MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

[redacted]

Massachusetts General Hospital
GRB 1003
55 Fruit Street
Boston, Massachusetts 02114

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[redacted]

American Kidney Fund Clinical Scientist in Nephrology Program Review Committee

To whom it may concern:

Presented for your review is the "Postprandial Hypocalcemia in Secondary Hyperparathyroidism in Early Chronic Kidney Disease" proposal. The applicant looks forward to your reviews.

Thank you,

[redacted]

[redacted]

AMERICAN KIDNEY FUND
CLINICAL SCIENTIST IN NEPHROLOGY PROGRAM

APPLICATION FOR ACADEMIC YEAR [redacted]

FORM A

Mail to: [redacted]
American Kidney Fund
6110 Executive Boulevard
Suite 1010
Rockville, MD 20852

CANDIDATE

Name [redacted]

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Soc. Sec. Number [redacted] Birthdate [redacted]

Citizenship [redacted] Signature [redacted]

DIRECTOR OF NEPHROLOGY PROGRAM

Name [redacted]

Academic Title [redacted]

Business Address [redacted]

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CLINICAL RESEARCH MENTOR

Name [redacted]

Academic Title Assistant Professor of Medicine

Business Address [redacted] Massachusetts General Hospital, 55 Fruit St., Boston, MA 02114

Telephone [redacted]

[redacted]

EDUCATION

Undergraduate Education

Institution	Location	Dates	Degree
[redacted]			

Medical School Education

[redacted]

Dates attended: [redacted] Date graduated: [redacted]

Graduate Medical Education

Dates	Institution	Location	Specialty
[redacted]			

List of Publications:

[redacted]

Fellowships

Name of Fellowship	Institution	Dates
[redacted]		

Student/Faculty Committees

Committee	Institution	Dates	Duties
[redacted]			

[redacted]

AWARDS, HONORS AND SCHOLARSHIPS

Name of Award and Award Citation	Institution	Dates
[redacted]		

PREVIOUS RESEARCH EXPERIENCE

Position	High School	College	Medical School	Other	Number of Months
Neuroscience Laboratory Technician		x			6
Research Coordinator		x	x		3
Research Coordinator			x		3
Co-investigator			x		4

ACADEMIC APPOINTMENTS

Title	Institution	Dates
Clinical Fellow in Medicine	Harvard Medical School	[redacted]

VOLUNTARY SERVICES OR OTHER RELEVANT EXPERIENCES

Name of Program	Location	Dates	Duties
[redacted]			

[redacted]

REFERENCES

List below the names and addresses of three individuals who can provide the American Kidney Fund with information regarding your personal and professional qualifications pertinent to this application. One of these individuals must be either the Chairman or the Director of the Internal Medicine or Pediatric Medicine Residency Program that you completed before beginning your subspecialty training in nephrology. Please have your three references mail their recommendations to the American Kidney Fund.

Name [redacted]
Academic Title Director of Residency Training, Clinical Director of Renal Unit
Business Address [redacted] Massachusetts General Hospital, 55 Fruit St., Boston, MA 02114
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Name [redacted]
Academic Title Associate Professor of Medicine, Harvard Medical School
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Academic Title Professor of Pediatrics, Harvard Medical School
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PERSONAL STATEMENT

Chronic kidney disease (CKD), a modern-day public health problem, has prompted calls for early disease recognition to prevent progression and development of complications, such as bone mineral metabolism abnormalities and their associated morbidity and mortality in this population. Having first learned during third-year medicine clerkship about the burden of CKD and its pervasive effect on a patient's daily life, the clinical year of Nephrology Fellowship afforded many opportunities to see firsthand the scope of this problem. Not only were the numbers of patients who carried a diagnosis of CKD staggering, the majority of these patients had numerous hospital admissions and some of them never left the hospital or reached end stage renal disease. These poor outcomes in millions of patients with CKD are the driving force for my dedication to clinical research in nephrology. Through patient-oriented physiological investigation of mineral metabolism abnormalities in CKD, I hope to enrich the scientific understanding of disease mechanisms and contribute to the development of new interventional strategies that will improve clinical practice.

The road map from a given scientific discovery to its integration into patient care is long and has many unexpected turns. Therefore, a successful journey requires the traveler to be passionately curious about what lies ahead, deeply motivated to reach the destination, patiently obstinate in this goal, well-equipped with necessary tools and appropriately guided by those who are further along. Having graduated from Downstate Medical School with a distinction in investigative scholarship, during residency training I pursued opportunities for further involvement in patient-oriented research at the Massachusetts General Hospital. Once I declared an interest in nephrology toward the end of internship, I was then able to join the Renal Clinical Research Unit during second year of residency training. I began by working on ongoing studies and soon moved on to new projects. This early experience introduced me to the process of designing a study, submitting an IRB application, recruiting subjects, collecting and analyzing data, presenting the results at institutional and national meetings and preparing a lead-authored manuscript which will be published in a well known peer-reviewed journal [redacted]

While the initial exposure to clinical research reaffirmed my desire to pursue an academic career in nephrology, it also taught me that patient-oriented investigators possess special knowledge and skills needed for study design and data analysis. It is with the goal to acquire these tools of the trade that I enrolled in the Harvard Medical School Scholars in Clinical Science Program [redacted]. The objective of this two-year Masters Degree program is to provide Scholars with expertise in epidemiology, biostatistics, genetics, pharmacology and new techniques of clinical research like genomics, proteomics and bioinformatics. Additionally, through conducting individual mentored clinical research projects students apply the theory learned during didactic coursework into practice and, as result, become fully trained in issues related to research involving human subjects, such as principles of informed consent and human safety protection. I am a more thoughtful and responsible investigator as a result of completing the coursework to-date and look forward to further growth.

Mentorship by Dr. [redacted] has been another key ingredient in my academic development. Dr. [redacted], himself a graduate of the Scholars Program and an RO1-funded investigator, has mentored several fellows who have successfully obtained research fellowship grants, lead-authored important publications and submitted NIH career development (K23) applications. Dr. [redacted] is well-versed in internal medicine and nephrology and is fascinated with human physiology and disease pathogenesis and their application to patient-oriented research. When Dr. [redacted] is on the wards he routinely connects observations in individual patients to scientific discoveries. Likewise, during meetings with collaborators who conduct basic science research he astutely relates latest breakthroughs to major clinical problems in the field of nephrology and provides relevant focus to ongoing joint projects. Through interaction with Dr. [redacted] I have learned to think about our projects on a deeper level, read the literature critically, write proposals that clearly convey ideas, present results in manner that can be readily understood by others, and, more importantly, not to get

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easily discouraged. On many occasions, when preliminary view of the data seemed disappointing, Dr. [redacted] would see patterns not initially observed, and the project would proceed with renewed vigor. Dr. [redacted] is dedicated to the development of the fellows in the Research Unit, and, in addition to weekly group meetings, he regularly meets individually with each fellow to discuss progress on their respective projects, provides scientific expertise on the design, data analysis and manuscript writing, assists with the grant application process, and directs fellows to important learning opportunities. Dr. [redacted] also encourages collaboration with leading investigators in the field by fostering the building of networks through introductions of fellows to potential future collaborators locally and nationally.

With the right set of tools, strong mentorship, established opportunities for collaboration and support from the AKF I am confident that I will be well prepared for a junior academic nephrology position at the completion of Nephrology Fellowship Training Program in 2010. As I progress through the research years of the fellowship, I will devote 90% of the total time to research and educational activities including the Scholars Program's didactic coursework and the departmental clinical conferences. The coursework will amount to about 7.5 credits per semester and it will allow sufficient time for the execution of the proposed project. Furthermore, the coursework content is directly applicable to the project and thus will enhance its integrity and feasibility. While the majority of the research time will be devoted to the proposed project, 5-10% of the research time will be spent on concurrent and related projects being conducted by Dr. [redacted] research group. The clinical responsibilities will include a half-day clinic once a week and coverage of the dialysis unit at MGH one half-day a month. Research related meetings will include weekly group meetings, individual weekly meetings with Dr. [redacted] monthly meetings with collaborators, and additional meetings with Dr. [redacted] as needed when questions arise. Finally, time will be allotted to independent study in areas related to the research project as well as internal medicine and nephrology.

Selection into the AKF Clinical Scientist in Nephrology Fellowship will allow me to implement into practice the acquired knowledge and skills, successfully complete the proposed mentored research project and prepare me for the next step in my academic journey, securing an NIH career development award (K23) to support my ongoing research training. This process will move me closer to the goal of becoming an independent patient-oriented investigator who is deeply committed to improving the outcomes of patients with CKD.

1 Specific Aims

Secondary hyperparathyroidism (sHPT) is a nearly universal complication of chronic kidney disease (CKD) that leads to bone and cardiovascular disease (CVD). While the abnormalities in mineral metabolism that maintain sHPT in renal failure are well established, the pathophysiological triggers that initiate sHPT in early CKD remain unclear. In early-stage CKD patients with normal fasting calcium (Ca) and PTH levels, we observed significant postprandial hypocalcemia, which followed early postprandial calciuria and was associated with subsequent significant increases in PTH levels. Relative postprandial hypocalcemia appears to be a previously unreported initiating factor in the pathogenesis of sHPT in early CKD. Understanding postprandial Ca and PTH metabolism and how to normalize these in early CKD is the subject of the current proposal. The results will be of immediate clinical relevance to millions of early-stage CKD patients for whom postprandial calciuria and hypocalcemia can be targeted to prevent or delay the development of sHPT.

Aim 1: Examine postprandial Ca-PTH metabolism over the course of 24 hours

PTH was still rising at the end of the 4-hour postprandial study period in our preliminary data. No studies have examined the daily PTH secretory pattern in CKD patients and its relationship with diet and serum and urinary Ca. We will examine the postprandial PTH secretory pattern in response to standard dietary Ca loads in CKD versus healthy subjects during a 24-hour stay at the General Clinical Research Center (GCRC) to test the following hypotheses:

1) CKD subjects will develop repeated episodes of relative postprandial hypocalcemia and increased PTH secretion following breakfast, lunch and dinner.

2) Sequential meals will produce a "stacking effect": greater increases in postprandial PTH levels after lunch and dinner with the shortest inter-meal interval (breakfast → lunch) leading to the greatest increase in postprandial PTH levels.

Aim 2: Examine the role of postprandial calciuria as a mechanism of hypocalcemia → increased PTH secretion

Our preliminary data suggested that postprandial calciuria contributed to hypocalcemia in CKD subjects. No previous studies have attempted to alter calciuria in order to test its impact on postprandial hypocalcemia and subsequent PTH secretion in CKD. We will study the renal and parathyroid responses to low and high protein meals (associated with increased calciuria) in CKD subjects and healthy volunteers to test the following hypotheses:

1) The calciuric response to a high protein meal will be greater than the response to a low protein meal in both groups.

2) Compared to a low protein meal, the increase in calciuria in response to a high protein meal within the CKD group will lead to a greater reduction in serum Ca levels and thus a greater postprandial rise in PTH.

Aim 3: Examine the role of postprandial hypocalcemia as a mechanism of increased PTH secretion

We hypothesize that postprandial hypocalcemia in CKD subjects results from their limited ability to offset urinary Ca losses with dietary Ca absorption due to calcitriol deficiency. We will study the effects of dietary Ca and calcitriol supplementation on postprandial Ca and PTH metabolism by testing the following hypotheses:

1) High Ca meals will *partially attenuate* postprandial hypocalcemia and increased PTH secretion in early CKD.

2) Calcitriol supplementation will *normalize* postprandial Ca and PTH levels in early CKD.

2 Background and Significance

CKD affects approximately 13% of the US population (1). Regardless of the etiology of CKD, most patients eventually develop sHPT beginning as early as stage 2 (2). sHPT leads to bone disease and, based on studies of stage 5 patients, is now considered a novel risk factor for CVD (3), the leading cause of death at all stages of CKD (4, 5). Thus, sHPT is an early and common complication of CKD that deserves aggressive treatment. Current management strategies are based on data from studies of dialysis patients, in whom hypocalcemia, hyperphosphatemia and calcitriol deficiency maintain sHPT. Importantly, elevated PTH levels are detectable early in the course of CKD when patients are normocalcemic (6). Thus, the stimuli that *initiate* sHPT are mostly unknown. Based on our preliminary data, we hypothesize that postprandial urinary Ca losses may lead to episodic relative hypocalcemia that stimulates increased PTH secretion in CKD patients who are normocalcemic at baseline. Our findings are supported by previous studies (7, 8). When calciuria was reduced with thiazide diuretics in subjects with hypercalciuria-induced hyperparathyroidism, PTH levels decreased (7). Furthermore, PTH levels increased in healthy volunteers after they developed hypercalciuria induced by furosemide administration (7). Other studies in healthy volunteers have shown that postprandial calciuria is immediate, increases after meals high in protein and starch, with greatest urinary Ca losses following protein meals (9-12), and if not accompanied by high dietary Ca can lead to negative Ca balance (13). While no such interventions have been carried out in CKD patients, CKD patients are known to take in less dietary Ca than the recommended daily allowance (14) and have decreased intestinal Ca absorption due to calcitriol deficiency (15). We propose that the dynamic postprandial hypocalcemia and increased PTH secretion we observed in early CKD subjects may result from calciuria induced by dietary macronutrients, insufficient dietary Ca intake, or inefficient intestinal Ca absorption due to calcitriol. We will use detailed physiological investigation to study these novel mechanisms of development of sHPT in early CKD and determine whether interventions that attenuate postprandial hypocalcemia might attenuate the increase in PTH secretion.

3 Preliminary Data

We studied 21 healthy volunteers and 13 early CKD subjects (eGFR 41 ± 8 ml/min/1.73 m^2) (16). Subjects consumed a standardized breakfast meal containing 300 mg of Ca, 15% protein, 55% carbohydrate following an overnight fast. A second isocaloric 200 mg Ca meal was administered 2 weeks later. We obtained blood and urine samples before the meal (time 0) and every 30 minutes thereafter for 4 hours. Compared with healthy subjects, CKD subjects demonstrated significantly decreased fasting fractional excretion of Ca (FECa) and calcitriol (1,25D) levels, but there were no differences in fasting serum Ca, 25D (all deficient subjects were repleted prior to the study to eliminate confounding by nutritional vitamin D deficiency) or PTH levels (Table). The Figures 1-3 illustrate fasting and postprandial measurements of (1) FeCa; (2) serum Ca; and (3) PTH in healthy volunteers (open circles) and CKD subjects (filled squares). Time 0 represents fasting measurements. While both CKD subjects and healthy volunteers demonstrated immediate increases in postprandial FeCa, only the CKD subjects developed significant postprandial reductions in serum Ca, beginning at 60 minutes, and then followed temporally by significant increases in PTH: up to a 21% increase from baseline by 240 minutes. Our results suggest that episodic, relative postprandial hypocalcemia may represent a previously unreported mechanism of sHPT in early CKD. We propose that postprandial urinary Ca losses in the face of limited intestinal Ca absorption due to 1,25D deficiency led to relative hypocalcemia that stimulated PTH secretion. This is supported by the results of the lower Ca meal in which the urinary Ca response was unchanged but the magnitude of reduction in serum Ca and increase in PTH were greater (data not shown). Importantly, PTH levels were still rising at the end of the 4-hour observation period. During the course of a day, as more meals are consumed and calciuria is repeated, acute changes in PTH levels following a single meal may impact the postprandial PTH response to the next meal, and this "stacking" effect may lead to long-term stimulation of PTH secretion in early CKD patients that would explain high PTH in the absence of hypocalcemia, the typical biochemical pattern of early-stage CKD. We will explore these hypotheses in detail in the current proposal.

	Healthy N = 21	CKD N = 13	P
Ca (mg/dl)	9.2 ± 0.3	9.3 ± 0.3	NS
FE_{Ca} (%)	0.9	0.5	<0.01
	0.7, 1.3	0.2, 0.7	
PTH (pg/ml)	30 ± 14	38 ± 19	NS
25-D (ng/ml)	39 ± 9	35 ± 8	NS
1,25-D (pg/ml)	41 ± 11	24 ± 10	<0.01

Figure 1

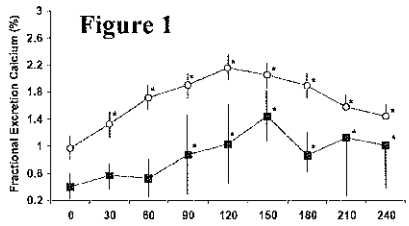


Figure 2

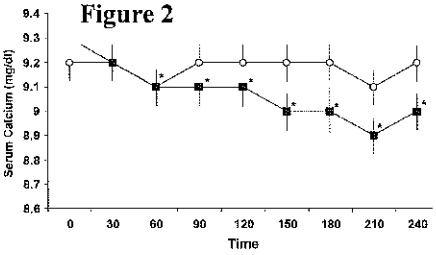
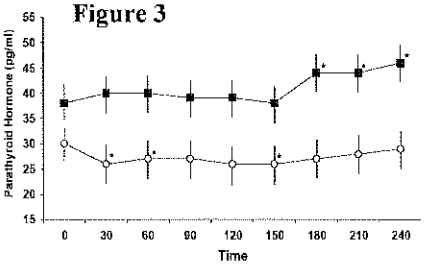


Figure 3



4 Methods

4.1 Broad Overview

Postprandial hypocalcemia and elevation in PTH in CKD subjects could be secondary to calciuria, low dietary Ca intake, or inefficient intestinal Ca absorption due to 1,25D deficiency. In order to examine these mechanisms of postprandial Ca handling and their effect on PTH, we will conduct detailed physiological investigation of human subjects on the GCRC. Aims 1 and 3 will be carried out in one efficient protocol: 1) 12 CKD subjects will be admitted to the GCRC twice to examine the duration of postprandial rise in PTH in response to 3 separate meals over 24 hours (Aim 1) before and after treatment with calcitriol; 2) during these admissions, CKD subjects will consume low (250 mg) and high (500 mg) Ca breakfast meals before and after 1 week of treatment with 0.25 mcg of calcitriol (with dose titration to 0.5 mcg based on follow-up serum and urine Ca levels) to examine whether augmenting dietary Ca intake or absorption to blunt postprandial hypocalcemia could prevent increases in PTH secretion (Aim 3). Twelve healthy volunteers will be admitted to the GCRC for one day as controls. On the day of admission, we will obtain blood and urine samples before the meal (time 0) and every hour thereafter for 15 hours. Subjects will consume 250 mg Ca breakfast on the morning of admission and 500 mg Ca breakfast on the following morning. During the day of admission, subjects will consume lunch and dinner on the GCRC, with the total daily dietary Ca intake of 750 mg. In Aim 2 we will study the postprandial response to low and high protein isocaloric and isocalcemic breakfast meals in 10 healthy volunteers and 10 CKD subjects.

4.2 Inclusion/Exclusion Criteria

Subjects will be ≥ 18 years old and have 25D stores ≥ 30 ng/ml. We will include CKD subjects with stage 3 CKD (eGFR 30-60 ml/min/1.73m^2) and fasting normophosphatemia (2.5 – 4.6 mg/dl) and normocalcemia (8.5 – 10.0 mg/dl). Healthy volunteers will have normal kidney function defined as creatinine ≤ 1.2 mg/dl for men and creatinine ≤ 1.0 mg/dl for women. To avoid confounding by age, we will use frequency matching to ensure that age distribution among CKD and healthy subjects is matched ± years. Subjects will be excluded if they: have a history of malnutrition (serum albumin <

3.0 mg/dl), gastrointestinal diseases, primary hypo- or hyperparathyroidism, previous parathyroidectomy, liver disease (ALT or AST > 100 U/L), cholestasis (direct bilirubin > 1.0 mg/dl), pregnancy, breastfeeding mothers or anemia; or use thiazide or loop diuretics, phosphate (P) binders, active vitamin D, anti-convulsants, or antacids.

4.3 Outcome Measures

Aim 1: The primary outcome measure, change in PTH levels over 24 hours, will be used in the following comparisons: 1) fasting PTH levels before breakfast, lunch and dinner; 2) postprandial change in PTH following breakfast, lunch and dinner; 3) daily postprandial PTH response curve in healthy volunteers and CKD subjects.
Aim 2: The primary outcome measures are changes in serum Ca, FeCa, and PTH following high and low protein meals.
Aim 3: The primary outcome measure is the percent change in postprandial PTH levels from baseline PTH levels (Δ PTH) in the CKD group. We will use this outcome measure for the following comparisons: 1) Δ PTH following the low and high Ca meals to test the effect of dietary Ca alone; 2) Δ PTH following the low Ca meal before and after calcitriol to test the effect of calcitriol alone; 3) Δ PTH following the high Ca meal before and after calcitriol to test the dual effects of calcitriol and dietary Ca supplementation. Secondary measures for all aims are serum P, FGF-23, 1,25D, FeCa and FeP.

5 Statistical Analyses

We will use mixed model ANOVA to test our hypotheses. In these analyses, time will represent the repeated measures factor, individual subjects will be represented as random effects terms and group (CKD subjects or healthy volunteers) or meal (low and high Ca meals before and after calcitriol treatment, high and low protein meals) will be treated as fixed-effects factors. We will test for interaction between time and group, and if interaction is present we will report postprandial differences separately for each group. When no significant interaction is identified, the interaction term will be removed from the model, and we will test for main effects of group and time. We will localize individually significant postprandial time points within the groups by comparing them with baseline fasting levels using multiple linear regression for repeated measures. Age, gender, race and BMI will be treated as potential confounders (17).
Sample size estimations for Aim 1 and 3: In our previous study (7), mean PTH levels among stage 3 CKD subjects were 39 ± 19 pg/dl and postprandial PTH levels increased from baseline levels by 21 ± 10% following a 300-mg Ca meal and by 38 ± 10% after a 200-mg Ca meal. To detect at least a 15% difference in the Δ PTH response in the CKD groups following a low Ca and high Ca meals alone and the Δ PTH response in the CKD groups following a low Ca and high Ca meal before and after calcitriol, with 90% power and 5% alpha, 12 subjects are required. Since this estimate is powered to detect a significant difference between 3 intervention groups vs. baseline (high Ca with and without calcitriol vs. low Ca) it will provide more than adequate power to detect significant main effects of either calcitriol or dietary Ca alone. As a secondary analysis, we will test for interaction (a multiplicative effect) between calcitriol and Ca and 12 CKD subjects will provide 80% power to detect a 12% difference in PTH. We will study 12 CKD and 12 healthy subjects before and after the intervention. Importantly, these estimates assume independent samples. Thus, our repeated measures approach will take into account the high within subject correlation and result in lower variability and greater power.
Sample size estimations for Aim 2: Previous studies of calciuria following high and low protein meals found a 60% greater FeCa in 3 hours following high protein meal as compared to FeCa after low protein meal (9). To detect a conservative 30 ± 20% difference between postprandial FeCa following high and low protein meals, with 90% power and 5% alpha, 10 subjects per group would be required. This same sample size will provide >90% power to detect a 20% difference between postprandial changes in PTH levels as we observed in our preliminary data.

6 Limitations and Alternate Approaches Considered

Race: Racial differences in Ca metabolism exist in health (19) and CKD (20). We will ensure that racial and ethnic backgrounds are not dramatically overrepresented in any group and will explore the effects of race in secondary, hypothesis generating analyses that will provide preliminary data for future studies dedicated to the effects of race.
Reduction of calciuria: While our goal is to alter calciuria to alter hypocalcemia, in this proposal we have elected to augment calciuria with high protein meals rather than propose strategies aimed at reducing calciuria which would be clinically desirable if our hypotheses are correct. We have chosen this approach because it is known to increase calciuria whereas potential strategies to reduce calciuria such as pre-treatment with indomethacin are also problematic in CKD and less reproducibly associated with changes in calciuria. If the current results support our hypotheses, in future studies, we will utilize salt restriction in an effort to decrease postprandial calciuria and associated increases in PTH levels.

7 Summary

The proposed studies are important scientifically and will allow the applicant to utilize knowledge and skills she has acquired from the Scholars in Clinical Science Program (SCSP) at the Harvard Medical School. The applicant has already obtained IRB approval and initiated recruitment of healthy volunteers. It is anticipated that the outlined proposal will take 2 years to complete. The mentor-guided research project, SCSP coursework and AKF support will prepare the applicant for her next career development milestone, an NIH K23 award to support ongoing research training.

8 Literature Cited

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AMERICAN KIDNEY FUND
CLINICAL SCIENTIST IN NEPHROLOGY PROGRAM

APPLICATION FOR ACADEMIC YEAR [redacted]

CONSENT FORM FOR RELEASE OF INFORMATION

In making this application to become an American Kidney Fund Clinical Scholar, I recognize my right under the "Family Educational Right and Privacy Act," Section 368 of the "General Education Provisions Act" 20 U.S.C. §1232g initially adopted by Section 513 of P.L. 93-380 dates August 21, 1974 and amended by P.L. 93-568 dated December 13, 1974. This statute as amended provides that information which could personally identify me may not be released except as this consent implies. I therefore agree that the AKF Selection Committee and their designee(s) are hereby authorized to release personally identifiable information from this application and in the course of my tenure as an American Kidney Fund Clinical Scholar, to the American Kidney Fund and to other organizations conducting studies for, or on behalf of, educational agencies or institutions for the purpose of administering or improving the American Kidney Fund Clinical Scientist in Nephrology Program or for improving the general weal. I shall expect the information which may be made available to the public (as itemized above) to be maintained in a separate file available to my inspection on demand. Such file shall contain a dated list of organizations or individuals to whom this information has been released.

Date [redacted]

Signature [redacted]

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

[redacted]
Chief, Renal Unit
Dir. Leukocyte Biology & Inflammation Program
Dir. Kidney Disease Program
Dir. Structural Biology Program
Professor of Medicine

Massachusetts General Hospital
[redacted]

[redacted]

American Kidney Fund

Re: American Kidney Fund Clinical Scientist in Nephrology Fellowship Application of [redacted]

Dear Committee Members:

I am delighted to write this enthusiastic letter of support for [redacted] who is applying for the American Kidney Fund Clinical Scientist in Nephrology Fellowship.
I have had the opportunity to know [redacted] for the last several years when she was a resident in Internal Medicine at the Massachusetts General Hospital and then as a clinical and research fellow in our combined nephrology training program at Massachusetts General Hospital and the Brigham and Women's Hospital. In short, [redacted] demonstrates all of the qualities that we look for in future staff members who graduate from our highly competitive fellowship program. [redacted] clinical efforts have been consistently rated as superior by her supervisors in medicine and nephrology. She has shown uncommon initiative and tremendous determination in laying the groundwork for a career in clinical investigation beginning at an early stage of her training. I have no doubt that [redacted] will develop into a successful clinician-scientist and anticipate her joining our faculty at the conclusion of her training.

[redacted] wisely chose to align herself with [redacted] who has served as her research mentor since she was a medical resident and initially became actively involved in clinical research activities in the Nephrology Division. [redacted] has an impressive track record of publication, funding and mentoring. As an expert in mineral metabolism in chronic kidney disease (CKD), [redacted] has presented his research at state of the art lectures at a variety of international meetings including the American Society of Nephrology, the National Kidney Foundation and the American Society of Bone and Mineral Research, among others. He has a strong record of continuous federal and foundation funding including career development awards from the American Heart Association, NKF, ASN and the National Institutes of Health. He is PI of an RO1 grant that began in 7/07 and has already submitted a second RO1 to extend his exciting research on phosphorus metabolism in CKD. These resources and his firmly established research infrastructure (study and data coordinators, blood technicians, statisticians, etc.) will be used to help support [redacted]

[redacted] also serves as an Associate Program Director for Internal Medicine Training for Career Development at MGH and it was in this role that he first met [redacted] With his guidance during the past 4 years, [redacted] designed and implemented several studies that examined the role of diet on mineral metabolism in early CKD. Her work was highlighted in poster presentations at the NKF Spring Clinical Meeting in Chicago and our own MGH Clinical Research Day. At the [redacted] ASN Renal Week in San Diego she was selected to present her work as an oral free communication. Perhaps most impressively, much of this work was accomplished in the little spare time our busy residency program affords, which demonstrates her strong commitment to clinical research. During her 1st year of fellowship, [redacted] completed an important physiological study that identified novel mechanisms of secondary hyperparathyroidism in early CKD. She lead-authored the paper detailing this work that was recently accepted by the *Journal of the American Society of Nephrology*. [redacted] generated new hypotheses based on these results and developed the studies outlined in her application. The Aims of the current proposal are the natural progression of her previous work, are important scientifically and are also an excellent tool for training in nephrology research.

[redacted] will continue to serve as research mentor to [redacted] for the duration of this award and the Nephrology Division and I will provide ongoing enthusiastic support for both [redacted] and her mentor. [redacted] will also benefit from the extensive research infrastructure provided by the Nephrology Division, MGH and Harvard Medical School. In addition to [redacted] and myself, she will be able to call on the guidance of [redacted] previously mentored [redacted] and is an internationally recognized, NIH-funded clinical investigator with significant expertise in the fields in which [redacted] has concentrated her interests. To complement her training, [redacted] enrolled in the Scholars in Clinical Science Program at Harvard Medical School. This program is designed to provide promising fellows with formal didactic and practical training in clinical research methodology. This elite program has trained many of our most promising clinical researchers, including [redacted] and will serve [redacted] well in preparing her for a career in clinical research.

As Chief of the Nephrology Division I am very satisfied about the rising trajectory of [redacted] early career. At this rate, [redacted] will become a successful academic nephrologist and an integral member of our Division. I am strongly committed to [redacted] ongoing career development and to clinical research in the Nephrology Division overall. I have made significant investments in our clinical research effort, securing and remodeling over 3,000 square feet of new research and office space where the clinical research program at MGH is based. I will ensure that [redacted] continues to have access to the hospital's extensive research infrastructure, and that during her years as a research fellow I will ensure that she will dedicate at least 75% of her time to research training.

I am confident that [redacted] is an ideal candidate for the [redacted] AKF Clinical Scientist in Nephrology Fellowship. I urge the AKF to support [redacted] in these endeavors.

[redacted]

Please indicate in the space below the period of time you have known the applicant, and in what capacity.

From_____Oct 2004_____ To ____Present_____

Relationship with Applicant _____Supervisor_____

Please rate the applicant by circling the appropriate number which most nearly represents your opinion of the applicant in comparison with a representative group of individuals you have known who have had approximately the same training and experience.

	Outstanding		Excellent		Fair		Poor				N/A
	Highest						Lowest				
	100%- 90%		80%-70%		60%-50%		40%-25%				
Industry/perseverance	10	9	8	7	6	5	4	3	2	1	N/A
Motivation/initiative	10	9	8	7	6	5	4	3	2	1	N/A
Maturity	10	9	8	7	6	5	4	3	2	1	N/A
Clinical ability	10	9	8	7	6	5	4	3	2	1	N/A
Interpersonal facility with peers/ patients	10	9	8	7	6	5	4	3	2	1	N/A
Research	10	9	8	7	6	5	4	3	2	1	N/A
Judgment/critical sense	10	9	8	7	6	5	4	3	2	1	N/A
Intellectual ability	10	9	8	7	6	5	4	3	2	1	N/A
Originality	10	9	8	7	6	5	4	3	2	1	N/A
Leadership capacity	10	9	8	7	6	5	4	3	2	1	N/A
Ability to communicate (written & spoken)	10	9	8	7	6	5	4	3	2	1	N/A
Overall Evaluation	10	9	8	7	6	5	4	3	2	1	N/A

AMERICAN KIDNEY FUND
CLINICAL SCIENTIST IN NEPHROLOGY PROGRAM

APPLICATION FOR ACADEMIC YEAR [redacted]

CONFIDENTIAL REFERENCE REPORT

PRECEPTOR STATEMENT

FORM C

TO THE APPLICANT This section is to be completed **by the applicant** before presenting to the Preceptor who will supervise the clinical research component of the program of study.

Name: [redacted]

TO THE PRECEPTOR

The above-named applicant to the American Kidney Fund Clinical Scientist in Nephrology Program has named you as his/her reference for the clinical research mentor field of study. We ask your cooperation in responding **soon.** All replies **must be received by December 1, 2007** and will be held in strict confidence. This section of the application is of crucial importance. Granting of the fellowship will depend critically upon the evidence provided here that the plan of study is sound, that it is in keeping with the overall goals of the American Kidney Fund as outlined in the announcement, and in that the candidate will be closely followed and supervised by a dedicate mentor in performing the research project. The completed form is not to be returned to the applicant, but mailed to:

Mail to: [redacted]
American Kidney Fund
6110 Executive Boulevard
Suite 1010
Rockville, MD 20852

Please indicate in the space below the period of time you have known the applicant, and in what capacity.

From_____October 2004_____ To ____Present_____

Relationship with Applicant ____ Research Mentor, Clinical Supervisor, Teacher_____

Please rate the applicant by circling the appropriate number which most nearly represents your opinion of the applicant in comparison with a representative group of individuals you have known who have had approximately the same training and experience.

	Outstanding		Excellent		Fair		Poor				N/A
	Highest						Lowest				
	100%- 90%		80%-70%		60%-50%		40%-25%				
Industry/perseverance	(10)	9	8	7	6	5	4	3	2	1	N/A
Motivation/initiative	(10)	9	8	7	6	5	4	3	2	1	N/A
Maturity	(10)	9	8	7	6	5	4	3	2	1	N/A
Clinical ability	(10)	9	8	7	6	5	4	3	2	1	N/A
Interpersonal facility with peers/ patients	(10)	9	8	7	6	5	4	3	2	1	N/A
Research	(10)	9	8	7	6	5	4	3	2	1	N/A
Judgment/critical sense	(10)	9	8	7	6	5	4	3	2	1	N/A
Intellectual ability	(10)	9	8	7	6	5	4	3	2	1	N/A
Originality	(10)	9	8	7	6	5	4	3	2	1	N/A
Leadership capacity	(10)	9	8	7	6	5	4	3	2	1	N/A
Ability to communicate (written & spoken)	(10)	9	8	7	6	5	4	3	2	1	N/A
Overall Evaluation	(10)	9	8	7	6	5	4	3	2	1	N/A

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

Renal Associates

Massachusetts General Hospital
GRB 1003
55 Fruit Street
Boston, Massachusetts 02114
[redacted]

[redacted]

Re: [redacted]

Members of the American Kidney Fund
Clinical Scientist in Nephrology Fellowship Review Committee:

I am writing in strong support of the application of Dr. [redacted] for the American Kidney Fund Clinical Scientist in Nephrology Fellowship. I have been extremely fortunate to serve as [redacted] research mentor over the past 3 years and am delighted to sponsor her current proposal and ongoing work as a research fellow in the Renal Unit at MGH.

Before coming to the MGH, [redacted] graduated summa cum laude from Downstate Medical College in New York where she was the recipient of numerous awards and a member of Alpha Omega Alpha. She first introduced herself to clinical research as a medical student, for which she received a prestigious award upon graduation in recognition of her outstanding work. [redacted] first approached me when she was a second year internal medicine resident interested in becoming involved in clinical research. Seeking me out as a potential research mentor was prompted by us having graduated the same medical school and sharing common interest in patient-oriented research in nephrology. During the past 3+ years, [redacted] has worked with me on several projects related to mineral metabolism in patients with CKD, first joining ongoing studies but later initiating her own studies. She presented her own preliminary results as a poster at the [redacted] National Kidney Foundation meeting and an oral presentation at the American Society of Nephrology meeting in San Diego in 2006. Most recently, [redacted] was the lead-author of the paper that detailed her important and novel findings and which was accepted by the *Journal of the American Society of Nephrology*.

In her published work, [redacted] observed that early-stage CKD patients developed subtle postprandial hypocalcemia in the immediate postprandial state that triggered subsequent secretion of parathyroid hormone. This observation has never been reported previously and may represent a novel early mechanism of secondary hyperparathyroidism. Importantly, although secondary hyperparathyroidism is a common and morbid complication that begins in early CKD, most prior work has focused on its mechanisms in end stage renal disease patients; much less is known of its early mechanisms. As an American Kidney Fund Clinical Scientist, [redacted] will further her work in this area. Through detailed physiological investigation, [redacted] will

expand our understanding of normal renal physiology and disease mechanisms while at the same time generating new data on the effects of readily available interventions to attenuate the development of secondary hyperparathyroidism in CKD, data that could eventually have a beneficial impact on millions of CKD patients. In addition, the studies she now proposes will promote her further development as a patient-oriented investigator. [redacted] developed all aspects of these studies herself with my guidance. She reviewed the literature, met with other experts in the field, designed the studies, wrote the protocols and informed consent forms for the IRB, and has begun the recruitment of subjects. None of the studies she proposes were "borrowed" from my own grants – these are new studies conceived by [redacted] with my mentorship.

In carrying out her work, [redacted] will continue to have access to the vast clinical research infrastructure at MGH, including its General Clinical Research Center where I am an active investigator with several ongoing protocols. I, along with [redacted] Chief of the Renal Unit and [redacted] Director of Renal Clinical Research, will ensure that [redacted] is provided with all the resources that she needs to succeed in her research training including 80% of her time protected for research training. She already has dedicated office space with a personal computer, phone, FAX and administrative support. Our blood technician, database manager and research coordinator will continue to be available to support her work. My own research funding is secure for the foreseeable future with RO1 funding as of July 2007 and a second RO1 under review. [redacted] will attend our weekly laboratory meetings and our clinical and research conferences and will continue to hone her clinical skills by seeing patients in her weekly outpatient continuity clinic with her staff preceptor, [redacted] She will attend the annual ASN and NKF conferences.

To complement the practical research experience she is gaining, [redacted] enrolled in the Scholars in Clinical Science Program at Harvard Medical School in order to obtain formal didactic training in the methods of human research. The Scholars Program is unique in that it focuses on patient-oriented research that involves direct patient contact, as [redacted] proposes. It covers study design, biostatistics, genetics, pharmacology, ethical conduct of human research and many other key topics. Several years ago, I was the first graduate of the Scholars Program and it was instrumental in my research career development. The program will provide [redacted] with the specialized tools required to conduct her current and future projects and will help prepare her for a career in academic medicine as it did for me.

[redacted] has thoroughly impressed me with her initiative in seeking out and executing clinical research opportunities but several elements of her accomplishments deserve special emphasis. [redacted] began to work in research during her extremely limited spare time as an internal medicine house officer and then as a clinical fellow in nephrology, all the while maintaining the highest standard of performance in her daily clinical duties. As the Associate Program Director for Housestaff Career Development at MGH, I can state with certainty that [redacted] is one of only a handful of residents to successfully initiate and recruit subjects into a patient-oriented clinical research study during our extremely rigorous residency program. While this considerable achievement

speaks to [redacted] determination to succeed in research, her motivation for a career in academic nephrology, and her scientific potential, these outstanding qualities must be considered in the broader context of [redacted] background. [redacted] In my opinion, her ability to not only transition seamlessly into a new country, new culture and new educational system using a new language, and at the same time, excel beyond her peers is truly remarkable.

In closing, I would like to reemphasize my unwavering support for [redacted] and this proposal. [redacted] early career development program which includes formal research education, an important patient-oriented clinical research project that will be performed in a supportive research environment is a recipe for success. The American Kidney Fund Clinical Scientist Fellowship is the next essential ingredient to help [redacted] achieve her lofty career goals.

Sincerely yours,

[redacted]

Assistant Professor of Medicine,
Harvard Medical School
Associate Program Director,
Internal Medicine Residency Program
Renal Unit, Massachusetts General Hospital

[redacted]

AMERICAN KIDNEY FUND
CLINICAL SCIENTIST IN NEPHROLOGY PROGRAM
APPLICATION FOR ACADEMIC [redacted]

BUDGET PROPOSAL

FORM D
This form is to be completed jointly by a representative of the Division of Nephrology and the person responsible for the clinical research area of study. Please indicate in the space below the institution or department which will be responsible for administering the financial aspect of the American Kidney Fund Clinical Scientist in Nephrology Program.

Applicant's Name [redacted]
Institution The General Hospital Corporation, dba Massachusetts General Hospital
Contact [redacted]
Title and Senior Grant and Contract Administrator
Telephone Number [redacted]

Please outline the expected annual budget for the applicant.

First Year Budget — Please provide a budget justification page
Applicant's Salary Including Benefits—First year of fellowship $ 37,037
(Must correspond to AKF's guidelines—see program description)

Please itemize your request for additional monies

1	Fringe	$ 12,963
2	Travel	$ 1,500
3	Laptop	$ 2,200
4	Training and Study Related Expenses	$ 26,300

Second Year Budget — Please provide a budget justification page
Applicant's Salary Including Benefits—First year of fellowship $36,765
(Must correspond to AKF's guidelines—see program description)

Please itemize your request for additional monies

1	Fringe	$13,235
2	Travel	$ 1,500
3	Training and Study Related Expenses	$ 28,500

Mail to: [redacted]
American Kidney Fund
6110 Executive Boulevard
Suite 1010
Rockville, MD 20852

[redacted]

Budget Justification Page (per year)

FIRST YEAR	**$80,000**
Salary	$37,037
Fringe	$12,963
Laptop and printer Software	$ 2,200
Travel	$1,500
Training and Study Related Exp	$26,300

Budget Justification - Year 1

$37,037	Salary (NIH PGY Level 5 of $46,992) will be supplemented by institutional funds.
$12,963	Fringe for professional staff at 35% in accordance with institutional policy.
$ 2,200	Laptop and printer software
$1,500	Travel
$26,300	Training and Study Related Expenses

Training and Study Related Expenses Justification

$ 1,000	Statistical programs, Endnote, and database software
$ 16,800	Laboratory Costs Money will be used to runs assays at research rates and purchase kits needed to run the following critical assays: 1,25-D, 25-D levels, PTH, FGF-23.
$ 6,000	Subject Payments
$ 1,000	Education - Books and fees for Harvard course
$ 1,000	Research Drugs
$ 500	General lab and office supplies

SECOND YEAR	**$80,000**
Salary	$36,765
Fringe	$13,235
Travel	$1,500
Training and Study Related Exp	$28,500

Budget Justification – Year 2

$36,765	Salary (NIH PGY Level 6 of $48,852) will be supplemented by institutional funds.
$13,235	Fringe for professional staff at 36% in accordance with institutional policy.
$1,500	Travel
$28,500	Training and Study Related Expenses

Training and Study Related Expenses Justification

$ 15,000	Laboratory Costs Money will be used to runs assays at research rates and purchase kits needed to run the following critical assays: 1,25-D, 25-D levels, PTH, FGF-23.
$ 4,000	Subject Payments
$ 8,000	Tuition for two additional courses at HSPH
$ 300	Education - Books and fees for Additional Courses
$ 700	Research Drugs
$ 500	General lab and office supplies

Two additional courses in biostatistics will be taken in academic year of [redacted] after completion of the Scholars Program and the cost for the enrollment is included in the second year budget justification. The two additional courses are offered at the Harvard School of Public Health and they provide in-depth training in basic statistical techniques that are commonly used in all aspects of human clinical investigation and specifically by our research group. The first course is Applied Longitudinal Analysis (BIO226-01) and it covers modern methods for the analysis

[redacted]

Budget Justification Continuation Page

of repeated measures, correlated outcomes and longitudinal data, including the unbalanced and incomplete data sets characteristic of biomedical research. Topics include an introduction to the analysis of correlated data, analysis of response profiles, covariance pattern models, random effects models, and generalized linear models for longitudinal data, including generalized estimating equations (GEE) and generalized linear mixed effects models (GLMMs). The studies described in this proposal will generate repeated measures data, and this course is well-suited for the kind of research projects I will be involved in throughout the duration of the AKF award and beyond. The second course is Applied Survival Analysis (BIO223-01) and it cover topics in both discrete data analysis and applied survival analysis, including logistic regression, hazard, survivor, and actuarial estimation of the survival distribution, comparison of survival using log rank and other tests, and regression models including the Cox proportional hazards model. This course is needed for the kind the survival analyses that are carried out by our group on observational data available from cohort studies of dialysis patients.

[redacted]

PLEASE NOTE
THIS FORM REQUIRES TWO SIGNATURES

[redacted]
Signature of Reference
(Nephrology Representative)

[redacted]
Print Name

[redacted]
Date

Chief of Nephrology
Title

Massachusetts General Hospital
Institution

[redacted]
Telephone Number

[redacted]
Signature of Reference
(Preceptor)

[redacted]
Print Name

[redacted]
Date

Asst. Prof. Medicine
Title

Harvard Medical School
Institution

[redacted]
Telephone Number

MASSACHUSETTS
GENERAL HOSPITAL

HARVARD
MEDICAL SCHOOL

Medical Services
55 Fruit Street, [redacted]
Boston, Massachusetts 02114-2696
[redacted]

[redacted]
Assistant Chief of Medicine
Director of Residency Training

[redacted]

[redacted]

American Kidney Fund
6110 Executive Boulevard, Suite 1010
Rockville, MD 20852

RE: [redacted]

Dear Sir or Madam:

It is my pleasure and privilege to write this letter of recommendation on behalf of Dr. [redacted] in support of the AKF Research Fellowship Award.

I have had the pleasure of working with [redacted] both as a resident in Internal Medicine as well as during her fellowship in Clinical Nephrology. To understand [redacted] is to appreciate the fact that she arrived here as a high school student from [redacted] without speaking any English and quickly established herself as an intellect to be dealt with. In [redacted] she entered the Sophie Davis School of Biomedical Education, which is part of the City University of New York, obtaining a Bachelor of Science. She subsequently entered the Downstate College of Medicine, State University of New York, obtaining her M.D. degree in [redacted] She graduated Suma Cum Laude at Downstate College of Medicine receiving numerous awards, including the Department of Internal Medicine Award for Academic Achievement in Clinical Performance at Downstate Medical Center. She was elected to membership in the Alpha Omega Alpha Medical Honor Society.

[redacted] outstanding performance stood out during our selection process, and we were fortunate to attract her to the Massachusetts General Hospital Internal Medicine Residency. [redacted] has an outstanding record as a resident in a very accomplished residency class. Her evaluations were consistently in our highest categories, superior. She has an outstanding knowledge base and has performed at the highest level on the In Service Exam. She is an avid reader of the medical literature. Accompanying this outstanding knowledge base are superb clinical skills. Her history, evaluations and clinical management were precocious and far ahead of her level of training. She was diligent, hardworking and tended to all of her responsibilities with the utmost of dedication, professionalism and maturity. She was no doubt one of the hardest working members of her peer group. She has incredible insight into her own strengths and areas for improvement. She has dealt with feedback with professionalism and responsiveness.

What is even more impressive is that during her residency and throughout her clinical year of fellowship, both settings with very demanding environments, she dedicated herself to clinical research. Beginning in June of [redacted] she has found and created time to contribute to several original works under the mentorship of Dr. [redacted] I remember many clinics in which [redacted] would come and recruit patients from my outpatient practice. She did this with diligence, regularity and professionalism. Patients always appreciated her professionalism and compassion during the recruitment phase. This effort has led to several publications, one of which she lead-authored. She was also selected to give an oral presentation at the ASN meetings in November, [redacted] She has coauthored several papers. Presently, the majority of [redacted] time is spent on research and research training, including her participation in the Scholars in Clinical Science Program at the Harvard Medical School.

Having arrived from [redacted] as a teenager, without a mastery of English to excelling at one of the most demanding residency and fellowship programs in the country and on top of that, having been productive from a research perspective during both residency and the clinical year of fellowship, speaks of incredible talent, unwavering dedication and an intense desire for academic success. Furthermore, this record is a testament to [redacted] ability to set goals and meet deadlines despite competing demands on her time. In my opinion, she is one of the most competitive candidates to come out of Massachusetts General Hospital for a career in academic nephrology and I would support her application with the utmost enthusiasm.

Sincerely,

[redacted]

HB/ts

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

Department of Medicine and Renal Unit
55 Fruit Street, Bulfinch 127
Boston, Massachusetts 02114-2696
[redacted]

[redacted]
Associate Professor of Medicine
Harvard Medical School

[redacted]

Re: American Kidney Fund Clinical Scientist in Nephrology Fellowship

Dear Committee Members:

It is with great pleasure that I provide this letter in strong support of Dr. [redacted] who is applying for the American Kidney Fund Clinical Scientist in Nephrology Fellowship. As the Director of Clinical Research in the Renal Unit at the Massachusetts General Hospital, I am excited about the potential [redacted] has already shown in only a brief time at MGH and have tremendous confidence that she will be able to carry out the project described in this proposal and in the process continue to develop into a high-caliber clinical investigator.

[redacted] strong interest and proficiency in clinical research date back to her residency when she designed and completed a physiological study that examined postprandial handling of dietary calcium and phosphorus in early chronic kidney disease. Guided by her research mentor, Dr. [redacted] [redacted] ultimately wrote a first-author publication that has been accepted by the *Journal of the American Society of Nephrology*. We were thrilled that she decided to enroll in our Nephrology Fellowship where she has continued to excel during the first clinical year as she did during residency.

In the five months of her first research year, [redacted] has designed a new protocol built upon preliminary data to formulate her proposal to study postprandial calciuria as a novel mechanism for the development of secondary hyperparathyroidism in early chronic kidney disease. [redacted] will use a rigorous physiological study design to test her well-researched hypotheses. The results will be of broad clinical interest, will suggest novel avenues for future research and perhaps most importantly, will serve as an outstanding research training vehicle for [redacted] scientific development. In addition [redacted] has enrolled in the Scholars in Clinical Science Program at Harvard Medical School. Through this program, [redacted] will receive exceptional training in the design and conduct of patient-oriented studies. Dr. [redacted] himself a graduate of the Scholars program, is specifically trained in physiological research and will continue to provide [redacted] first-rate mentoring. Finally, I will personally oversee [redacted] research development and ensure her access to the full extent of our clinical research infrastructure.

I look forward to continuing to support [redacted] early research career development. I highly recommend [redacted] to the committee with my full support and without reservations.

Sincerely yours,

[redacted]

Renal Unit, Department of Medicine
Massachusetts General Hospital
Associate Professor of Medicine
Harvard Medical School

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

Endocrine Unit
50 Blossom Street, [redacted]
Boston, Massachusetts 02114-2696
[redacted]

[redacted]

Members of the American Kidney Fund Review Committee:

It is with great pleasure that I write this letter of enthusiastic support for the [redacted] AKF Clinical Scientist in Nephrology Fellowship application of Dr. [redacted]. I have known [redacted] through our research collaborations in the past 4 years, during which time I have been very impressed with her development as a budding clinical investigator.

Although [redacted] has only been involved with clinical research at the MGH for the past 4 years, she has sought out every opportunity to participate and excel in clinical research since the time of her arrival at MGH. [redacted] chose to work with Dr. [redacted] an RO1-funded clinical investigator and an expert on the design and conduct of physiological studies. By working closely with Dr. [redacted], she developed an exciting project looking at the postprandial handling of dietary calcium and phosphorus in healthy volunteers and subjects with chronic kidney disease. With the guidance of Dr. [redacted] [redacted] designed an original patient-oriented study for which she obtained IRB approval, recruited all of the participants in the study, analyzed the data, and prepared the manuscript that will be published in the *Journal of American Society of Nephrology*. What is most impressive is that [redacted] did this while still carrying out her many responsibilities as a resident in Internal Medicine and later a clinical fellow in Nephrology. [redacted] presented the results of her efforts both at local research conferences as well as the national meetings. At the American Society of Nephrology Renal Week Meeting she delivered an oral presentation that was very well received. By studying the handling of dietary calcium and phosphorus in healthy volunteers and CKD subjects, she found that while postprandial calciuria was observed in both groups, only the CKD subjects developed relative hypocalcemia and a consequent rise in parathyroid hormone levels. Her findings made important contributions to the understanding of physiologic mechanisms of the development secondary hyperparathyroidism in early chronic kidney disease. [redacted] work has also contributed to the ongoing collaboration between the Renal Unit and the Endocrine Unit at MGH.

The current proposal represents the next phase of [redacted] development as an independent clinical investigator. The innovative and important study she now proposes was conceived and initiated with close collaboration with Dr. [redacted], her primary research mentor. This work was built on [redacted] preliminary data and proposes to determine whether offsetting the postprandial calciuria by increasing the dietary absorption of calcium will prevent the postprandial rise in PTH observed in the CKD cohort. This project will dovetail nicely with future work on bone mineral metabolism in CKD that is currently under way in my laboratory, and I look forward to ongoing collaboration with [redacted].

In closing, I would like to express my strong enthusiasm for Dr. [redacted] and her bright future as a clinical researcher. I firmly believe that the AKF Clinical Scientist in Nephrology Fellowship is the ideal support mechanism for this next important phase of Dr. [redacted] career development and that as an AKF Fellow, Dr. [redacted] will be an outstanding ambassador for the American Kidney Fund. I hope the AKF will invest in her future.

Sincerely yours,

[redacted]

Professor of Pediatrics,
Harvard Medical School