

Position Paper: Ph.D. Training in Cancer Biology

Frank M. Torti, Dario Altieri, James Broach, Hung Fan, Michael Lotze, James Manfredi, Lynn Matrisian, Dihua Yu and Amato Giaccia for the Cancer Biology Training Consortium

Affiliation of authors: Department of Cancer Biology, Wake Forest University School of Medicine (FMT); Department of Cancer Biology, University of Massachusetts Medical School (DA); Department of Molecular Biology, Princeton University (JB); Department of Molecular Biology and Biochemistry, University of California Irvine (HF); Department of Surgery, University of Pittsburgh (ML); Department of Oncology Sciences, Mount Sinai School of Medicine (JM); Department of Cancer Biology, Vanderbilt University (LM); Department of Cancer Biology, University of Texas/M.D. Anderson Cancer Center (DY); Department of Radiation Oncology, Stanford School of Medicine (AG)

Correspondence to: Amato J. Giaccia, Ph.D., Director, Cancer Biology Graduate Program, Stanford University School of Medicine, Department of Radiation Oncology, CCSR - South, Room 1255, 269 Campus Drive, Stanford, CA 94305-5152 Telephone 650-723-7366 (e-mail: giaccia@stanford.edu)

Introduction

Cancer is one of the major afflictions of mankind. In recent years, knowledge about the origins, growth, tissue interactions and spread of cancer has burgeoned. Descriptive knowledge has been replaced by mechanistic understanding of cancer behavior at a molecular, cellular and organismal level. Concomitant with the development of this extensive body of knowledge has been the development of scientists devoted to the elucidation and solutions of problems of cancer biology.

Cancer biology is a unique, interdisciplinary biomedical science that encompasses experimental approaches and didactic knowledge from biochemistry, cell biology, epidemiology, genetics, immunology, microbiology, pharmacology, molecular biology, pathology and physiology. Cancer biology also is closely allied to the clinical oncologic sciences that are involved in human cancer prevention, detection, diagnosis and treatment.

The Cancer Biology Training Consortium involves leaders of pre-doctoral and post-doctoral research and educational training at institutions in the United States. Recognizing that cancer biology is a distinct, but highly interdisciplinary scientific discipline, our goal is to define a curriculum that will train new investigators intensively in fundamental and translational approaches to cancer biology and to provide lifelong skills that will enable students to contribute to extinction of cancer as a major problem of human health.

To this end, a major goal of the Consortium is to establish guidelines for trainees in cancer biology including:

- Education in the experimental science of cancer biology that encompasses both didactic and non-didactic learning
- Research training in the experimental science of cancer biology
- Career development as independent cancer biologists

These aims are closely allied to those of the National Cancer Institute (NCI). The NCI provides funding for both individual and institutional pre-doctoral and post-doctoral training grants with the intent to develop individuals with long term commitment to cancer research. The following recommendations for training of Ph.D. students in cancer biology represent the deliberations and consensus of a working group of Cancer Biology Chairs and Program Directors that represent more than 50 academic medical centers.

Part I: Foundation Courses

The following subjects are considered prerequisites for training in cancer biology.

These may be satisfied prior to entry into a cancer biology program or during the first year of graduate study as individual courses or as part of a core curriculum.

- Genetics
- Cell and Molecular Biology
- Biochemistry
- Experimental Design / Biostatistics
- Ethics

Part II: Essential Elements of Training in Cancer Biology

A1. Training in Basic Science of Cancer Biology

Students need to be exposed to a discipline that emphasizes cancer in the context of human disease. A cancer biology curriculum should provide significant exposure to the core areas of cancer training listed below. How these topics are divided into courses is left to the individual training programs.

- Dysregulation of Signal Transduction Pathways
- Oncogenes and Tumor Suppressor Genes
- Control of Cell Proliferation, Cell-Cycle and Cell Death
- Carcinogenesis, DNA Damage and Repair
- Tumor Angiogenesis, Invasion and Metastases
- Cancer Virology
- Histopathology of Neoplasia
- Tumor Microenvironment and Stromal interaction
- Cancer Genetics and Epigenetics
- Cancer Immunology
- *In vitro* and *in vivo* Tumor Models
- Cancer stem cells

A2. Training in the Translational Science of Cancer Biology

A unique aspect of training in cancer biology is the focus on human cancer. Therefore, in addition to these basic topics in cancer biology, a cancer biology training program should provide exposure to the following topics that provide a bridge between the fundamental biology of cancer and clinical

cancer. Core elements of this bench to bedside (and vice versa) training would include:

- Molecular diagnosis and prognosis, including unbiased approaches to discovery using genomic, proteomic and metabolomic analyses
- Molecular imaging
- Systems Biology and Bioinformatics
- Bioenergetics, endocrinology and nutrition, as they are altered in cancer
- Therapeutic strategies: Targeted and cytotoxic therapies, including immunotherapy, hormone therapy, small molecules, proteins, RNAi, etc.
- Chemoprevention

A3. Training through exposure to the problems of human cancer

Interaction of cancer biology trainees with clinicians is encouraged, and might take one or more of the following forms:

- Student Attendance at Tumor Boards. A student would choose one particular cancer that they are interested in studying and attend an interdisciplinary tumor board to understand the clinical presentation of the disease, diagnostic and imaging tests, as well as patterns of cancer dissemination and the clinical management of the cancer.
- Observing cancer clinicians manage patients. A student may “shadow” an oncologist in their management of specific cancer

patients. An alternative possibility is matching a graduate student with an oncology fellow/resident as they develop and present cases to attending physicians.

- **Clinical Trial Team Experience.** A student may be involved in the development of a cancer clinical trial with a correlative component. The student might help with background and introductory materials, for example. This would provide the student insight into how a therapeutic is developed and provide experience in a multidisciplinary team approach to translational research.

Some graduate programs are not associated with medical schools. In this case, graduate students should rely on a combination of invited speakers, local medical centers and support groups for cancer patients and their families.

B. The Laboratory Research Experience in Cancer Biology

- **Rotations:** Students are encouraged to experience at least three research rotations, thus exposing the students to different aspects of cancer biology, regardless of when they decide on their primary laboratory mentor. Multiple rotations foster learning of multiple approaches to solving complex biological problems, as well as mastering additional techniques.
- **Thesis Research:** No matter how basic the research thesis, it should address an important scientific issue that the student can understand and articulate as a problem in cancer biology. Cancer biology research is defined as any research

investigating the molecular, cellular and organismal basis of tumors, then prevention, detection and treatment.

- **Advancement to Candidacy:** There are many variations of the preliminary examinations. However, three components that are recommended as a part of the examination are 1) a written proposal in the form of an abbreviated “NIH-style” grant on a defined problem in cancer biology that the student proposes to study, 2) an oral presentation and defense of that proposal, and 3) demonstration of general knowledge of cancer biology.
- **Dissertation Research Advisory Committee:** The faculty preceptor that will advise the student on their thesis research must be conducting cancer-related research as defined above. In cases where the principal laboratory preceptor is not a member of the thesis advisory committee, at least one member should have a cancer related research focus. Additionally, in certain circumstances, it might be useful to have a physician on a thesis committee to provide clinical insight into the thesis question. The Consortium recommends that the meetings of this committee should be held at least once a year, and at the end of these meetings progress should be assessed and reported to the mentor and student formally.

Part III: Other Research-Related Experiences in Cancer Biology

In addition to formal course work and research training, a fully developed program should provide exposure to advances in the discipline as a whole:

- **Research Presentations:** An essential element of training for students should be an opportunity to present their ongoing research at institutional, national and/or international cancer meetings at least yearly.
- **Journal Clubs:** Journal clubs are an essential element of student training. They provide needed exposure to new research methodologies and their application to specific cancer problems, hone critical thinking, enhance communication skills, and provide lifelong tools for keeping current in cancer research.
- **Seminar Speakers:** Seminars provide students with the opportunities to interact with leaders in the cancer field. Every effort should be made to have both local and external speakers, and to have the students host and meet with speakers before or after the formal seminar. Such meetings provide an opportunity for students to obtain career counseling from invited speakers.
- **Training Courses:** Courses that allow for intensive investigation of a particular subject matter, often requiring immersion in a topic for several weeks or months, can complement education at the student's home institution. These courses can be particularly valuable if knowledge on a certain technique or topic is limited at the student's institution. Examples of such intensive study are the courses given at Woods Hole, the Jackson Lab, the AACR or Cold Spring Harbor.
- **Teaching Cancer Biology:** A teaching experience for graduate students in which the student lectures on a topic in cancer biology is highly encouraged. This experience could be fulfilled by serving as teaching assistants for graduate or undergraduate classes in cancer biology or cancer-related courses.

Summary

Cancer biology is a young field. The science continues to evolve rapidly. Students now identify the field of cancer biology as a primary area of lifelong learning and research; they often make this career choice early in their scientific training. The goal of the Cancer Biology Training Consortium is to promote consistent, high quality training for this new generation of cancer biologists. This curriculum for these students recommended here is based on a consensus of viewpoints of cancer biology educators throughout the United States, and provides the framework for training in this distinct scientific discipline.

In support of this manuscript:

Steven Akman, M.D.	Wake Forest University School of Medicine
Dario Altieri, M.D.	University of Massachusetts Medical School
James Alwine, Ph.D.	University of Pennsylvania Cancer Research Institute
Don Ayer, Ph.D.	University of Utah
Richard Baer, Ph.D.	Columbia University
Steven Balk, M.D., Ph.D.	Beth Israel Deaconess Medical Center
Bruce Blumberg, Ph.D.	University of California, Irvine
Susann Brady-Kalnay, Ph.D.	Case Western Reserve University School of Medicine
James Broach, Ph.D.	Princeton University
James Casey, Ph.D.	Cornell University College of Veterinary Medicine
Sunita Chaudhary, Ph.D.	University of Medicine and Dentistry of New Jersey
Jonathan Cooper, Ph.D.	Fred Hutchinson Cancer Research Center, Seattle
Jess Cunnick, Ph.D.	West Virginia University
Beverly Delidow, Ph.D.	Marshall University, Joan C Edwards School of Medicine
Channing J. Der, Ph.D.	University of North Carolina, Chapel Hill
Frederick Domann, Ph.D.	University of Iowa
Daniel Donoghue, Ph.D.	University of California, San Diego
Alan Eastman, Ph.D.	Dartmouth Medical School
Hung Fan, Ph.D.	University of California, Irvine
Amato J. Giaccia, Ph.D.	Stanford University
Wade Gibson, Ph.D.	Johns Hopkins University
Barbara Graves, Ph.D.	University of Utah, Huntsman Cancer Institute
Kathleen Green, Ph.D.	Northwestern University
Geoffrey Greene, Ph.D.	University of Chicago
Diane Hayward, Ph.D.	Johns Hopkins University
David Helfman, Ph.D.	University of Miami, Miller Medical School
Michael Imperiale, Ph.D.	University of Michigan, Ann Arbor
Susan Kane, Ph.D.	Beckman Research Institute of the City of Hope
Sohaib Khan, Ph.D.	University of Cincinnati
Barbara Knowles, Ph.D.	Jackson Laboratory
Paul Lambert, Ph.D.	University of Wisconsin, Madison
Timothy Lane, Ph.D.	University of California, Los Angeles
Edmund Lattime, Ph.D.	University of Medicine and Dentistry of New Jersey
Michael Lotze, M.D., Ph.D.	University of Pittsburgh
James Manfredi, Ph.D.	Mount Sinai School of Medicine
Susan Marriott, Ph.D.	Baylor College of Medicine
Jesse Martinez, Ph.D.	University of Arizona Cancer Center
Lynn Matrisian, Ph.D.	Vanderbilt University
W. Stratford May, Jr., M.D., Ph.D.	University of Florida
Maureen Murphy, Ph.D.	Fox Chase Cancer Institute
Marja Nevalainen, M.D., Ph.D.	Thomas Jefferson University
Matthew O'Connell, Ph.D.	Mount Sinai School of Medicine
Anna Riegel, Ph.D.	Georgetown University
Ann Roman, Ph.D.	Indiana University School of Medicine
Yoji Shimizu, Ph.D.	University of Minnesota
William Sugden, Ph.D.	University of Wisconsin, Madison
James Trempe, Ph.D.	University of Toledo
Frank M. Torti, M.D.	Wake Forest University School of Medicine
Dennis Watson, Ph.D.	Medical University of South Carolina

Scott Weed, Ph.D.,
Zena Werb, Ph.D.
Kenneth Wright, Ph.D.
Dihua Yu, Ph.D.

West Virginia University
University of California, San Francisco
H. Lee Moffitt Cancer Center and Research Institute
University of Texas, MD Anderson Cancer Center