/IMMUNOGENETICS

### Geoffrey Hill, Track Leader

This track will conduct research of the specificity and function of human T cell responses to pathogens with the overall goal of understanding the biology of host-pathogen interactions. After initial pioneering human trials of adoptively transferred T cell clones to prevent cytomegalovirus (CMV) infection after allogeneic HCT, human trials of T cell therapy including the use of gene-modified T cells are now a strong research focus and area for training. These studies require the development of techniques for viral antigen discovery, and for isolation, expansion, characterization, engineering and reinfusion of T cells into patients. Additional studies are directed at defining intrinsic qualities of T cells that enable superior persistence and efficacy after adoptive transfer with specific emphasis on the identification of a novel memory T cell subset in humans that is distinct in phenotype, gene expression profile, response to homeostatic cytokines, and functional properties. The role of antibodies in control of viral disease (including CMV and respiratory viruses) is another area of research, energized by the work of Dr. Geoffrey Hill and an animal model for CMV now available in his lab. Another focus of this track is to study factors associated with vaccine responses in the immunocompromised host. Immunocompromised hosts are often excluded from standard vaccinations during the time of maximum need; however, recent studies using novel CMV and varicella zoster virus (VZV) vaccines specifically target immunocompromised patients. This track also offers research opportunities to define pathogen-specific and immune reconstitution dynamics in immunosuppressed populations and to characterize and optimize vaccine responses using state of the art computational methodologies. Another area covered in this track is the genetic basis of infectious diseases. A unique cohort of 5,000 HCT recipients/ donors have undergone genotyping facilitates genome wide association studies (GWAS) of infectious phenotypes as well as associated validation experiments. Gene expression studies characterizing host signatures associated with progressive infectious diseases in immunocompromised hosts are another area for prospective trainees. Senior faculty with top credentials, computational expertise, and state-of-the-art technologies in labs and shared resources (including strong genomics facilities) support these studies.

## 3) MICROBIOME AND PATHOGENESIS

### David Fredricks, Track Leader

This research track provides trainees with the opportunity to study the role of individual microbial pathogens in transplant outcomes and infectious complications in the immunocompromised host (e.g., CMV, respiratory viruses, *Clostridium difficile*, *Enterococcus faecalis*, *Aspergillus fumigatus*, and others). For example, postdoctoral fellows can investigate how CMV and HSV subvert the human immune response to establish lifelong infection, and the factors leading to reactivation of viral infection in the immunocompromised host. To facilitate studies, stool, mouth and skin samples from prospective cohort studies are available to trainees (as well as samples from our general repository). In addition, this track will provide a rich training environment for studying human-associated microbial communities (the indigenous microbiota) and their genes (the microbiome), with a focus on how bacterial communities at particular epithelial surfaces impact risk of infection and outcomes, such as graft-versus-host disease after HCT. Fred Hutch and the UW have a deep and diverse community of investigators studying aspects of the human microbiome and pathogenesis, providing many opportunities for rigorous laboratory-based investigation and career development. . In 2017, Dr. Fredricks launched the Microbiome Research Initiative, which serves as an incubator for new scientific opportunities by galvanizing investigators who are pursuing microbiome studies, capitalizing on recent advances in the field and catalyzing nascent research on the microbiome that impacts cancer and infectious diseases

## PROGRAM DIRECTOR

Michael Boeckh, MD, PhD, Head of the Infectious Disease Sciences Program, will serve as Program Director for the training program contributing 10% effort. This effort will be concurrent with his Program Head responsibilities and is compensated through funds provided by the Vaccine and Infectious Disease Division (VIDD) of Fred Hutchinson Cancer Research Center. As Program Director, Dr. Boeckh's responsibilities are to administer and oversee the training program, interact with NIAID and the different committees, oversee the integration of the training grant program into program activities to ensure the success of each trainee, and manage all other aspects of the training program.

## ASSOCIATE DIRECTORS

Joshua Schiffer, MD, MSc, Associate Professor at Fred Hutch/UW and Catherine Liu, MD, Professor at Fred Hutch and Associate Professor at UW, will serve as Associate Directors. Dr. Liu also serves as Director of the Antimicrobial Stewardship and Outpatient Parenteral Antimicrobial Therapy Programs at the SCCA. As Associate Directors of the training program, Drs. Schiffer and Liu's responsibilities are participating in the selection process for trainees, creating mentorship committees; participating in the trainee evaluation process; participating in EAC and IAC meetings; curriculum planning and execution, and preparation of annual training grant progress reports.

## EXTERNAL ADVISORY COMMITTEE

The External Advisory Committee (EAC) comprises four distinguished individuals (Kieren Marr, Nina Singh, David Snyderman, John Zaia) outside of our consortium organizations with strong credentials in both laboratory sciences and clinical research, expertise in obtaining NIH funding, and training the next generation of scientists.

## INTERNAL ADVISORY COMMITTEE

The Internal Advisory Committee (IAC) comprises all track leaders as well as distinguished individuals from inside of Fred Hutch and our consortium organizations with strong credentials in training, laboratory sciences and clinical research expertise as well as familiarity with the mission of our training program. The IAC committee members are Nancy Davidson, Lisa Frenkel, Rhoda Morrow, Barry Stoddard, David Fredricks, Geoffrey Hill, Ajit Limaye, and Michael Boeckh.

## SENIOR, JUNIOR AND SUPPORTING MENTORS

Training faculty with an especially strong expertise and track record in the fields of virology, molecular immunology, immunogenetics, microbial pathogenesis, epidemiology, clinical trials conduct and biostatistics, will serve as mentors. Senior mentors were selected based upon the excellence of their research, ability to secure competitive extramural funding, and mentoring records. Junior mentors have less mentoring experience, and mentorship skills will be developed by pairing them with a senior and a supportive mentor. All have a unique set of skills and achievements for which they were selected to serve on the training faculty. We anticipate that some of the junior mentors will move into the senior mentor rank during the next five-year grant period.

This co-mentoring approach has been a highly successful concept in our experience. It will not only increase access to mentors for the trainees but also provide leadership and guidance as the younger faculty member develops mentoring skills. Overall, this approach will enrich the training experience of co-mentored trainees.

# Training Program Organization

## Principal Investigator

Michael Boeckh

## Associate Directors

Joshua Schiffer  
Catherine Liu

### External Advisory Committee

Kieren Marr  
Nina Singh  
David Snyderman  
John Zaia

### Internal Advisory Committee

Nancy Davidson  
Lisa Frenkel  
Rhoda Morrow  
Barry Stoddard

All track leaders

Tracks	Clinical Research, Infection Prevention and Stewardship	Immunology/ Immunogenetics	Microbiome and Pathogenesis
Track Descriptions	Study the epidemiology, pathogen dynamics, biomarkers/diagnostics, and risk factors, as well as potential interventions for reducing risk, of infections in HCT and SOT recipients through the design, conduct, and analysis of observational and interventional clinical trials.	Study the immunopathogenesis of infections, immunologic mechanisms, immunoreconstitution, vaccine responses, genetic bases of disease, genetic signatures of disease, systems biology approaches of immune and vaccine responses.	Study the human microbiome, with a focus on how bacterial communities at particular epithelial surfaces impact risk of infection and outcomes, such as GVHD after HCT. Study the mechanisms of individual microbial pathogens on outcomes in the immunocompromised host.
Senior Mentors	<b>Michael Boeckh</b> <b>Ajit Limaye</b> Janet Englund David Fredricks Keith Jerome Christine Johnston Ollivier Hyrien Joshua Schiffer Anna Wald	<b>Geoffrey Hill</b> Larry Corey Tom Hawn David Koelle Martin Prlic Cameron Turtle	<b>David Fredricks</b> Michael Boeckh Adam Geballe Geoffrey Hill Ollivier Hyrien Keith Jerome David Koelle Joshua Schiffer Cameron Turtle
Junior Mentors	Rachel Bender-Ignacio Guang-Shing Cheng Helen Chu Cindy Fisher Josh Hill Catherine Liu Steven Pergam Alpana Waghmare	Aude Chapuis Warren Phipps Justin Taylor	Alex Greninger Christopher Johnston Steven Pergam Michael Wu
Supporting Mentors	Theodore Gooley Wendy Leisenring Danielle Zerr	Stephen DeRosa Evan Newell Jia Zhu	

NOTE: **Bold** indicates Track Leaders

## Additional Information

For further information, please contact:

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