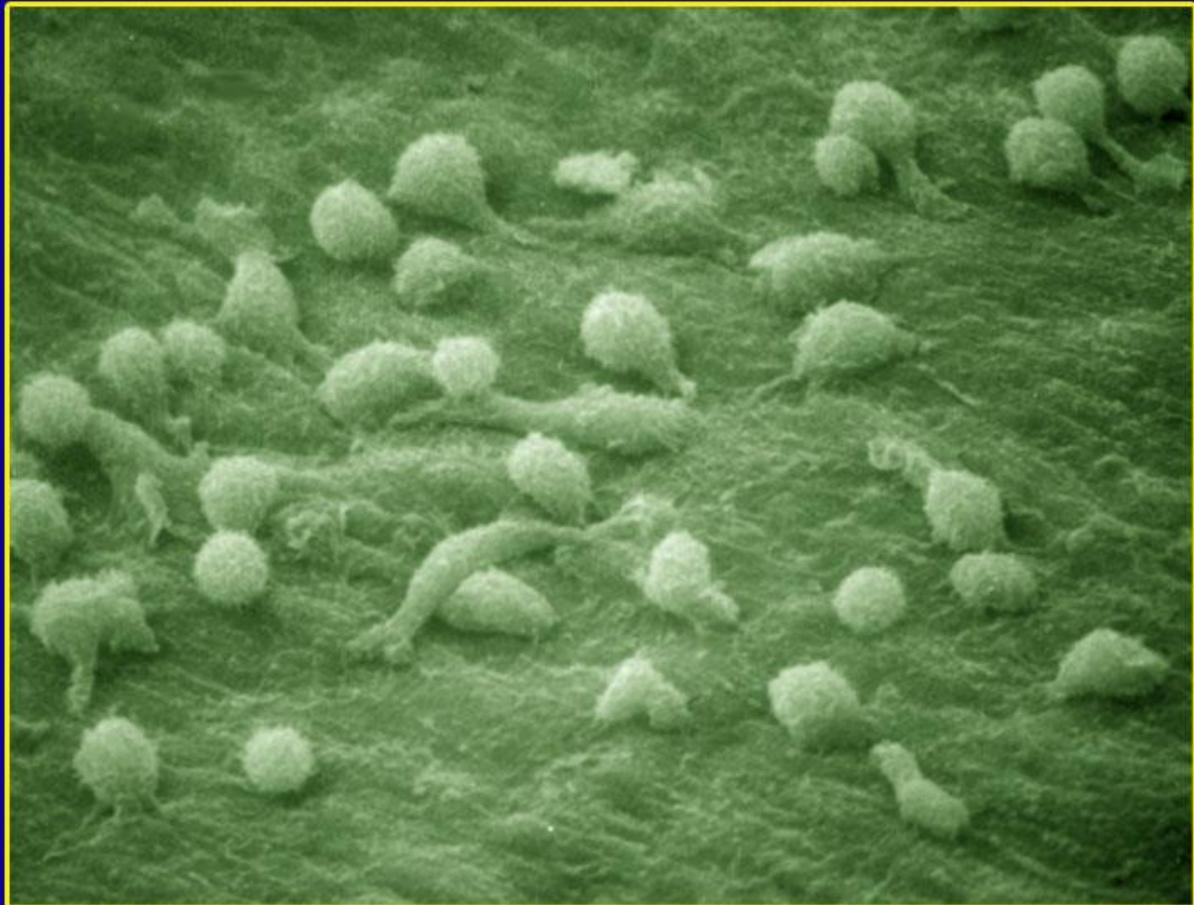


**GRADUATE PROGRAM IN
CELLULAR AND MOLECULAR
PATHOLOGY
2016-2017**



**Department of Pathology, Microbiology
and Immunology**

FACULTY ACCEPTING STUDENTS 2016-2017

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Research Key Words: Blood coagulation, Fibrinolysis, Enzyme mechanisms, Protein structure, Biochemistry, Biophysics, Fluorescence spectroscopy, Bacterial virulence factors, Pathology, Infectious diseases, Cardiovascular diseases, Bacteria, Biochemistry, Enzyme action, Pathology, Protein Structure, Spectroscopy

Research Description: Research in this laboratory is focused on molecular mechanisms of human blood coagulation and fibrinolysis and their roles in cardiovascular and infectious diseases. Biochemical and biophysical techniques are being used to determine how the proteolytic enzymes of blood coagulation and fibrinolysis are regulated through interactions with specific physiological and pathological proteins, and the membrane surfaces of vascular cells. Present work focuses on three areas: (1) The mechanism by which coagulation factor Va regulates the formation of the active blood clotting proteinase, thrombin, from its inactive precursor, prothrombin, and the mechanisms of thrombin regulation; (2) The mechanism of non-proteolytic activation of prothrombin by the *Streptococcus aureus* protein, staphylocoagulase and its homologs, and their roles in the molecular pathology of infections of heart valves in acute bacterial endocarditis; and (3) The mechanism of activation of plasminogen by the streptococcal protein, streptokinase, which is the basis for its critical role as a virulence factor in life-threatening streptococcal infections. Fluorescence spectroscopy, protein chemistry, enzyme kinetics, and molecular biology approaches are being used to define the roles of protein conformational changes and the assembly of macromolecular complexes in these mechanisms. The goal of the research is to develop molecular descriptions of these systems, which are necessary for development of new therapeutic approaches for treatment of thrombosis, and for inhibitory targeting of bacterial pathogenicity factors that usurp the human coagulation and fibrinolytic systems to propagate infectious diseases.

Publications: Kroh, HK, Panizzi, P, Tchaikovski, S, Baird, TR, Wei, N, Krishnaswamy, S, Tans, G, Rosing, J, Furie, B, Furie, BC, Bock, PE. Active site-labeled prothrombin inhibits prothrombinase in vitro and thrombosis in vivo. *J Biol Chem*, 286(26), 23345-56, 2011

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Research Key Words: progression of kidney disease angiotensin PAI-1
regression of sclerosis, Kidney, Knockout, Pathology

Research Description: Research efforts primarily concern renal pathology and involve: 1) basic research in mechanisms and pathophysiology of progression of chronic renal disease; including regression/remodeling of sclerosis; 2) basic research in mechanisms and pathophysiology of the renin angiotensin system; and 3) applied renal pathology with emphasis on prognostic features in minimal change disease/focal glomerulosclerosis.

Chronic rat animal models and knock-out mice are used to investigate the interactions of fibrotic and thrombotic mechanisms. Our work focuses on contributions of the renin angiotensin system to structural damage, and its interactions with other growth factors, and with mechanisms of thrombosis (i.e. plasmin/plasminogen activator system). Approaches include classical pathology, molecular biology and functional assessments.

Publications: Kaikita K, Fogo AB, Ma L-J, Schoenhard JA, Brown NJ, Vaughan DE: Plasminogen activator inhibitor-1 deficiency prevents hypertension and vascular fibrosis in response to chronic nitric oxide synthase inhibition. *Circulation* (in press)

Wallace, E, Fogo, AB, Schulman, G. Imatinib Therapy for Non-Infection-Related Type II Cryoglobulinemia With Membranoproliferative Glomerulonephritis. *Am J Kidney Dis*, 59(1), 122-5, 2012

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Yang HC, Rossini M, Ma LJ, Zuo Y, Ma J, Fogo AB. Cells derived from young bone marrow alleviate renal aging. *J. Am. Soc. Nephrol* [print-electronic]. 2011 Nov; 22(11): 2028-36. PMID: 21965376, PMCID: PMC3231782, PII: ASN.2010090982, DOI: 10.1681/ASN.2010090982, ISSN: 1533-3450.

Basford AW, Lewis J, Dwyer JP, Fogo AB. Membranous nephropathy with crescents. *J. Am. Soc. Nephrol* [print-electronic]. 2011 Oct; 22(10): 1804-8. PMID: 21903992, PII: ASN.2010090923, DOI: 10.1681/ASN.2010090923, ISSN: 1533-3450.

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Research Key Words: Biochemistry, Enzyme action, Gene regulation, Knockout, Mouse, Polymorphism, Protein structure

Research Description: A dynamic balance exists between the processes that form a blood clot at the site of blood vessel injury (coagulation) and the processes responsible for removing the clot once healing has occurred (fibrinolysis). This equilibrium, referred to as hemostasis, is required to prevent excessive blood loss from a wound (bleeding) while avoiding occlusion of normal blood vessels (thrombosis). My laboratory is involved in studying the contribution of certain plasma clotting factors to the formation of fibrin clots in normal and pathologic conditions. We are particularly interested in the plasma serine proteases factors IX and XI. These enzymes appear to be required for consolidating the hemostatic process after initial clot formation. Excessive activity of either protein has been linked to formation of pathologic blood vessel thrombosis. Utilizing a combination of site-directed mutagenesis, production of recombinant proteins in mammalian tissue culture, enzymology and classic coagulation assays we are investigation structure/function relationships as they relate to the activation, the activity, and binding interactions involving factors IX and XI. We are applying similar approaches to investigations of the proteases responsible for converting inactive factor XI to the active form factor XIa.

More recently, we have been investigating the contributions of factors IX and XI to hemostasis and thrombosis in vivo, using factor IX and factor XI deficient mice. These proteins appear to play important roles in the formation of abnormal occlusive thrombi in mouse models, and may be attractive targets for drugs to prevent or treat blood vessel thrombosis in human patients.

Publications: Cheng Q, Zhao Y, Lawson WE, Polosukhin VV, Johnson JE, Blackwell TS, Gailani D. The effects of intrinsic pathway protease deficiencies on plasminogen-deficient mice. *Blood* [print-electronic]. 2005 Nov 11/1/2005; 106(9): 3055-7. PMID: 15985536, PMCID: PMC1895339, PII: 2005-02-0577, DOI: 10.1182/blood-2005-02-0577, ISSN: 0006-4971.

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Research Key Words:

Mammary gland development; Breast Cancer; Signal Transduction; Drug Development

Research Description:

The laboratory uses techniques from modern molecular biology and biochemistry, microscopy, primary 3D culture of human breast tissue and rodent models to identify mechanisms that are important in normal development and that are coopted in breast cancer.

Publications:

1. Mrozowski, R.M., Vemula, R., Wu, B., Zhang, Q., Schroeder, B.R., Hilinski, M.K., Clark, D.E., Hecht, S.M., O'Doherty, G.A. and **Lannigan, D.A.** (2012) Improving the affinity of SL0101 for RSK using structure-based design. *ACS Med. Chem. Lett* 4:175-179 PMID: PMC3601785
2. Pasic, L., Eisinger-Mathason, T.S., Velayudhan, B.T., Moskaluk, C.A., Brenin, D.R., Macara, I.G. and **Lannigan, D.A.** (2011) Sustained activation of the HER1-ERK1/2-RSK signaling pathway controls myoepithelial cell fate in human mammary tissue. *Genes Dev.* 25:1641-1653. PMID: PMC3182019
3. Groehler, A.L. and **Lannigan, D.A.** (2010) A chromatin-bound kinase, ERK8, protects genomic integrity by inhibiting HDM2-mediated degradation of the DNA clamp, PCNA. *J. Cell Biol.* 190:575-586 PMID: PMC2928013
4. Eisinger-Mathason, T.S.K., Andrade, J., Groehler, A.L., Clark, D.E., Muratore, T.L, Pasic, L., Smith, J.A., Shabanowitz, J., Hunt, D.F., Macara, I.G. and **Lannigan, D.A.** (2008) Co-dependent function of RSK2 and the apoptosis promoting factor, TIA-1, in stress granule assembly and cell survival. *Mol. Cell* 31:722-736 PMID: PMC2654589

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Research Key Words: Epigenetics, cancer, chromatin

Research Description: Epigenetic reprogramming of chromatin structure during neoplastic transformation and malignant progression.

Publications: Prusevich P, Kalin JH, Ming SA, Basso M, Givens J, Li X, Hu J, Taylor MS, Cieniewicz AM, Hsiao PY, Huang R, Roberson H, Adejola N, Avery LB, Casero RA, Taverna SD, Qian J, Tackett AJ, Ratan RR, McDonald OG, Feinberg AP, Cole PA. A selective phenelzine analogue inhibitor of histone demethylase LSD1. *ACS Chem. Biol* [print-electronic]. 2014 Jun 6/20/2014; 9(6): 1284-93. PMID: 24707965, PMCID: PMC4076021, DOI: 10.1021/cb500018s, ISSN: 1554-8937.

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Hansen KD, Timp W, Bravo HC, Sabunciyan S, Langmead B, McDonald OG, Wen B, Wu H, Liu Y, Diep D, Briem E, Zhang K, Irizarry RA, Feinberg AP. Increased methylation variation in epigenetic domains across cancer types. *Nat. Genet*. 2011 Aug; 43(8): 768-75. PMID: 21706001, PMCID: PMC3145050, PII: ng.865, DOI: 10.1038/ng.865, ISSN: 1546-1718.

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Research Key Words:

Breast Cancer, Sarcoma, chromatin, transcriptional regulation, next generation sequencing, RNAseq, ChIPseq, Exome sequencing

Research Description: Large cancer re-sequencing projects like the TCGA have shown that transcriptional regulators, including chromatin readers, chromatin modifying enzymes and transcription factors, are recurrently mutated in many different cancers. We are interested in understanding how the function of the genes, how they shape the transcriptional programs in cancer cells, and how mutation of these genes contributed to carcinogenesis.



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Research Key Words: acute lung injury, coagulation, fibrinolysis, biomarkers, ARDS, sepsis, alveolar epithelium, alveolar epithelial fluid transport, respiratory failure

Research Description: Our lab does basic and translational research on the role of the alveolar epithelium in the pathogenesis and resolution of acute lung injury and the acute respiratory distress syndrome. Current projects include investigation of the role of alveolar epithelium in modulating intra-alveolar fibrin deposition in the injured lung, translational studies of biomarkers for diagnosis and prognosis in acute lung injury and studies of the pathogenesis and biomarkers of reperfusion pulmonary edema after lung transplantation.

Publications: Brittain EL, Janz DR, Austin ED, Bastarache JA, Wheeler LA, Ware LB, Hemnes AR. Elevation of plasma cell-free hemoglobin in pulmonary arterial hypertension. *Chest*. 2014 Dec; 146(6): 1478-85. PMID: 24945582, PMCID: PMC4251612, PII: 1883303, DOI: 10.1378/chest.14-0809, ISSN: 1931-3543.

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Research Key Words: cancer invasion, membrane trafficking, cytoskeleton, systems biology, secreted exosomes, extracellular RNA

Research Description: Cancer metastasis--the spread of cancer cells to distant organs--is what kills the majority of cancer patients. In order for cells to metastasize, they must acquire an invasive and motile phenotype, degrading and moving through tissue barriers. In addition, they must be able to survive and grow at distant sites in the body. The Weaver laboratory studies all aspects of this process. We are particularly focused on how secretion of small extracellular vesicles called exosomes from cells promotes aggressive, invasive behavior and facilitates tumor growth and metastasis. Current projects include: 1) Function of exosomes in cell migration and invasion; 2) The role of exosome secretion in additional tumor phenotypes; 3) How RNAs and proteins are trafficked to extracellular vesicles; and 4) How release of extracellular vesicles from cells is controlled, especially in response to deregulation of signaling in cancer cells. We use a variety of approaches, including live imaging and other microscopy approaches, in vivo tumor studies, biochemical purification and analysis, and bioinformatics/systems approaches.

Publications: Sinha S, Hoshino D, Hong NH, Kirkbride KC, Grega-Larson NE, Seiki M, Tyska MJ, Weaver AM. Cortactin promotes exosome secretion by controlling branched actin dynamics. *J. Cell Biol* [print-electronic]. 2016 Jul 7/11/2016; PMID: 27402952, PII: jcb.201601025, DOI: 10.1083/jcb.201601025, ISSN: 1540-8140.

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Research Key Words: Regenerative Medicine, Wound healing, Mesenchymal stem cells (MSCs), Fibrosis, Wnt pathway, Cardiac regeneration, Plaque instability, Atheroma progression

Research Description:

My laboratory studies the cellular drivers and signaling mechanisms that regulate tissue repair and regeneration. We use mouse models of myocardial and complex cutaneous tissue injuries to study endogenous regulators of repair as well as exogenous factors, including the role of stem cell-mediated cellular therapies, that regulate repair. My research interests dovetails well with my clinical role as Medical Director of Transfusion Medicine and of the Stem Cell Laboratory. In addition, I am dedicated to training future biomedical scientists and medical residents. Our long term goal is to identify signaling pathways which can be targeted to improve tissue repair.

Project 1 Role of Wnt signaling in repair vs. regeneration. Using both genetic models and novel small molecule Wnt pathway modulators, we have identified a pro-regenerative role in both cardiac and complex cutaneous wounds for the canonical Wnt pathway. Our current efforts are to dissect the cellular drivers of regeneration and to identify Wnt targets which mediate the pro-reparative phenotype.

Project 2 How do stem cells mediate repair and can we develop new bioengineered platforms to improve stem cell-based therapeutics? We have partnered with Vanderbilt Bioengineers to develop stem cell-based treatments for ischemic vascular diseases which seek to understand and optimize both stem cell and scaffold properties which result in improved blood flow restoration.

Project 3 We have developed a mouse model which demonstrates that deletion of a vascular smooth muscle cell protein, SPRR3, results in progression of atherosclerosis and ultimately to its most serious consequence, plaque rupture. Current projects are focused on identifying the molecular partners of SPRR3 and testing it as a novel therapeutic using a novel transgenic mouse as well as state-of-art peptide replacement approaches.

Project 4 As a Transfusion Medicine physician, I am involved in multiple clinical/translational projects involving blood and blood products in clinical medicine.

Publications: Saraswati S, Guo Y, Atkinson J, Young PP. Prolonged hypoxia induces monocarboxylate transporter-4 expression in mesenchymal stem cells resulting in a secretome that is deleterious to cardiovascular repair. *Stem Cells*. 2015 Apr; 33(4): 1333-44. PMID: 25537659, PMCID: PMC4376598, DOI: 10.1002/stem.1935, ISSN: 1549-4918.

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Research Key Words: Cancer, Metastasis, Dissemination, Clinical Translation, Adhesion, Invasion, Migration, Tetraspanin, surface protein organization, Integrin, Tumor Biology, Cancer, Malignancy, Membrane, Translation, Vascular Biology

Research Description: Cancer Metastasis is the primary cause of cancer-related deaths. Research in the laboratory is dedicated to understanding the molecular biology of cancer metastasis and translating this knowledge to clinical application.

The research program is based on three central themes: A) Investigating the molecular mechanisms of tumor cell migration, B) Evaluating and validating these mechanisms in the patient population, and C) developing research and clinical tools to advance our studies.

The laboratory pursues three primary research objectives: 1) Characterization of the molecular mechanism of migration regulated by the tetraspanin CD151, 2) Identification and characterization of the metastatic cell population within a primary tumor, and 3) clinical implementation of molecular markers of migration as biomarkers of tumor progression and metastasis.

Specific mechanistic studies include: The regulation of migration by tetraspanins: Among the molecular regulators of motility, we have found the tetraspanin CD151 to be a particularly critical component of metastasis. Interfering with its function through antibody binding inhibits extracellular matrix mediated migration and blocks >95% of the tumor cell dissemination in a spontaneous metastasis model. Using a newly-established in vivo motility assay, we have been able to demonstrate that altering the function of CD151 results in complete inhibition of in vivo motility for several tumor cell types. Ongoing studies try to determine the molecular mechanism by which this regulation of migration occurs.

Specific translational studies include: Molecular mechanisms of migration contribute to metastasis and subsequently thought to be central to the cancer progression poor clinical outcome for cancer patients. We have developed a series of preclinical tests that determine the status of pro migratory mechanisms within the tumor. Using this technology it becomes possible to diagnose patients with aggressive disease, predict clinical outcome, and possibly anticipate treatment response. Ongoing studies are expanding biomarker studies to a variety of cancers, including renal, bladder, prostate, lung, and breast cancer.

Publications: Arnold SA, Loomans HA, Ketova T, Andl CD, Clark PE, Zijlstra A. Urinary oncofetal ED-A fibronectin correlates with poor prognosis in patients with bladder cancer. *Clin. Exp. Metastasis* [print-electronic]. 2015 Oct 10/11/2015; PMID: 26456754, PII: 10.1007/s10585-015-9754-x, DOI: 10.1007/s10585-015-9754-x, ISSN: 1573-7276.

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CELLULAR AND MOLECULAR PATHOLOGY GRADUATE FACULTY

Name	Room	Phone No.
Abel, Ty, M.D., Ph.D.	U-2216A MCN	2-9451
Arnold, Shanna, Ph.D.	C-2103 MCN.....	3-1205
Atkinson, James B., M.D., Ph.D.	C-3320 MCN	3-9576
Bock, Paul E., Ph.D.	1205A- Stallworth	3-9863
Boyd, Kelli, Ph.D., D.V.M.	AA-6220 MCN	2-3596
Cates, Justin, M.D., Ph.D.....	C-2310C	6-6694
Davidson, Jeffrey M., Ph.D.	F-527 Acre Bldg.	873-7087
Fogo, Agnes B., M.D.	C-3310 MCN	2-3114
Gailani, David, M.D.	538 PRB	6-1505
Hoover, Richard L., Ph.D.	CC-2213 MCN	3-8845
Hudson, Billy G., Ph.D.	B-3102 MCN	2-7298
Jerome, Walter G. (Jay), Ph.D.	U-2206 MCN	2-5530
Lannigan, Deborah, Ph.D.	712 B PRB.....	2-5460
Majka, Susan, Ph.D.....	P405 MRBIV.....	2-5206
Major, Amy, Ph.D.	383 PRB	6-1816
McDonald, Oliver, M.D., Ph.D.....	CC-2201A	3-1101
Mosse, Claudio, M.D., Ph.D.	A-19 Acre Bldg.....	873-6976
Osteen, Kevin G., Ph.D.	B-1100 MCN	2-4196
Santoro, Samuel A., M.D., Ph.D.	C-3322 MCN	2-3234
Schoenecker, Jonathan, Ph.D.	4202 DOT.....	3-5875
Seegmiller, Adam, M.D., Ph.D.	4918B TVC	2-0858
Sephel, Gregg C., Ph.D.	F-318 Acre Bldg.	873-7524
Stricker, Thomas, M.D., Ph.D.....	CC-3309 MCN.....	3-4008
Swift, Larry L., Ph.D.	CC-3327 MCN	3-2646
Valentine, William M., D.V.M., Ph.D.	CC-3303 MCN	3-5836
Verhamme, Ingrid M., Ph.D.	T-2309 MCN	3-6563
Wallace, Jeanne, D.V.M.	AA-6224 MCN	2-6852
Ware, Lorraine B., M.D.	B-1321 MCN.....	2-3412
Weaver, Alissa M., M.D., Ph.D.	748 PRB	6-3529
Young, Pampee, M.D., Ph.D.	C-2217 MCN	6-1098
Zijlstra, Andries, Ph.D.	C-2104A MCN	2-3295
Zutter, Mary, M.D.	T-3218B MCN	3-1095

OVERVIEW OF THE GRADUATE PROGRAM IN CELLULAR AND MOLECULAR PATHOLOGY

I. GOALS

The graduate program in Cellular and Molecular Pathology provides training in biochemical, cell and molecular biological research to elucidate the fundamental mechanisms of human disease processes. The program emphasizes training in experimental laboratory investigation leading to the Ph.D. degree for students interested in pursuing careers in basic biomedical research and teaching. Graduate study in this area offers students the opportunity to integrate principles of molecular genetics, cell biology, biochemistry, and biophysics into research relevant to improving the quality of life through the discovery of new avenues for treatment of disease. The research interests of the faculty are diverse and include vascular biology, tumor pathology, neurobiology, infectious disease, and tissue repair and remodeling. Major areas of research in the department are vascular biology and tumor pathology.

II. PROGRAM

A. First Year

The first year of graduate study in Biomedical Sciences at Vanderbilt is under the direction of the Interdisciplinary Graduate Program (IGP). All graduate students in the Biomedical Sciences, regardless of their specific interests will be enrolled in this program for their first year of study. During this year, the students take a common curriculum that is designed to provide a solid core of knowledge in all of the disciplines of basic biomedical science. Even though the students entering this program come from diverse academic backgrounds, it is the aim of this program to prepare students to enter any department with the foundation to perform effectively in any advanced course and to complete the requirements for the Ph.D. degree. During the first year of study, students identify the laboratory in which they will pursue their thesis research through research project rotations, undertaken in each of four laboratories of their choice. At the end of the Spring semester, the students declare their choice of a department and laboratory for their thesis research.

B. Course Requirements — Ph.D.

Required:

Pathology 8331	Seminar in Experimental Pathology
Pathology 8332	Current Topics in Experimental Pathology
M&IM 8335	Research Proposals: Preparation & Critical Review
Pathology 8351	Cellular and Molecular Basis of Disease
Pathology 8352	Cellular and Molecular Basis of Disease
Pathology 8999	Non-Candidate Research (<i>research prior to entering into candidacy</i>)
Pathology 9999	Research (<i>research after entering into candidacy</i>)

Elective courses in the Department of Pathology:

Pathology 8322	Experimental Methods in Pathology
Pathology 8335	Molecular Pathology of Extracellular Matrix
Pathology 8337	Cellular and Molecular Basis of Vascular Disease

Students must make a grade of B or better in PATH 8351 and 8352 (Cellular and Molecular Basis of Disease), complete at least 24 hours of didactic work, and maintain an overall B average in didactic courses. Satisfactory (S) and unsatisfactory (U) grades are given for Pathology 8999 and Pathology 9999. Three unsatisfactory grades will result in dismissal from the program.

C. COURSE REQUIREMENTS — MSTP (Medical Scientist Training Program)

Required

MEDICAL SCHOOL (VSMI and VSMII years)

Foundations of Medical Knowledge (VSMI)
Foundations of Clinical Care (VSMII)
MSTP Seminar Series (IGP 8310)- Fall and Spring of VSMI and VSMII years

GRADUATE SCHOOL

Seminars in Experimental Pathology (PATH 8331)
Current Topics in Experimental Pathology (PATH8332)
One semester of Cellular & Molecular Basis of Disease (either PATH 8351 or PATH 8352)
Research Proposals: Preparation & Critical Review (M&IM8335)
MSTP Seminar
Electives

D. Selection of Thesis Advisory Committee

The Thesis Advisory Committee will administer both Phase I and Phase II of the Qualifying Exam. The committee will consist of at least five faculty members, with at least three members, including the Thesis Advisor, being from the Division of Investigative Pathology (IP), Department of PMI and at least one but no more than two with Graduate Faculty Appointments from other programs/departments. The members from the IP Division may have primary or secondary appointments in PMI. In selecting members of the Thesis Advisory Committee, it should be kept in mind that this committee will provide oversight and direction for the student through the final defense. Consequently, members should be selected carefully, based on their specific areas of expertise and their expected contributions in advising the student during the dissertation research. In the first step of the selection process the student and preceptor, in consultation with the DGS, should develop a list of faculty for the committee. When the list has been approved by the preceptor and the DGS, the student should then contact the faculty to determine their willingness and availability to serve. Faculty members should not be asked to serve on the committee until the list has been approved by both the preceptor and the DGS. The Chair of the Thesis Advisory Committee should be selected by the Thesis Advisor and the student in consultation with the DGS, prior to the first committee meeting. In general, the Chair of the committee should hold a primary faculty appointment in the Department of Pathology, Microbiology and Immunology; faculty holding secondary appointments in the Department may serve as Chair only with the approval of the DGS.

After faculty members have agreed to serve on the committee, a "Request to Appoint a Thesis Committee" form should be completed and submitted to the Graduate School. The Graduate School then officially appoints the committee and notifies each member. The "Request to Appoint a Thesis Committee" form and other forms can be found on the Graduate School website (http://www.vanderbilt.edu/gradschool/form_locator/).

E. Qualifying Examination Phase I

A student must have completed at least 24 hours of didactic work prior to taking Phase I of the Qualifying Exam. The Phase I Qualifying Examination should be completed in the summer of the second year. The examination will be administered by the student's Thesis Advisory Committee. The DGS and Program Manager must be notified of the date of the exam. Notification of the exam date and scheduling of a room for the exam should be completed no less than four weeks in advance of the exam.

The purpose of the Phase I Qualifying Examination is twofold:

- a) To test the student's ability to define a basic scientific research question, evaluate relevant literature, and propose critical experiments to address the question;
- b) To test the student's depth and breadth of knowledge of basic cell and molecular pathology.

For this examination, the student is required to develop a novel proposal based on the research she/he plans to undertake in the Thesis Advisor's laboratory and defend the proposal before the Thesis Advisory Committee. The proposal should follow the Research Plan section of the NIH R01 grant format and be no more than 10 pages, double-spaced, with no more than 30 lines of text per page and type face with an average spacing of no more than 15 characters per inch. The written proposal should include the hypothesis to be tested, specific

aims, sufficient background to provide rationale for the study, experimental approach and design, anticipated outcomes, possible problems, and interpretations of data. The proposal should be submitted to the Thesis Advisory Committee and DGS at least 10 days prior to the date of the exam.

The examination will begin with the student presenting a brief overview of the proposal (15-20 minutes) followed by questions from the committee. It is important that the committee ask questions focused on the proposal to be able to evaluate the student's ability to define a basic research question and propose experiments to address that question. Equally important, the committee should ask questions to test the student's breadth of knowledge of basic cell and molecular biology and pathology. While the amount of time for examination in each of these areas is not specified, it is important that sufficient questions are asked to determine if the student is prepared to proceed with the dissertation proposal and thesis research.

The examination should last no longer than two hours. During the examination, the thesis advisor may ask questions, but should not assist the student in answering questions. Unsatisfactory performance may require additional coursework or study followed by reexamination. The student is allowed to consult the Thesis Advisory Committee and/or Thesis Advisor for advice on how to address weaknesses identified in the proposal or examination, and how to improve the proposal or performance in the examination. The reexamination may focus on the identified weaknesses or may be comprehensive. A student may be dismissed from the program if performance on the re-examination is not deemed satisfactory by a majority vote of the Thesis Advisory Committee.

F. Qualifying Examination Phase II

For this examination the student must submit to the Committee and to the DGS a dissertation research proposal in the format of an NIH R01 grant proposal. (Use Arial, Helvetica, Palatino Linotype, or Georgia typeface, and a font size of 11 points or larger with 0.5 inch margins, no more than 6 lines/inch, and no more than 15 characters/inch average spacing.) The proposal should include a Specific Aims page and Research Strategy (Significance, Innovation, and Approach) up to a maximum of 13 pages. The Phase II proposal could be an extension or refinement of work proposed in Phase I or could be based on a new research direction as decided by the student and her/his mentor. The student in consultation with the committee will set a date and will notify the DGS who in turn notifies the Associate Dean of the Graduate School. The DGS and Program Manager must be notified four (4) weeks prior to the date of the exam. The written proposal must be submitted to the members of the committee **at least 10 days prior to the examination.**

The format for the examination includes a 30-45 minute oral presentation by the student followed by a question/answer period. All questions must be related to the proposal. The Thesis Advisor may ask questions and may provide points of clarification if requested; however, the Advisor should not assist the student in answering questions. If the student passes the examination, they are admitted to candidacy for the Ph.D. degree. If the committee feels that certain areas of the proposal are weak or need refocusing, or if clarification concerning the research protocol is needed, the student can be asked to re-write all or part of the proposal and re-schedule another committee meeting. The committee may also specify a time period in which the students must respond to the concerns. If the student does not successfully address the concerns of the committee at the re-examination, the student will be asked to withdraw from the Ph.D. program. With the passing of this examination the student is admitted to candidacy for the Ph.D. degree. By the regulations of the Graduate School the candidate has a maximum of 4 years from the date of passing the qualifying examination to complete the Ph.D. degree. The Phase II Qualifying Examination should be completed preferably in the fall but no later than the spring semester of the third year.

G. Role of Thesis Advisory Committee

It is the responsibility of the Thesis Advisory Committee to assure that the requirements of the department and the Graduate School are met by the candidate for the degree. In addition to reviewing the scientific progress of the student, the committee should be generally concerned with the student's development during the program. Students should feel free to seek help from any member of the Thesis Advisory Committee.

The Thesis Advisory Committee should meet with the student and Advisor at least every 6 months to review progress and to assist the student in planning the direction of research. The DGS should be notified of the committee meetings. Prior to these meetings the student will develop a progress report for the period of time since the last meeting. This report should be given to each committee member at least one week prior to the meeting. The Chair of the Thesis Advisory Committee will use the Student Advisory Committee report form (see p. 14) to record the results of each meeting. The report form should be signed by the student after discussion with the committee Chair. In addition, the Chair should provide a letter to the applicant detailing the results of the meeting. Copies of the letter should be sent to each member of the Thesis Advisory Committee. Copies of the report and letter also must be filed with the Program Manager and copies sent to the DGS. This procedure will help maintain open communication between student, thesis advisor, DGS, and the Committee. If a student receives two unsatisfactory reports they must schedule a meeting with the DGS to discuss the situation.

H. Thesis

Thesis Preparation

The Thesis Advisory Committee, in consultation with the student, the thesis advisor, and the DGS, will determine when the student has completed the requirements for the dissertation research and is prepared to write the thesis. It is also important at this time for the student to submit the "Intent to Graduate Form" to the Graduate School, signed by the DGS. Since the publication of original research is felt to be an integral part of graduate education, the student cannot defend the thesis until at least one first-authored manuscript has been accepted for publication by a refereed journal.

Thesis Defense

The Thesis Advisory Committee will examine the student and thesis. If possible, the defense should be scheduled during one of the regular departmental seminars, such as Works in Progress (WIP) or Journal Club (PATH 8331 and 8332). In some instances it might be possible to schedule a defense during Seminars in Pathology. The student should contact the program manager who will arrange to have the student added to the appropriate schedule.

The final examination begins with the student presenting a seminar of approximately 45 minutes in duration. This portion of the examination is open to the public. At the end of the seminar, questions from non-committee members are entertained. After those questions have been addressed, the public is dismissed, and the Thesis Advisory Committee administers the final examination. At the end of the examination, the student is asked to leave the room while the committee discusses the examination and evaluates the student's performance. The student is then informed of the results of the examination. If successful, the members of the examining committee sign the appropriate forms and, if appropriate, the first page of the thesis. It is the prerogative of the committee as to whether they sign the thesis at this time or whether they sign it when final revisions, if any, are made. The form declaring successful completion of the final examination must be signed and sent to the Graduate School.

I. Graduate Student Travel

The Department of Pathology encourages graduate students to participate in regional and national meetings, realizing that this represents an important facet of graduate education. In order to facilitate student travel, the BRET office has developed guidelines to help students navigate the process of planning a trip and getting reimbursed for the expenses associated with the travel. Students in all of our graduate programs are expected to follow these guidelines. By following these expectations and guidelines, students' needs will be met in the most efficient manner. Kristi Hargrove is the contact for graduate student travel.

III. SUGGESTED TIME SCHEDULE FOR GRADUATE TRAINING

	Year 01			Year 02			Year 03			Year 04-?		
	F	S	S	F	S	S	F	S	S	F	S	S
IGP Core Curriculum	X	X										
Lab Rotations	X	X										
‡ Path 8331 / Seminar Exp. Path.				X			X			X		
‡ Path 8332 / Current Topics					X							
M&IM 8335/ Research Proposals: Preparation & Critical Review		X			X							
Path 8351(A) 8352 (B)/ Cellular and Molecular Basis of Disease				B	A							
Electives		X		X	X							
Selection of Thesis Advisor		X										
Selection of Thesis Advisory Committee					X							
Qualifying Exam Phase I						X						
Qualifying Exam Phase II							VARIES					
Path 8999/ Non-Candidate Research			X	X	X	X	X					
Path 9999/ Research								X	X	X	X	X

‡ Students take PATH 8331 & 8332 for credit one time, but they must participate in the courses as long as they are in residence in the program.

DETAILS OF CELLULAR AND MOLECULAR PATHOLOGY GRADUATE PROGRAM

Elective Courses 2016-2017

NOTE: Vanderbilt Course Numbering System Subject to Change

PATH 8351(A) – Cellular and Molecular Basis of Disease

An introduction to human disease and the accompanying changes in normal structure and function. The course consists of modules focused on a physiologic system and its related diseases. Each module includes a review of normal anatomy and physiology and the pathological changes occurring with the disease, an in-depth discussion of the molecular and cellular mechanisms of the disease along with clinical correlates, as well as a discussion of high-profile papers relevant to the disease. 8351A-(Spring) and 8352B-(Fall) are offered as a series, but they can be taken in any order. Prerequisite: basic knowledge of biochemistry, cell, and molecular biology. [3-3] McDonald, Stricker and Staff.

PATH 8352(B) – Cellular and Molecular Basis of Disease

An introduction to human disease and the accompanying changes in normal structure and function. The course consists of modules focused on a physiologic system and its related diseases. Each module includes a review of normal anatomy and physiology and the pathological changes occurring with the disease, an in-depth discussion of the molecular and cellular mechanisms of the disease along with clinical correlates, as well as a discussion of high-profile papers relevant to the disease. 8351(A)-(Spring) and 8352(B)-(Fall) are offered as a series, but they can be taken in any order. Prerequisite: basic knowledge of biochemistry, cell, and molecular biology. [3-3] McDonald, Stricker and Staff.