2011

Chemistry/Biology Interface Training Program (CBITG)

Goals of the Program and Rationale for the Program Organization

Predoctoral trainees will be selected from a pool of graduate students who have been recruited by the Chemistry, BMBB, Medicinal Chemistry and Microbiology Departments, at a stage in their graduate careers when their talents and motivations can be gauged by their performance in University of Minnesota coursework and their interactions with several of the faculty. Thus, trainees will generally be chosen from the pool of graduate students in participating departments at the end of their first or second year. Once appointed, trainees will become immersed in an enriched menu of training experiences. After a maximum of two years' support by the training grant, students will normally be supported by the NIH (or other) research grants of their primary advisors. *The defining characteristic of our program will be to continue to allow first-rate students to grow into accomplished professionals both in their primary area of interest (e.g., synthetic/mechanistic chemistry, molecular biology, mechanistic enzymology, medicinal chemistry) and in a complementary field by cross-discipline research interactions and experiences.*

Research Opportunities and Cross-Discipline Training

Research opportunities are available in each of 30 training faculty laboratories. *Each trainee will have a research advisor in his/her major field of interest and a coadvisor in the complementary area chosen from among the members of the CBITG faculty.* As an additional mechanism to ensure cross-training, the trainee will generally spend a significant period of time during their training period (i.e. ~3 months) in the laboratory of the co-advisor to learn skills in the other discipline. In other words, the trainee's project will be set up to have both chemistry and biology components, and the trainee will be involved in both aspects. Thus, trainees would not only develop skills corresponding to their natural background and interests, but also become knowledgeable and proficient in new research environments. By spending a significant amount of time in a laboratory other than that of their primary advisor, students would learn new techniques and experience first-hand the obstacles, failures, tricks, and triumphs of the 'other half' of the chemistry/biology interface.

Due to the unpredictable nature of scientific research, a trainee's project may either move forward too slowly (e.g., a total synthesis is not completed in the first two years so biological testing is not possible), or move in a direction that is not compatible with hands-on cross training in the co-advisor's lab during the 2-year period of training grant support. In these cases, the cross-training will be expected to occur later in the student's graduate training. To ensure that significant exposure to the complementary discipline is still received during the period of training grant support, *all trainees will be asked to attend group meetings in the co-advisor's lab on a regular basis and also to present their work at regular intervals. Students will be expected to participate in the planning and running of the Annual Training Grant Symposium (see http://www.chem.umn.edu/bio/symposium2011) and attend appropriate seminars in the disciplines of their advisor and co-advisor.*

Coursework

The program described below is based on a requirement of six semester courses as the minimum for an acceptable graduate program. *The training program requires that at least two of these six courses will be taken in the complementary discipline.* In other words, students whose primary focus is biochemistry will be required to take at least 2 chemistry and medicinal chemistry courses, whereas students whose primary focus is chemistry will be required to take at least 2 biochemistry or biology courses. All trainees are also required to take an ethics course by the end of the first year of their traineeship. Such courses are currently offered by the Chemistry and BMBB Departments.

All trainees will be required to take the following course:
Chem 8011 Mechanisms of Chemical Reactions: A graduate chemistry core course that covers principles that govern organic, inorganic, and enzyme reaction mechanisms.

All trainees will be required to take one of the following courses:
BioC 8002 Molecular Biology: A graduate biochemistry course that covers the fundamentals of modern molecular biology at an advanced level. This course is appropriate only for Chemistry students with a solid background in the fundamentals of biochemistry.
BioC 4331 Biochemistry I: Structure, catalysis, and metabolism in biological systems. Advanced survey of structure/catalysis, metabolism/bioenergetics.
BioC 4332 Biochemistry II: Molecular mechanisms of signal transduction and gene expression. Advanced survey of molecular biology, mechanisms of gene action, and biological regulation.

To satisfy the diverse needs of our trainee population, four of the following courses can be chosen to complete the minimum course requirements for a graduate program:

Chem 8411 Introduction to Chemical Biology: Covers the chemistry of amino acids, peptides, proteins, lipids, and carbohydrates; enzyme chemistry and fundamentals of enzyme catalysis; overview of gene cloning and basic techniques in molecular biology.
Chem 8412 Chemical Biology of Enzymes: Covers structure, thermodynamics, and kinetics of enzymes. Also presents an overview on the major techniques in enzyme structure determination: CD, UV, EPR, NMR (solution and solid state), X-ray crystallography.
Chem 8413 Nucleic Acids: Covers the chemistry and biology of nucleic acids, including structure, thermodynamics, reactivity, DNA repair, chemical oligonucleotide synthesis, antisense approaches, ribozymes, techniques used in nucleic acid research, interactions with small molecules and proteins.
Chem 8735 Bioinorganic Chemistry: Covers metalloenzyme structure and function, model complexes, metal-nucleic acid interactions, and metals in medicine.
Chem 8134 Bioanalytical Chemistry: Covers analytical techniques with important applications to biochemical problems.
BioC 5527 Introduction to Modern Structural Biology: Methods employed in modern structural biology to elucidate macromolecular structures. Primary focus on X-ray diffraction, nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry. Principles underlying structural biology and structure/function relationships.
BioC 5528 Spectroscopy and Kinetics: Biochemical dynamics from perspectives of kinetics and spectroscopy. Influence of structure, molecular interactions, and chemical transformations

on biochemical reactions. Focuses on computational, spectroscopic, and physical methods. Steady-state and transient kinetics. Optical and magnetic resonance spectroscopies.
BioC 5331 Macromolecular Crystallography I: Fundamentals and Techniques. Macromolecular crystallography for protein structure determination/engineering. Determining macromolecule structure by diffraction.
BioC 5332 Macromolecular Crystallography II: Techniques and Applications. Determining structure of macromolecule by diffraction. Using software in macromolecular crystallography.
BioC 8213 Advanced Molecular Biology: A special topics course based on the primary literature. Current topics such as DNA replication, recombination and gene conversion, regulation of gene expression, chromatin structure and transcription, developmental gene regulation, organellar gene expression, RNA splicing, initiation/control of translation, animal viruses, transposable elements, somatic recombination.
BioC 8216 Signal Transduction and Gene Expression: Covers the regulation mechanisms of signal receptors and second messengers, including cyclic nucleotides, calcium, and phosphoinositol derivatives; polypeptide and catecholamine hormone-mediated processes; molecular basis of neurotransmitter signaling and ion-channels.
GCB 8131 Advanced Genetics I: Covers the comparative organization of genetic material in prokaryotic and eukaryotic organisms with an emphasis on mutation, complementation, and recombination as operational criteria for genetic analysis.
MedC 5245/Chem 5245 Introduction to Drug Design: Concepts that govern design/discovery of drugs. Physical, bioorganic, medicinal chemical principles applied to explain rational design, mechanism of action of drugs.
MedC 8700/Chem 8700 Combinatorial Methods in Chemical Biology: The emphasis in this course is on understanding the general principles of current combinatorial methods for the generation of biological and chemical libraries with an emphasis on their utility in biology and drug design.

Trainee Candidates
Trainees are selected by an ad hoc committee appointed by the CBITG Director. *Nomination materials will consist of the results of all courses taken during the first year, two nomination letters (typically from the advisor and the co-advisor), and a short (1-2 page) description of the research project that is written by the candidate and clearly outlines the goals of the research project and its cross-disciplinary features.* A candidate will not be appointed a trainee unless the project has both chemistry and biology components. Because of the large number of highly qualified candidate trainees anticipated, each trainee will be appointed with the likelihood of receiving two years (24 months) of support.

Monitoring Trainee Progress
Re-appointment for the second year of CBITG support requires that the trainee submit evidence that satisfactory progress has been made toward meeting the departmental requirements for completion of written and oral Ph. D. candidacy examinations and that the trainee has actively participated in training activities. Each year, the trainee will submit a short written report to the training grant Director detailing research progress, current and future directions, and efforts to incorporate cross-disciplinary training. A meeting between the trainee, the trainee's advisor and co-advisor, and the steering committee will be held to discuss the report and the trainee's

progress. These meetings will provide another opportunity for trainees to discuss their research with faculty in an informal setting, and will also provide students with valuable feedback at a relatively early stage in their graduate training. *Re-appointment for a second year will be denied if there is not satisfactory progress or a plan in place to incorporate cross-disciplinary training.*