ATP APPLICATION

(all materials due July 19, 2010)

Name of Student:_____

Pitt Student ID:_____

US Citizen* YES Permanent Registered Alien** YES

Current PhD Program_____

Current or Proposed Faculty Mentor_____

Student e-mail_____

Mentor e-mail_____

References (minimum 2):

1. Name and e-mail_____
2. Name and e-mail_____
3. Name and e-mail_____

Please also submit the following information:

1. Personal Statement from applicant, including career objectives and rationale for joining the ATP (1 page limit).
2. Brief description of research project to be completed during the training program, highlighting how it fit within the ATP goals (1 page limit).
3. Personal Statement from mentor, highlighting student strengths and how the proposed research would integrate within the ATP (1 page limit).
4. GRE/MCAT scores
5. Current student CV including presentations and publications
6. Current mentor NIH Biosketch, directed towards training grant
7. Transcripts (undergraduate and graduate)
8. Proof of Eligibility:
   *US citizen: copy of birth certificate, passport, or naturalization papers
   **Permanent Registered Alien: copy of Alien Registration card or other legal verification.

Please submit this form and have all reference letters and admission materials on or before July 19, 2010 sent to:

Wendy M. Mars, PhD
University of Pittsburgh
Department of Pathology
S411B South BST
Pittsburgh, PA 15261

Direct any questions concerning this nomination form to Dr. Mars at 412-648-9690 or wmars@pitt.edu

Background

A functional vasculature is an absolute requisite for all organs and tissues. Hence, although the term "vascular dysfunction" tends to cognitively be linked with heart disease, in reality the vasculature plays a significant role in multiple pathologies such as stroke, diabetes, and cancer. As there is a commonality to the mechanisms driving many aspects of vascular biology, a thorough understanding of vascular remodeling and regeneration can be considered as essential to all areas of biomedical research. Recognizing the general importance of vascular biology to the study of medicine as a whole, The University of Pittsburgh (**UOP**) has established a cross-campus, pre-doctoral training program focusing on both pathological and physiological aspects of vascular remodeling and regeneration. Although it is administratively housed within an established graduate program (Cellular and Molecular Pathology, or **CMP**, directed by Wendy Mars) within the School of Medicine (**SOM**) the Angiopathy Training Program (**ATP**) is closely affiliated with the University-wide Center for Vascular Remodeling and Regeneration (**CVRR**, directed by David Vorp, grant co-PI) and hence, open to graduate students working with CVRR faculty who hail from a variety of departments, who have affiliated with various programs from across the University, and who already demonstrate a commitment to the fields of vascular remodeling and regeneration. Comprehensive training will be met through a combination of an established curriculum, dedicated facilities, and an interactive training faculty. The focus of the ATP is organ-specific biology, angiogenesis, and vascular imaging. With this combination, our intent is to provide a foundation of vascular scientists able to populate all areas of biomedical research upon graduation.

Specifics of the Angiopathy Training Program (ATP)

Curriculum Rationale

The program is open to and, actively recruiting, mature (second year and beyond) students throughout the UOP. Students who enter the ATP, but who are affiliated with faculty members in one of the other UOP graduate programs other than CMP or CBMP will be required to take courses from either the CBMP or CMP "track", while simultaneously meeting any other graduation requirements their parent program may impose. *In most programs many of the core requirements are met during the first year of entry, before students are able to participate in the ATP*. Hence, this strategy allows **all** students to take advantage of ATP training and will not adversely affect the progress of those students who work with faculty that are not affiliated with CMP or CBMP.

The selection of CBMP and CMP tracks is based upon the goal of a strong background in organ/tissue-based biology in conjunction with vascular-centric training; both programs require students to take a set of core courses that comprehensively examine both normal and abnormal tissue biology. In the first year after joining ATP, those who choose the CBMP track will be expected to complete *"Cell Biology in Normal and Disease States"* (3 credits) and either *"Cell and Molecular Physiology*" (2 credits) or *"Regulation of Membrane Traffic"* (2 credits). For those who choose the CMP track, the required courses will be *"Normal Tissue Growth and Differentiation"* and either *"Molecular Pathobiology"* (3 credits), or *"Cancer Biology and Therapeutics"* (3 credits). Students on either track will also be required to take the *"Angiogenesis"* course offered through CMP (3 credits) as well as the "*Multiparametric Microscopic Imaging Course"* offered by CBMP (3 credits). In addition, during the fall and spring semesters throughout their training, all ATP students will be expected to enroll in the Pathology Research Seminar (**PRS**, q credit). PRS is formal course where students learn to "teach" and "critique" their peers by formally presenting and evaluating selected topics from the literature. Students on either track who enter ATP through any UOP program other than CMP or CBMP will also be required to exhibit proficiency in statistics, ethics, and grant writing. The former two courses are already required by most UOP training-programs. IMM offers a grant writing course (2 credits) that has students prepare a grant for submission as part of their training and which

will be used to fulfill the ATP grant-writing requirement. Finally, students in the ATP will be expected to participate in events sponsored by the CVRR, including the CVRR retreat in order to effectively network with UOP vascular scientists from all educational levels and disciplines. The ATP will also require participation in the annual CMP Research Day and retreat and strongly recommends membership in an international vascular-oriented organization such as either the North American Vascular Biology Organization (**NAVBO**), an affiliate of the American Society for Investigative Pathology (**ASIP**), the International Society for Applied Cardiovascular Biology (**ISACB**), or the American Heart Association (**AHA**).

In summary, students entering the ATP from various graduate programs are already expected to have a strong and broad-based scientific background in their chosen discipline, including preliminary laboratory research under the guidance of their ATP mentor. To develop a strong background in tissue- and organ-based biology, students will choose either a CBMP or CMP track. In either track, by completing the two required core courses, students can obtain a comprehensive introduction to both normal and abnormal organ biology. Second, in addition to a thesis project centered upon a vascular biology theme under the guidance of an ATP mentor, formal training in vascular biology will be obtained via the "*Angiogenesis"* course offered through CMP. Third, to assure advanced proficiency in basic biological imaging techniques that are crucial for vascular investigations, students will take a course in "*Multiparametric Microscopic Imaging"* that is offered through CBMP. Fourth, as the ability to formally present and critique research is essential for all scientists, each semester until graduation all ATP students will be required to participate in the PRS, a forum that continually develops these skills. This latter arrangement will have a secondary advantage of providing constant interaction between the junior and senior ATP students with both each other and, with students from other, related programs. Fifth, students will be required to complete graduate courses in statistics, ethics and grant writing as these areas are felt to be central for all biomedical disciplines. Finally, to obtain both general and vascular-specific networking experiences, ATP students will be required to participate in the annual CMP Research Day, CVRR-sponsored events (i.e. lectures, retreats and symposia) and will be strongly encouraged to participate in a vascular-oriented international organization such as NAVBO, ISACB and/or AHA.

Course Descriptions

As mentioned above, there will be two "tracks" for ATP certification, one in CMP and one in CBMP. These tracks will fulfill the graduation requirements for either CMP or CBMP, respectively, for students who enter via the IBGP or MSTP programs. Students from other programs (BioEng, EOH, PIMB) will select one of these tracks and complete additional home program requirements as necessary. The following is a short description of the various required ATP courses. A proposed timeline for IBGP students is also shown. Note that although they are not listed below, formal courses in statistics, ethics and grant writing are also offered through various UOP venues and will be required by the ATP. It is highly recommended that students take the grant writing course offered through the IMM program in the IBGP.

Courses specific to the CMP track

Molecular Mechanisms of Tissue Growth and Differentiation (required); MSCMP 2730-3 credits. The course covers the anatomy, embryology, histology, function, and growth regulation (growth factors, receptors, and signaling pathways) of various differentiated tissues (central nervous system, lung, liver, pancreas, urinary and reproductive systems, breast, endocrine system, skin, bone, skeletal muscle, bone marrow). Multidisciplinary lectures are given by the members of the various departments including pathology, cell biology and physiology, medicine, and surgery who have on going research in these areas. The course is designed to offer detailed information on specific tissues, tissue-tissue interactions, and overlapping cellular and molecular pathways that exist in multiple tissues.

Molecular Pathobiology (option 1); MSCMP 2740-3 credits. This course is structured to introduce students to the integration between basic and clinical research on the molecular pathogenesis of relevant human diseases. The course provides students with an overview of the natural history of selected diseases, their diagnosis and clinical management. This is followed by in-depth discussions concerning the pathologic substrate of the disease, with particular attention focused on molecular mechanisms of disease progression. In addition to current basic science research, students are exposed to the clinical impact of basic science discoveries upon the development of new therapeutic interventions. Discussions of current research trends and factors that enhance fundability of research projects are included. Each disease module contains lectures from the faculty followed by presentations of current research papers by the students. These presentations and discussions are peer reviewed by fellow students and faculty, forming the basis of the final grade.

Cancer Biology and Therapeutics (option 2); MSCMP 3710-3 credits. This course presents biochemical and clinical aspects of cancer biology and therapy, and is designed for graduate students training in the basic sciences or medicine. The lectures cover: the biology of normal and neoplastic cells; mechanisms of neoplastic transformation; chemical and environmental carcinogenesis; viral oncogenesis; breast and prostate cancer; chemotherapy; radiotherapy; gene therapy; tumor immunology; and nutrition and cancer.

Note: CMP track students must take either option 1 or option 2 above.

Courses specific to the CBMP track:

Cell Biology of Normal and Disease States (required); MSCBMP2880-3 credits. This course explores three topics in current day cell biology and physiology, using both lectures and "in class" discussions of primary literature. Basic biology, the cellular basis of disease processes, and recent advances in translational research that may lead to cures for common disease processes are covered. The section on stem cell biology, diabetes, and translational research focuses on understanding how cells divide and how all of the body's different tissues stem from a master cell with the potential to generate all of the different cell types present in the body. In addition to understanding normal stem cell biology, the potential for use of stem cells to regenerate organs and to cure ailments such as diabetes is explored. A section on cellular polarity explores early events in polarity establishment including endocytic signaling and establishment of specialized membrane domains in epithelia and neurons. Discussion also focuses on disease processes such as autosomal dominant kidney disease, an ailment characterized by altered and dysfunctional polarity. The third section examines ion channels and disease: CFTR and cystic fibrosis. This section explores the role of RAD in protein quality control, the traffic and transport of CFTR, the functional role of CFTR and the epithelial sodium channel in the lung, and promising new therapies to alleviate the morbidity and mortality associated with CFTR mutations.

Cell and Molecular Physiology (option 1); MSCBMP 2830-2 credits. This course consists of problem-solving sessions and examination of original papers. A main focus is on the application of modern biophysical and molecular-genetic approaches for the analysis of cellular function. Topics include: 1) membrane transport: pumps, channels and bioelectrical potentials; 2) excitable membranes; 3) regulation of ion channels; 4) absorptive and secretory functions of epithelia; 5) signal transduction; 6) molecular motors, cell motility and muscle contraction.

Regulation of Membrane Traffic (option 2); MSCBMP 2740-2 credits. This course analyzes membrane/protein traffic along both the biosynthetic and endocytic pathways. Emphasis is placed on how this traffic is regulated. Topics include the role of g-proteins (both heterotrimetric and small), coat proteins (coatamer 1 & 2 & adaptions), signal transduction cascades (PKC, PKA, IP3, etc.), and snare complexes in protein trafficking. The role of the cytoskeleton in transporting cargo and signal transduction is also discussed. Membrane traffic

in several specialized cell types is covered including polarized epithelial cells, cells of the immune system, and neurons.

Note: CBMP track students must take either option 1 or option 2 above.

Angiopathy Training Program

Proposed Curricula Time Frame for IBGP Students*

CBMP Track		CMP Track	
Course	**Credit Hours**	**Course**	**Credit Hours**
Year 1 – Fall Term		**Year 1 – Fall Term**	
Foundations	8	Foundations	8
Foundations Conference	4	Foundations Conference	4
Laboratory Research	1	Laboratory Research	1
Year 1 – Spring Term		**Year 1 – Spring Term**	
Cell Biology in Normal & Disease States	3	Tissue Growth & Differentiation	3
Cell & Molecular Physiology (program opt. 1)	2	Molecular Pathobiology (program opt. 1)	3
Laboratory Research	1	Laboratory Research	1
Year 1 – Summer Term		**Year 1 – Summer Term**	
Statistics Course	3	Statistics Course	3
Scientific Ethics	1	Scientific Ethics	1
Grant Writing	2	Grant Writing	2
Membrane Trafficking (program opt. 2)	2		
Laboratory Research	1	Laboratory Research	1
Year 2 – Fall Term		**Year 2 – Fall Term**	
		Cancer Biology & Therapeutics (program opt. 2)	3
Pathology Research Seminar	1	Pathology Research Seminar	1
Year 2 – Spring Term		**Year 2 – Spring Term**	
Angiogenesis	3	Angiogenesis	3
Pathology Research Seminar	1	Pathology Research Seminar	1
Year 2 – Summer Term		**Year 2 – Summer Term**	
Multiparametric Microscopic Imaging	3	Multiparametric Microscopic Imaging	3
Year 3 – Fall Term		**Year 3 – Fall Term**	
Pathology Research Seminar	1	Pathology Research Seminar	1
Year 3 – Spring Term		**Year 3 – Spring Term**	
Histology (optional)	(5)	Histology (optional)	(5)
Grand Total	35 (40)	Grand Total	36 (41)

***Students entering via the MD/PhD program complete statistics, ethics, and grant writing as part of their MSTP training and are not required to take Foundations/Foundations Conference due to their medical course work credits. Similarly, students entering via other University graduate programs such as PIMB or BioEng are not required to take the Foundations "core" and must complete their statistics, ethics and grant writing requirements through either their home programs or those offered by the ATP. Funding from this T32 would begin in Year 2 in the above example.**

Courses required by both tracks

Multiparametric Microscopic Imaging; MSCBMP 2860-2 credits. This is a lecture/lab course that immerses students in the theory and practical aspects of modern microscopic imaging. The fields cover the theory and implementation of all types of light and electron microscopy and computer aided imaging. Students are expected to reach a functional capability in a selected technology.

Angiogenesis-MSCMP 3750-3 credits. This course provides extensive basic knowledge of develop-mental, cellular, and molecular biology aspects of vascular remodeling and regeneration, as well as the most recent advancements in its clinical applications. Topics include: 1) angiogenesis in physiological and pathological processes; 2) molecular and cellular regulation of angiogenesis; 3) current advances in angiogenic therapies. Recent outstanding research publications are also discussed.

Pathology Research Seminar-MSCMP 2750. Students either present their research (allowed one semester only) or a recent research article from a broad range of biomedical topics selected by the student in consultation with a faculty advisor. The course meets weekly except in the summer. Emphasis is placed on a careful analysis and critical evaluation of the manuscript as well as the development of teaching and public speaking skills needed for a scientific presentation via written and oral feedback. The student is expected to elucidate issues relevant to the topic and to answer questions from other graduate students and faculty.

Note: All students must participate in the Pathology Research Seminar throughout the course of the ATP.