Training Program in Cancer Research – University of Michigan

Overview

The Biostatistics Training Program in Cancer Research at the University of Michigan provides support for pre-doctoral training at the interface of Biostatistics and Cancer research under support from the National Cancer Institute of the National Institutes of Health.

The program, which began in 2002, will support four trainees each year. Training support is typically for two or three years. United States citizens and permanent residents are eligible to apply. Trainees can be new applicants to the Biostatistics graduate program or continuing Michigan students at any stage in their graduate studies. Trainees from other departments (e.g. Statistics and Epidemiology) can be considered. Trainees are expected to enroll in, or have the eventual intention of enrolling in, the Ph.D. program.

Trainees are expected to undertake a curriculum of coursework in Biostatistics and Cancer, learn about the science of cancer and become involved in cancer research projects.

Pre-doctoral trainees are provided with full tuition (two semesters) and a stipend ($30, 598.00 for 2017-2018) each year. Trainees also receive travel funds towards attendance at a scientific meeting.

Introduction

The role and future of biostatisticians in cancer research: Rationale for the training program

It is widely recognized that biostatistical collaboration and methodology are essential components of research into the underlying mechanisms, causes, risk factors and therapeutic interventions for cancer. The long term aim of this program is to increase the participation in cancer research of biostatisticians who are educated not only in the powerful methods of modern statistics, but also in the biology, genetics and epidemiology of cancer, the current body of knowledge about the etiology of the disease, its natural history, prevention and treatment.

Cancer is a leading cause of mortality and morbidity among people throughout the world. It has a devastating effect on individuals and the society in which they live. Over 40 percent of us will develop cancer; 20 percent of us will die from cancer. There is a tremendous amount of active and ongoing research into understanding the basic mechanisms of cancer and developing methods to prevent and treat cancer. The science of cancer is multifaceted, as illustrated by the breadth of scientists involved in the research efforts to fight cancer which includes

pathologists, immunologists, virologists, population scientists geneticists, radiation biologists, and clinical trialists to name a few.

There has been a long tradition of involvement by statisticians in cancer research. A major emphasis and achievement of statisticians in cancer research has been in developing the discipline of clinical trials and in developing methods for epidemiological studies. These areas can and will continue to play important roles. The phenomenal expansion in the knowledge of the underlying mechanisms of cancer indicates a need for statistical scientists with a greater understanding of the science of cancer. The astounding advances in molecular biology and genetics will have a substantial impact on the role that biostatisticians play in the future. They are likely closer to the cutting edge in advances in basic science. One area where they will play important and crucial roles are in the field of bioinformatics and data science.

In the future, biostatisticians will be working more and more in multidisciplinary cancer research teams. A premise of this training program is that such teams will be greatly enhances if the biostatisticians have a substantial knowledge of the molecular biology, the biological mechanisms and the genetics of cancer.

With advances in the medical science and the associated technology, the types of data which statisticians are seeing and the types of issues they face are becoming more complex. As medical science becomes more complex the demands for statistical expertise will increase as well. In modern biostatistical research, the statistician scientist must be trained not only in the theory of statistics, but also be an interested and knowledgeable scientist, as well as having the interpersonal skills to work with investigators who are not trained as statisticians.

The outcomes used in clinical trials and epidemiological studies are becoming more diverse. There is a need for more advanced statistical methods and individuals that understand their use and interpretation in the context of cancer.

Another example in the advances of medical science, which are likely to have a profound effect on biostatisticians, is the area of drug development. Advances in combinational chemistry and high through-put assays will inevitably lead to more potential therapies to evaluate on the limited number of patient resources available. These high through-put technologies will lead to very high dimensional datasets, an unfamiliar problem for the classical clinical biostatistician. Future therapies are also likely to be increasingly based on gene and protein targets. Thus, genetic or protein expression data will be the likely type of information used to evaluate therapy as well as the traditional response rate and survival time.

Another area where involvement of statisticians is crucial, is for research that uses data from electronic medical records, claims data and cancer registries. Data from these sources can be used for many different purposes, including patterns and trends in cancer incidences, medication usage, as well as discovery of associations and evaluation of therapies. However, because of the nature of the data it is big, messy and not collected for research purposes, there are considerable challenges.

We believe that the training program is quite novel and unique amongst departments of Biostatistics. The program is designed to respond to the changing environment for biostatistics, and the special need for biostatisticians to understand biology more than ever.
The overall purpose of this training program is to provide biostatisticians with the requisite scientific knowledge to understand current issues in cancer research, and to provide training in statistical and epidemiological techniques and research methodology related to cancer. The methods of education will include formal coursework in biostatistics, epidemiology, and biology relating to cancer; interdisciplinary seminars on current research and biostatistical topics in cancer research; a Cancer Biostatistics Seminar; a journal club; mentored research in collaboration with cancer investigators; and presentation of research products in national statistical and cancer conferences.

Training Environment at the University of Michigan

The primary biostatistical training facility will be the Department of Biostatistics in the School of Public Health at the University of Michigan. The department is top ranked in the United States, with many internationally regarded faculty and a vibrant research and teaching program. It is one of the six departments in an outstanding School of Public Health, with close links to the Statistics Department and the Bioinformatics Program at the University of Michigan. It is located in close proximity to the University of Michigan Medical Center and the Cancer Center.

The Department of Biostatistics is a leader in the development and application of statistical methods in the biomedical sciences. It is an expanding department with over 40 faculty and more than 130 graduate students. The faculty includes leading researchers in the areas of survival analysis, missing data, longitudinal and correlated data analysis and statistical genetics. It has extensive collaboration with The University of Michigan Medical Center in many areas, including cancer, diabetes, kidney diseases, imaging, genomics and Alzheimer's.

The Comprehensive Cancer Center at The University of Michigan is a very successful cancer center with over 70 million dollars in grant funding. The University of Michigan is consistently ranked very highly in cancer research funding from the NCI. It has an extensive research program, including clinical research in many disease sites (prostate, breast, head and neck, skin cancer, leukemia etc.) It has successful programs in basic science, behavioral science, epidemiology and genomics. It has very active research programs in imaging, genomics and proteomics.

Many faculty and students from the Department of Biostatistics are involved in cancer related research projects. The list below gives cancer related research of faculty in the Department of Biostatistics:

Jeremy Taylor: Methods for evaluating biomarkers, cure models, phase I design, longitudinal modelling and risk prediction models.

Alex Tsodikov: Demography of cancer, cellular stochastic models and survival analysis.

Tom Braun: Novel designs for phase I studies.

Tim Johnson: Bayesian modelling of spatial and imaging data.

Bhramar Mukherjee: Methods for estimating gene-environment interaction, data integration.

Rod Little: Missing data, survey methods of casual modelling in cancer.

Kerby Shedden: Computational methods for high dimensional genomics and imaging data.

Hui Jiang: Computational methods for genomics data.

Mousumi Banerjee: Health services research, tree based survival analysis methods.

Yun Li: Causal Inference.

Phil Boonstra: Shrinkage estimators, hierarchical models, and problems of measurement error, Cancer-related applications, including cancer epidemiology and cancer genetics/genomics.

Kelley Kidwell: Survival analysis, adaptive treatment strategies, and applications to cancer research.

Lili Zhao: Bayesian statistical methodology and its application in cancer research.

Matthew Schipper: Early phase oncology trial design predictive risk modeling and use of biomarkers to individualize and adapt treatment.

Participating Faculty

The faculty associated with the training program consist of primary faculty and supporting faculty. The primary faculty are biostatisticians and epidemiologists, who participate in cancer research, and can direct the statistical research activities of trainees. The supporting faculty are cancer researchers who can provide scientific expertise and researcher opportunities for the trainees.

Program Director Jeremy Taylor has led the Training Program in Cancer Research since 2002. Dr. Phil Boonstra serves as Program Associate Director, working with Dr. Taylor to organize and manage the program. Dr. Taylor also leads a Steering Committee that includes, in addition to himself and Dr. Boonstra, members who bring valuable and wide-ranging expertise to the program. Along with the members of the Steering Committee, additional Primary Faculty serve as advisors to the program trainees as well as teach the Biostatistics courses that are required for the program. Supporting faculty are available to mentor trainees, as well as to provide projects and hands-on experience.

Primary Faculty

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Program Description

Overview of the departmental program

The graduate program in the Department of Biostatistics provides individualized programs of study directed towards applications of Biostatistics in a spectrum of biomedical areas, including health services, epidemiology, genetics, survey, population studies, and clinical research. The existing program consists of three components: (1) A Biostatistics Core of courses required by all students; (2) a Breadth/Depth requirement of 15 credit hours of formal course work in biostatistics beyond the required core courses; the depth requirement must be based on a coherent advanced quantitative area on which study will be focused; and (3) A cognate requirement (a minimum of 9 credits) in an area of application of biostatistics.

Specific Cancer Training

The goals of the training program are to give students who are obtaining a degree in Biostatistics, (i) a solid understanding of cancer biology, (ii) experience and ability to communicate and collaborate with cancer scientists, (iii) understanding of recent developments in cancer requiring innovative statistical research and (iv) independent research skills to identify new statistical research problems arising out of cancer research and the ability to write research papers and grant applications.

The proposed training will adopt the basic structure of the existing graduate program, but will tailor the breadth/depth and cognate components to provide basic science, epidemiological and statistical training appropriate for a cancer researcher. The trainees may be required to

take additional didactic courses, beyond those required to satisfy the cognate requirement, to enhance their knowledge in the areas of molecular biology, cancer biology and cancer genetics.

The potential courses are described in the Coursework tab on cognate courses. The trainee will also be expected (a) to participate in interdisciplinary seminars involving topics in cancer research; (b) to become involved in a current cancer research project, mentored jointly by a supporting faculty member of the Cancer Center and a member of the Biostatistics faculty, to apply biostatistical skills learned as part of his/her training and to learn more about cancer as a participant in the research process; and (c) to develop a thesis topic in an area of biostatistics of particular relevance to some aspect of cancer studies.

Courses

The required Biostatistics class for trainees is a "Statistics in Cancer" seminar class, which will be held every other semester. The seminar class will be a mechanism for the trainees to interact with each other, the program director and the associate director.
This course will allow the trainees to learn about specialized topics in Cancer Research and to see specific examples of high level biostatistics input in a Cancer Research project.
Presentations will be made by the trainees, instructor and guest speakers on current research. We will bring in Cancer statisticians to give seminars to the trainees. The trainees will have the opportunity to meet with visiting speakers.

The Biostatistics department teaches a broad range of classes every year, including core and elective classes. The elective classes that are potentially relevant to the training program are:

- Biostatistics 606: Biocomputing
- Biostatistics 619: Clinical Trials
- Biostatistics 675: Survival Analysis
- Biostatistics 646: High throughput molecular genomics and Epigenomic Data Analysis.

Other Program Activities

Trainees will be expected to participate in a Journal Club, in which presentations will be made by trainees on an article from recent literature. There will be occasional tours of laboratories, to expose trainees to the type of equipment and technology that is used in Cancer research. Other programmatic activities includes presentations on topics such as, "what is on an NIH grant", "How to make a poster" and "Recent results of clinical trials"

Collaborative Experience

An important part of this training program is collaborative experience. We will organize for each trainee hands on experience with Cancer data. This experience will consist of spending time in a collaborative research setting working on one of the supporting faculty member's research projects. It will be the responsibility of the program director to place each of the trainees in a research setting. This will be done on an individual basis and will depend on the

needs, ability, experience and interests of the trainee, as well as the availability and needs of the Cancer researcher. This part of the training will be mentored jointly by a member of the Cancer Center (a supporting faculty member) and a member of the key Biostatistics faculty from the steering committee.

Time in Program

We would expect each trainee to be supported financially by the program for two to three years, by which time they will have completed most of their exams, finished their cognate course work relating to cancer, had experience working with a cancer investigator, and be working on their dissertation.

Dissertation Research

It is expected that the topic of a student's Ph.D. dissertation would be relevant to cancer. The primary Ph.D. advisor can be anyone eligible from the Department of Biostatistics. The expectation is that it would be someone who has a research interest in cancer. There would be at least one member of the training program steering committee on the student's Ph.D. dissertation committee.

Trainee Travel

Active and early participation in annual meetings of the American Statistical Association, the Biometrics Society, the American Public Health Association, specialized clinical trials and Cancer meetings will be encouraged. We believe this to be a very useful educational tool as it exposes the student to a broader understanding of the meaning and role of statistical science. We would expect the more experienced trainees to present papers at these meetings.

Opportunities after Traineeship

Upon completion of training, graduates of the program are expected to take positions in academia, government, and industry. Graduates are expected to be involved in a host of research areas which may include: design and analysis of epidemiologic or clinical studies, bioinformatics, collaboration with geneticists and basic science researchers.

Coursework

Trainees will take the regular coursework required by the Department of Biostatistics. Trainees will be expected to take additional coursework to learn about the science and biology of cancer. These courses can count towards the School of Public Health cognate requirement.

Cognate Requirement

The School of Public Health cognate requirement is that students take 12 units of credit outside of their main area of study (9 cognate credits plus the EPID requirements). Knowledge of basic

epidemiology (Epidemiology 601) is required plus two or three other courses. The Epidemiology requirement can be satisfied by taking Epidemiology 621 instead of Epidemiology 601. In addition to this SPH requirement, students in this training program would be required to take additional courses to bring their knowledge of molecular biology, cancer biology and cancer genetics to a higher level. A required course for all trainees would be Epidemiology 621, Cancer Epidemiology. After EPID 601 and 621 the recommended classes are Bioinformatics 523 and Cancer Biology 554. The other courses required by the trainees of this training program would vary depending on the background biological knowledge of the trainees and their interest.

The course descriptions of possible cancer related courses are given below.

Cancer Related Courses

Environmental Health Sciences 504: Genes and the Environment
In past years disease causation frequently was thought of as a "dichotomy" between genes ("nature") and the environment ("nurture"). More recently this view has been replaced with a more holistic perspective that emphasizes the importance of interactions between genes and environmental and/or occupational exposures. The focus of this course will be on interaction between genes and specific environmental and/or occupational exposures. The course will consist of detailed evaluation of specific examples of gene-exposure interaction (e.g., beryllium-related lung disease, peripheral neurotoxicity from organophosphate pesticides, bladder cancer and amine exposure) the underlying science of such examples, medical consequences, potential policy and social implications of current and future scientific knowledge, and review of current and pending legislation that address these issues. The course will meet for one two-hour session per week, and will be conducted in an advanced seminar-style format. Student will be expected to make presentations and lead discussion, in addition to presentations by faculty and outside guests. Student evaluations will be based on written reports, class participation and class presentation.

Environmental Health Sciences 602: Essentials of Toxicology
This course examines basic concepts of occupational and environmental toxicology, including uptake, distribution, metabolic conversion, and elimination of toxic agents, as well as the fundamental models used to describe the interaction of xenobiotic agents with biological systems. The course focuses on the application of these concepts to the assessment of exposures, estimates for risk of disease, establishment of appropriate limits on exposures and ambient levels of toxic materials/agents, and understanding and prevention of mortality and morbidity resulting from environmental exposure to toxic substances through a case format study.

Epidemiology 511: Introduction to Public Health Genetics
This course is designed for those interested in a basic understanding of human genetics who have had only a very limited exposure to biologic sciences. This course will cover the basics of genetics at both the molecular and population level. In addition to the basic science, some

ethical, legal, and social implications of genetics research will be examined. Examples relevant to public health will be emphasized.

Epidemiology 512: Biological Basis of Disease
This course will examine the major pathological processes of interest to practitioners of Public Health. Specifically, the physiological mechanisms of disease will be examined with a view to understanding the cellular, biochemical and molecular processes that underlie diseases of major public health impact.

Epidemiology 515: Genetics in Public Health
This course is designed for students with biology or genetics background, that are interested in understanding genetics in public health. This course will provide an in depth examination of genetics in public health including newborn screening diseases and practices, fundamentals of population genetics, and the genetics of common chronic diseases.

Epidemiology 516: Genomics in Epidemiology
This course relates genomics to the core public health discipline of epidemiology emphasizing the use of genomics to help describe disease frequency and distribution and to gain insights into biological etiologies. Topics include genetic material in disease, in families and in populations; the investigation of multifactorial traits; model-based linkage analysis; model-free linkage analysis; segregation analysis; allele association and linkage disequilibrium; and gene-gene interactions and gene-environment interactions. Issues related to implementing studies are considered.

Epidemiology 621: Cancer Epidemiology
The course will review the socio-demographic magnitude of cancer, basic concepts of cancer biology and the causes of cancer. Methods for evaluating genetic factors, tobacco, alcohol, radiation, chemicals, pharmaceuticals, viruses and nutrition will be reviewed in lectures and by classroom discussion of selected publications.

Epidemiology 636: Cancer Risk and Epidemiology Modeling
This course will introduce 1) the concepts of multistage carcinogenesis and the analysis of cancer epidemiology using mathematical models of carcinogenesis; 2) the analysis of cancer prevention strategies using Markov cancer natural history models. Students will learn how to develop and fit multistage and cancer natural history models in R.

Bioinformatics 523: Bioinformatics Basic Biology Lab
Introduces basic biology to graduate students without any prior college biology. Geared towards students pursuing training in Bioinformatics or Biostatistics who have quantitative training (computer science, engineering, mathematics, statistics, physics). After a brief introduction to organic and biochemistry, boot camp will have lectures on molecular biology, cell biology and laboratory tools used in both, as well as introductory molecular biology laboratory experiments.

Bioinformatics 525: Foundations in Bioinformatics and Systems Biology.
This course is comprised of three modules. Each module is one credit hour and consists of one lecture and one lab.

- Module One: Bioinformatics on the Web- An introduction to the web resources and tools that researchers use for the retrieval of public data and the analysis of public and laboratory data. Includes: accessing NCBI data resource, related tools, other public databases, and the analysis of sequence data in a biological context.
- Module Two: Introduction to Statistics- The section on statistics starts from first principles- probability distributions, sampling, independence, estimation, confidence intervals, and hypothesis tests. Concepts are illustrated using biological examples including distributions of phenotypes in populations, treatment comparisons, genetic association tests, and multivariate profiles of "omics" data. More advanced topics may include simultaneous inference in screening studies, survival analysis, or regression techniques for decomposing variance in multi-factor experiments.
- Module Three: Bioinformatics and Systems Biology: Integration of genome-wide data sets into their functional context. Analysis of protein-protein interactions, pathways and networks. Modeling and simulation of systems and networks. Example applications from translational medicine and cell biology.

Bioinformatics 527: Introduction to Bioinformatics and Computational Biology
This course introduces students to the fundamental theories and practices of Bioinformatics and Computational Biology via a series of integrated lectures and labs. These lectures and labs will focus on the basic knowledge required in this field, methods of high-throughput data generation, accessing public genome-related information and data, and tools for data mining and analysis. The course is divided into four areas: Basics of Bioinformatics, Computational Phylogeny (includes sequence analysis), Systems Biology and Modeling. There will be weekly homework, two take-home exams, and students will prepare and present group projects.

Cancer Biology 554: Cancer Pathogenesis and Treatment
This is a team-taught class comprised of a combination of didactic and paper-based discussions. Topics covered are:

- The Pathogenesis of Cancer
- Examples of Neoplastic Disease
- Traditional Cancer Therapies
- Emerging Therapies for Combating Cancer

Admission/Application Procedure

Applicants who are interested in the Cancer/Biostatistics training program should contact the training program director, in addition to applying to the department. The training program is restricted to students who are citizens or permanent residents of the US.

Departmental Admission Requirements

Admission to the graduate program in the Department of Biostatistics is the responsibility of the faculty in the department. An admissions committee undertakes the task of screening all applicants to the department. The procedures for applying and the requirements for admission are described on the department's website. The admissions committee takes into consideration undergraduate and graduate transcripts, GRE scores, letters of recommendation, personal statement of research interest, experience and goals.

Students applying to the Epidemiology Department will be responsible for following those department's admissions policies and guidelines. For more information, please the Epidemiology Department webpage.

Training Program Requirements

All trainees in the Cancer/Biostatistics training program will be expected to display an interest in cancer research. Prior knowledge of cancer is not required.

Applications to the Cancer/Biostatistics training program should be sent to:

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A statement should be included explaining the applicant's interest in the training program. This can be incorporated in the personal statement. The steering committee will select trainees based on their academic credentials and potential, and their interest or potential for interest in cancer.

Links

- University of Michigan School of Public Health
  https://sph.umich.edu/
- Department of Biostatistics
  https://sph.umich.edu/biostat/
- Department of Epidemiology
  https://sph.umich.edu/epid/
- Department of Statistics
  https://lsa.umich.edu/stats

Other Sites

- University of Michigan Cancer Center
  https://www.mcancer.org/
- National Cancer Institute
  https://www.cancer.gov/
- American Statistical Association
  http://www.amstat.org/
- International Biometrics Society
  https://www.biometricsociety.org/