David P. Basile, Ph.D.

Research or Creative Activity Section

Item from Promotion and Tenure Dossier Checklist	Location
Research and Creative Activity Statement	This section
Peer evaluation of research or creative activity – See Nine (9) External letters of evaluation	General Summary section
Evidence of scholarly products and presentations	
Most significant papers (5), including in rank	
Basile et al AJP 2001.pdf	Appendices
Basile Spurgeon-Pechman_AJP2007.pdf	Appendices
Basile et al AJP 2008.pdf	Appendices
Basile Leonard et al. AJP 2008.pdf	Appendices
Basile Philips et al AJP 2010.pdf	Appendices
American Society of Nephrology Renal Week 2010 Distinguished Faculty Invitation	Appendices
World Congress of Nephrology 2009 Speaker Invitation	Appendices
FASEB Summer Research Conference 2010 Speaker Invitation	Appendices
American Society of Nephrology Association of Specialty Professors Workshop Invitation	Appendices
Departmental evaluation of stature of journals in which publications appear	This section
ISI Web of Knowledge citation index	Appendices
Research load information; amount of time devoted to research	This section
List of grants applied for in rank	Appendices
Summary statements from NIH, AHA	Appendices
Documentation of individual contributions to collaborative work	This section
See internal letters of evaluation	General Summary section

Section IV: Research and Creative Activity

1. Research and creative activity narrative

My overall research program is directed primarily at understanding the nature of both acute and chronic kidney disease. More specifically, I have a long standing interest in acute kidney injury (acute renal failure), which is a significant clinical problem and the single largest kidney related disorder requiring hospitalization. Acute renal failure has a severe mortality rate, ranging between 30-70% depending on the specific population or cause of the disorder. Acute kidney injury results in tissue damage and impaired function. Repair processes are thought to allow the recovery of function if the patient survives the episode.

My initial interest in the area stemmed from a philosophy that understanding this repair response might allow the evolution of a therapeutic strategy in treating patients with acute kidney injury. Such strategies might include treatment of patients with agents designed to improve blood perfusion or enhance endogenous growth responses. Several years ago my interests expanded to investigate aspects of kidney injury that were not reversible. Our recognition that small blood vessels of the kidney were permanently lost in an animal model of acute kidney injury was a major finding in this area and coincided with an increased clinical awareness that patients following recovery from AKI were developing chronic kidney disease. We recognized that impaired perfusion of blood within the kidney would substantially alter its function and may predispose the development of chronic kidney disease and hypertension.

Work related to this topic has been the centerpiece of my research program over the last several years and has led to the funding of an NIH RO-1 grant entitled "Long-term effects of acute renal failure", which was competitively refunded in rank. The funding of this award since my arrival in 2005 to 2012 will be ~$1.4 M. We have published 14 papers while in rank. A thorough description of my most significant publications is included in this section, which are geared toward elucidating alterations in kidney function following AKI and the nature of the impaired vascular repair response. ***To further expand on the significance of our work, peer evaluations from internal reviewers have been solicited by the Department Chair, Dr. Sturek.***

As discussed in *Section II Personal Statement*, our work on the long-term effects of acute kidney injury is likely to remain the centerpiece of our research program, however its specific focus is evolving and ongoing studies related to the cellular and molecular mechanisms of altered kidney function post-AKI will provide an exciting new direction for our work, with potential clinical implications. As such, work in collaboration with Dr. Mervin Yoder, a Co-Investigator on our RO-1 grant, is geared toward understanding the intrinsic repair potential of endogenous kidney endothelial cells. In general, kidney endothelial cells have a much reduced capacity to proliferate vs. cells from other tissues; we have begun to screen microRNAs from these cells in an effort to understand the epigenetic factors that may underlie the impaired responses of the kidney vasculature. Such work will be a major focus of the next renewal of this application.

Additional studies related to our interest on acute renal failure have driven an expansion of these ideas and will generate new applications within the 12 months. For example, Dr. Yoder and I have collaborated on a study regarding the potential protective effects of endothelial colony forming cells on the manifestation of acute kidney injury. This work will extend beyond the original scope of the existing RO-1 application and we have already published some of this work in abstract form (Abstract #36). Currently, we are in the planning stages of an additional grant application related to protective effect of endothelial colony forming cells and their potential therapeutic use.

Studies related to the inflammatory contribution of salt sensitive hypertension have driven the development of a grant idea based on the effects of immune cells on renal hemodynamic function. This application is currently in the planning stages and will utilize my expertise in the study of AKI on renal hemodynamics with the immunology expertise of Dr. Hamid Rabb, from Johns Hopkins University. Our plans include the submission of an RO-1 application using a Co-PI mechanisms which will allow portions of work to be carried out at Indiana University and Johns Hopkins University. Finally, I am in the process of revising an NIH grant entitled "Mitochondrial response and resistance to acute kidney injury".

My expertise in kidney pathophysiology has led to a number of collaborative opportunities both inside and outside IUSM. I am a co-investigator on an NIH grant submitted by Dr. Timothy Sutton (Division of Nephrology). Dr. Sutton's work and my own mesh well together, as he is interested in the effect of kidney injury on vascular permeability. I am also a co investigator on a grant from Dr. Beth Lee of Ohio State University related to the effects of an mRNA stabilizing protein in injured kidney cells. We carry out the animal portions of these studies and have already generated one-peer reviewed manuscript. We have also generated preliminary data required for the renewal of this NIH project. I have also begun an active collaboration with Dr. Matthias Clauss (Cellular & Integrative Physiology); Dr. Clauss has submitted an NIH grant related to activation of the endothelium as a factor leading to inflammation in kidney disease. I am a co-investigator on this grant. Some of the preliminary data for this grant was generated in my laboratory using staining methodologies developed in my laboratory. Dr. Clauss and I are currently in the process of writing our first manuscript together based on these data.

My expertise in kidney pathophysiology provided me an opportunity to take an active role in the planning and development of a program project grant entitled "**Coronary and renal vascular disease in metabolic syndrome: Molecular to Integrative**". This program project application was submitted by Dr. Michael Sturek (Chairman, Department of Cellular & Integrative Physiology) which seeks to understand the basis for progressive cardiovascular dysfunction in the development of obesity and metabolic syndrome in Ossabaw swine. The development of this program project involved extensive planning and collaboration involving multiple investigators. I wrote and directed Project 1 "**Hypertension and kidney disease in the metabolic syndrome".** The program received a priority score of 30 and is currently pending. Preliminary studies geared toward evaluating alterations in kidney function and vascular structure was generated for this proposal and has been published in abstract form. The preliminary studies conducted during the generation of this program project resulted in the publication of one abstract and we anticipate that it will be assembled into manuscript form during 2010. ***To expand on the nature of these collaborative interactions, letters from collaborators have been solicited by the Department Chair, Dr. Sturek.***

In closing, I have been fortunate to develop a productive research career related to the pathophysiology of an important clinical problem, i.e., acute kidney injury. To the extent that I have been able, I have strived to capitalize on opportunities to expand on our research findings and build collaborative relationships that can move this research into exciting new areas with potential therapeutic implications. I anticipate that the next several years will be fruitful and will generate exciting new results. I further anticipate that these new studies will serve as the basis for future research funding opportunities.

2. Peer evaluation of research and creative activities

In addition to the external peer review letters in Section I, internal evaluations from the following individuals has been solicited by the Chair:

- Dr. Bruce Molitoris
- Dr. Robert Bacallao

3. Evidence of scholarly publication and presentations.

Evidence of scholarly publications and presentations are listed in Section VI: Curriculum Vitae (Publications and Invited Lectures) and in Section II: Candidate's statement. First and last author placement on publications, and corresponding author/senior authorship are highly significant in the biomedical science journals. In some cases, placement as a middle author represents variable levels of contribution from very minor to substantial. In the majority of publications listed in my CV, I am listed as the primary or senior author. I also highlight some cases in which I am a middle author (#28, #32, #33 in the publication list), which represent significant contribution to a collaborative effort with individuals outside the IUSM. In the following section, I have identified 5 highly significant publications and relevant discussion pertaining to the impact of each of these.

Basile DP, Donohoe D, Roethe K^U, and Osborn JL. Renal ischemic injury results in permanent damage to peritubular capillaries and influences long-term function. *Am J Physiol Renal Physiol.* 281:F887-899, 2001.

This article was the first to demonstrate that renal blood vessels are lost following ischemic acute kidney injury. This represented a significant shift in thinking about acute kidney injury for several reasons. Historically, acute kidney injury has been thought of as a reversible disorder due primarily to a recovery and regenerative response. In this paper, we used a rat model of acute kidney injury and demonstrated that not all aspects of kidney function were restored. We demonstrated that there was a urinary concentrating defect in animals after the normal recovery period and demonstrated that this was due to impairment in the ability to generate a hypertonic renal medulla. We hypothesized that this may be due to impaired medullary blood flow and used a vascular filling technique to demonstrate that the small blood vessels of the kidneys were rarefied. We observed that rats never recovered vascular density and also observed that they manifested elements of chronic kidney disease. In a subsequent manuscript, (not listed here) we demonstrated that resultant hypoxia was a driving force in the development of chronic kidney disease.

This manuscript was written and conceived of by me and I was the corresponding author. The work on this manuscript was carried out at the Medical College of Wisconsin prior to my time in rank but I include it here because this observation remains at the center of our current research plan. A significant degree of our current research efforts at IUSM are based on continuing to understand the significance of this observation. Subsequent studies in rank have been geared toward elucidating the cellular mechanisms of vascular cell dropout, as well as to increase our understanding about the physiological implications of altered renal vascular density.

Spurgeon-Pechman KR [G], Donohoe DL, Mattson DL, Lund H, James L, and **Basile DP**. Recovery from acute renal failure predisposes hypertension and secondary renal disease in response to elevated sodium. *Am J Physiol Renal Physiol* 293: F269-78, 2007.

This study follows up on our interest in understanding the alterations in renal function following the standard recovery from acute kidney injury. Based on our understanding of sodium handling by the kidney, we hypothesized that rats following acute kidney injury would be prone to develop hypertension when consuming high salt diets. We demonstrated that acute kidney injury had no direct effect on blood pressure regulation. Interestingly, rats developed significant hypertension after 5 weeks of recovery from acute kidney injury when placed on a high salt diet. Moreover, rats on a high salt diet developed dramatic chronic kidney disease characterized by robust interstitial inflammation and protein excretion. The time course of chronic kidney disease development was dramatically hastened when rats were placed on elevated salt diet.

This manuscript was written and conceived of by me and I was the corresponding author. The majority of this study was carried while I was in rank at IUSM. These studies were funded by my NIH grant "Long-term effects of acute renal failure". A portion of these studies were carried out under subcontract with Medical College of Wisconsin. This subcontract allowed for my graduate student, Dr. (Spurgeon) Pechman, to complete her dissertation project at that institution.

Basile DP, Fredrich K, Chelladurai B, Leonard EC, and Parrish AR. Renal ischemia reperfusion inhibits VEGF expression and induces ADAMTS-1 a novel VEGF inhibitor. *Am J Physiol Renal Physiol* 294: F928-F936, 2008.

These studies sought to understand the molecular and genomic factors contributing to vascular dropout in the injured kidney. Our hypothesis was that vasculotrophic factors were inhibited following AKI and/or that vasculotrophic inhibitory factors would be induced following injury. Using multiple techniques we demonstrated that there was a transient reduction in VEGF (vascular endothelial cell growth factor) expression following the induction of acute kidney injury which persisted for up to 1 week at both the protein and mRNA level. These data led us to suggest that loss of vascular trophic support by VEGF derived from injured nearby tubular epithelial cells compromised renal blood vessel stability.

In addition, we built our own custom gene chips, which targeted genes associated with angiogenesis, and screened gene expression in sham-operated and post ischemic rat kidneys. The most interesting and consistent result from this study was the identification of a gene coding for ADAMTS-1, a molecule with known negative effects on vascular stability. This molecule may inhibit endothelial cell proliferation directly or indirectly by blocking VEGF activity. This was the first description of ADAMTS-1 expression in a setting of kidney disease. This paper was conceived of by me, written by me and I was the corresponding author. The ideas for these studies were contained within my NIH grant.

Leonard, EC, Friedrich JL [U], and **Basile DP**. VEGF-121 preserves microvessel structure and ameliorates secondary kidney disease following recovery from acute kidney injury. *Am J Physiol Renal Physiol* 295:F1648 - F1657, 2008.

These studies sought to address the functional importance of reduced VEGF activity in kidney. It was reasoned that if the loss of VEGF represented a potential factor leading to disrupted vascular function, that supplementation with VEGF might provide a beneficial long term effect on

kidney blood vessels and a protective effect of chronic kidney disease. VEGF-121 was used in these studies and was administered to rats at various times during the recovery response. It was observed that VEGF was effective at ameliorating the chronic effect of high salt diet on the chronic kidney disease that could be provoked with a high salt diet. Interestingly, VEGF was effective only when it was administered in the early post-injury period and it had no effect when administration was delayed for up to 3 weeks following injury. VEGF preserved renal blood vessels, and this correlated with the protection from chronic kidney disease.

This manuscript is of critical importance as it demonstrates clearly not only that vascular density influences chronic kidney function, but also that this is potentially reversible within a defined and limited period of time. This paper was conceived of by me, written by me and I was the corresponding author. The ideas for these studies were contained within my NIH grant.

Philips SA, Pechman KR[G], Leonard EC, Friedrich JL, Bian JT, Beal AG[U],and **Basile DP**. Increased angiotensin II sensitivity following recovery from acute kidney injury: role of oxidant stress in skeletal muscle resistance arteries. *Am J. Physiol. Regul Integrative Physiol* In press, 2010.

These studies reflect an evolving interest in other aspects of the chronic effects of acute kidney injury as it may relate to impaired vascular control. Specifically, we demonstrated that rats following recovery from acute kidney injury show an increased blood pressure response to the hormone angiotensin II. Remarkable features from these studies include the fact that the increased pressor response was located at sites outside the kidney, such as skeletal muscle arterioles. The increased pressor response could be recapitulated in an isolated system by evaluating the contractile response of small skeletal muscle blood vessels. We demonstrated that the increased response was the result of a persistent increase in oxidative stress. The increase in oxidative stress occurs in blood vessels in which expression of genes known to contribute to oxidative stress are diminished.

This study is highly significant as it extends the possibility that the alterations in vascular function post acute kidney injury (AKI) is more complicated than previously realized. Rather than mediating effects of kidney blood vessel loss alone, AKI chronically alters the function of existing blood vessels outside the kidney. This suggests that circulating factors outside the kidney alter global cardiovascular function. Because of the realization that acute kidney injury may be associated with increases in non-renal cardiovascular complications, this discovery may lead us to understand signals derived from kidney that impair cardiovascular function. The investigation of humoral/inflammatory factors that contribute to chronic effects of AKI represents an important target for future funding opportunities in the next year.

4. Evaluation of stature of journals in which publications appear

The stature of journals in I have published while in rank are listed at the end of this section. Included in this is a list of each journal's impact factor and citation half life, as provided by the Institute for Scientific Information (ISI). This is followed by a description of each journal and a summary of its status among comparable journals. In general, the journals which I have published in are among the most well respected journals in his field.

The impact factor of a journal relates the average number of times a work published in that journal is cited by other published work over the next two years. Although it is often useful to evaluate the stature of journal in which work is published by the journal impact factor, a more

direct measurement of impact relates the citations of an individual author's work, which is currently being tracked by the Institute for Scientific Information (ISI) Web of Knowledge. The table below is based on a search of the ISI Web of Knowledge database in April of 2010 and illustrates the number of times my publications have been cited by subsequent papers. Years prior to rank are listed only as averaged values over a 4 year period. Individual years during time in rank at IUSM are listed as well as an average during the period in rank from (2005-2009). The table indicates a steady increase in the impact of previous publications during time in rank.

Year	**Citations per year**
Average (1996-2000)	22.8
Average (2001-2004)	39
2005	68
2006	58
2007	64
2008	113
2009	113
Average (2005-2009) In rank at IUSM	**83.3**

5. Research Load information: amount of time devoted to research

At least 80% of my time is devoted to research. This effort includes research activity in the laboratory as well as the design and implementation of experiments, supervision of research technicians, and analysis of data. The time devoted to research also includes reading of related scientific literature and the organization, planning and participation of group meetings designed to move the research program forward. These meetings include my own research group, transient student lab trainees, and/or other scientists around IUSM with whom I collaborate. I am a Co-investigator on 2 NIH applications, one in the IUSM Division of Nephrology and one from Ohio State University. I am also a co-Investigator on several pending applications within the Department of Cellular & Integrative Physiology. In addition to these activities, this effort also includes scientific writing of manuscripts, grants applications and progress reports to the NIH (See appendix for list of grants submitted while in rank).

A significant portion of this research time could also be classified as service. Such activity would include work as a reviewer for professional journals and grant funding agencies. See Section VI: CV, for a list of these scientific related service activities and Section V: Service, for a more detailed description of these activities.

6. Documentation of individual contributions to collaborative work.

Section II (Candidate's Statement) contains a section outlining collaborative efforts both inside and outside the IUSM. Some of these collaborative efforts have already been successful in helping to attract outside funding and generated publications. In this section, I outline in more detail the nature of some of these collaborative efforts. In addition, letters from the following individuals have been solicited by the Chair to clarify the nature of these efforts and describe the specific roles in these collaborations:

Dr. David Mattson (Department of Physiology; Medical College of Wisconsin). Dr. Mattson is an expert on the control of renal medullary hemodynamics and we have published several papers together on renal hemodynamic regulation following acute kidney injury. Dr. Mattson took over as the advisor of Dr. Pechman and provided laboratory space and additional supervision after I transitioned to the IUSM.

Dr. Van Why (Department of Peditrics, Medical College of Wisconsin). Dr. Van Why and I have published 1 paper on the protection from ischemic acute kidney injury. We have also published in abstract form the effects of chromosomal substitution on protection mediated by allelic differences in Brown Norway rats. Once published in manuscript form, theses data will be useful as we move forward on our studies of protective states of ischemic injury in the kidney.

Dr. Beth Lee (Department of Physiology, Ohio State University). Dr. Lee is an expert at transcriptional control mechanisms in epithelial cells of the kidney. Dr. Lee's research suggested a potential role for a specific mRNA regulatory protein HuR in the setting of cellular repair. We began collaborating on the possibility that HuR regulation may be important in the setting of kidney repair following ischemia reperfusion injury and I participated as a Co-Investigator on her RO-1 application.

Dr. Tim Sutton, (Division of Nephrology, Indiana University School of Medicine). Dr. Sutton's research, like my own, is highly focused on understanding alterations in the renal microvasculature in the setting of ischemic injury. I have participated as Co-Investigator in Dr. Suttons RO1 application and have helped in providing insight into experimental design for studies to elucidate early alterations in endothelial structure following ischemia.

Dr. Mervin Yoder (Department of Pediatrics, Indiana University School of Medicine). Dr. Yoder's expertise in endothelial progenitor cells has provided an important new direction for our future work on the vascular repair mechanisms within the kidney following ischemia reperfusion injury. Dr. Yoder is a Co-Investigator on my NIH RO-1 grant entitled "Long term effects of acute renal failure. The interaction with Dr. Yoder has provided an entirely new context for us to study the problems associated with acute kidney injury.

Dr. Frank Witzmann (Department of Cellular & Integrative Physiology, Indiana University School of Medicine). Dr. Witzmann is an expert in proteomic techniques and toxicology. He has been involved in planning and writing our pending R0-1 application on mitochondrial function in the setting of acute kidney injury.

Dr. R. Mark Payne (Department of Pediatrics, Indiana University School of Medicine). Dr. Payne is an expert in mitochondrial function and has developed important methodology that will be helpful in developing new tools for targeting mitochondria. He has been involved in the planning and execution of our pending R01 application on mitochondrial function in the setting of acute kidney injury.

Note: Dr. Basile, Dr. Witzmann and Dr. Payne are all Co-Principal Investigators on this application.

Dr. Matthias Clauss (Department of Cellular & Integrative Physiology, Indiana University School of Medicine. Dr. Matthias Clauss is an expert in endothelial cell biology with an interest in signaling pathways and angiogenesis. Dr. Clauss has developed a model of mice in which endothelial activation is associated with increased inflammation in the kidney and demonstrates features of chronic kidney disease. I have been working with Dr. Clauss to help develop preliminary data for his RO-1 on this topic and I am a co-investigator on this application (Submitted in January 2010).

Dr. Michael Vasko (Department of Pharmacology & Toxicology, Indiana University School of Medicine. Dr. Vasko is interested in neurotoxicology and the effects of an agent called Paclitaxol, which is an anti cancer drug associated with severe pain. Dr. Vasko developed an interest in understanding the effects of Paclitaxol on local blood flow. I consulted with Dr. Vasko and helped train his graduate student on technical aspects required for studies conducted by his graduate student to investigate this question. This work has been submitted for publication.

Definition of role on middle author papers:

In most of the papers in my C.V., I am listed as the primary or senior author indicating a primary role in the project. Middle authorship may indicate a range of diverse roles in which either minor or significant roles would be played in the generation of the resultant manuscript. Therefore, I will make a brief comment regarding the nature of these collaborations in which I am a middle author and will limit these descriptions to those manuscripts published in rank.

Manuscripts #28 and 32 represent part of my long standing collaboration with Dr. David Mattson and the Medical College of Wisconsin. These studies were part of the dissertation project of Dr. Kimberly Pechman, who was continuing on the studies originating in my laboratory prior to my departure. One study, #28, was conceived by Dr. Mattson who had been developing a keen interest in the role of immune cells in hypertension. We combined these interests with mine related to acute kidney injury. Manuscript #32 was largely conceived of by me and was described in my RO-1 grant, which included Dr. Mattson as a consultant. However, Dr. Mattson was the senior author due to significant mentorship role with Dr. Pechman after I moved to IUSM and his expertise in renal blood flow measurements. The collaboration in both of these manuscripts was manifested by significant discussion regarding experimental design and data analysis. Significant portions of the experiments were carried out in both laboratories; renal blood flow studies were carried out in Dr. Mattson's laboratory, immunohistochemisty studies and the measurements of renal interstitial hydrostatic pressure were carried out in my laboratory.

Manuscript #33 represents part of my collaboration with Dr. Beth Lee at Ohio State University. Dr. Lee is interested in mRNA regulation in renal epithelial cells. One part of these studies involved animal models if epithelial injury. To that end, I participated in the design and execution of the of the animal portions of these studies. The molecular and histochemical analysis of these studies was carried out in Dr. Lee's laboratory.

Manuscript #26 and #35 represent studies in which my laboratory provided roles that were largely technical and supportive of other investigators' research. In one study, I helped to fluid and sodium content in the gallbladder of obese mice. In another study, we helped to design experiments in which blood flow could be measured in hindlimb of rats in response to paclitaxol using laser Doppler flow methods. The experiments were initially carried out in my laboratory after training personnel from the collaborators laboratory.

EVALUATION OF THE STATURE OF JOURNALS IN WHICH PUBLICATIONS APPEAR

Journal Name	**2008-Impact Factor (ISI cited half life)**
American Journal of Physiology-Renal (Fluid, Electrolyte) Physiology	3.9 (6.8 yrs)
American Journal of Physiology-Regulatory, Integrative and Comparative Physiology	3.2 (7.2 yrs.)
Current Opinion in Nephrology and Hypertension	4.0 (4.8 yrs)
Kidney International	6.4 (6.6 yrs.)
Experimental Cell Research	3.4 (8.0 yrs)
Microcirculation	2.5 (5.2 yrs)
Journal of the American Society of Nephrology	7.5 (5.1 yrs)
American Journal of Physiology-Gastrointestinal Liver Physiology	3.6 (7.1 yrs)
Neurotoxicology	2.4 (6.7 yrs)

Most of the journals in which Dr. Basile has published represent those that are highly respected in the fields of nephrology or renal physiology research. A description of each of these journals is provided below.

The American Journal of Physiology - Renal Physiology: This journal is published by the American Society of Physiology, the largest professional association of physiologists in the world. The American Society of Physiology publishes up to 13 different journals related to different aspects of physiological research. *The American Journal of Physiology-Renal Physiology* publishes original manuscripts on a broad range of subjects relating to the kidney, urinary tract, and their respective cells and vasculature, as well as to the control of body fluid volume and composition. Studies may involve human or animal models, individual cell types, and isolated membrane systems. *The American Journal of Physiology - Renal Physiology* has an ISI impact factor of 3.9 and is rated 10th of 57 of journals listed in the category of "Nephrology and Urology" research and 13th of 74 of journals listed in the field of "Physiology".

The American Journal of Physiology - Regulatory, Integrative and Comparative Physiology: This journal is published by the American Society of Physiology, the largest professional association of physiologists in the world. The American Society of Physiology publishes up to 13 different journals related to different aspects of physiological research. This journal publishes

original investigations that illuminate normal or abnormal regulation and integration of physiological mechanisms at all levels of biological organization, ranging from molecules to humans, including clinical investigations. Major areas of emphasis include regulation in genetically modified animals; model organisms and comparative functional genomics; development and tissue plasticity; neurohumoral control of circulation and hypertension; local control of circulation; cardiac and renal integration; thirst and volume, electrolyte homeostasis; appetite and obesity, and inflammation and cytokines. *The American Journal of Physiology - Regulatory, Integrative and Comparative Physiology* has an ISI impact factor of 3.3 and is ranked 23 of 74 journals listed in the field of "Physiology".

Current Opinion in Nephrology and Hypertension delivers unvarnished, expert assessments of developments from the previous year. Insightful editorials and on-the-mark invited reviews cover key subjects, spanning topics such as circulation and hemodynamics; pathophysiology of hypertension; epidemiology and prevention; mineral metabolism; and pharmacology and therapeutics. *Current Opinion in Nephrology and Hypertension* has an ISI impact factor of 4.0; it is ranked 8th of 57 journals listed in the category of "Nephrology and Urology".

Kidney International is the official Journal of the International Society of Nephrology. *Kidney Internationa*l devotes itself to renal research. It aims to inform the renal researcher and practicing nephrologist on all aspects of renal research. It includes the highest level of original research studies of clinical and basic renal research as well as editorials on matters of international nephrology and mini-reviews on hot topics. *Kidney International* has an ISI impact factor of 6.4 and is ranked 3 of 57 journals in the category of "Nephrology and Urology".

Experimental Cell Research promotes the understanding of cell biology by publishing experimental studies on the general organization and activity of cells. The scope of the journal includes all aspects of cell biology from the molecular level to the level of cell interaction and differentiation. *Experimental Cell Research* has an ISI impact factor of 3.9 and is ranked 62 of 157 journals in the category of "Cell Biology".

***Microcirculation* is the official journal of the** Microcirculatory Society, Inc, whose goal is to actively encourage and promote all forms of innovative research and teaching, leading to an increase in understanding of microcirculatory function in health and disease. The journal publishes original manuscripts and review articles related to all aspects of microcirculatory function. *Microcirculation* has an ISI impact factor of 2.5 and it is ranked 27 of 56 journals listed in the field of "peripheral vascular disease".

The Journal of the American Society of Nephrology is the official journal of the American Society of Nephrology. *The Journal of the American Society of Nephrology* publishes highly competitive original manuscripts, brief reviews, and special articles in areas of basic and clinical science relevant to the broad discipline of nephrology. Subject matter includes but is not restricted to cell biology, developmental biology, genetics cell and transport physiology, hemodynamics and vascular regulation, immunology and pathology, and the pathophysiology of renal disease and progression. *The Journal of the American Society of Nephrology* has an ISI impact factor of 7.5 and is ranked 1 of 57 journals in the field of "Nephrology and Urology".

NeuroToxicology is a bimonthly international journal which specializes in publishing the best peer-reviewed original research papers dealing with the effects of toxic substances on the nervous system of humans and experimental animals of all ages. The Journal emphasizes papers dealing with the neurotoxic effects of environmentally significant chemical hazards, manufactured drugs and naturally occurring compounds. Neurotoxicology has an ISI impact factor of 2.4 and is ranked 29 of 75 journals in "toxicology" and 100 of 219 of journals in "pharmacology & pharmacy".