Promotion Narrative: Associate Professor to Professor, Tenured

TEACHING NARRATIVE

Teaching Philosophy

● My philosophy in teaching is that as faculty we should strive to extract the best possible performance and potential for academic growth from every student. The most capable students should be encouraged to perform at the highest level, while those requiring more help should receive it. There is no single method or formula for achieving this goal, but the commonality amongst all students is that they arrive at OUHSC with a variable, but nonetheless partially developed potential for academic excellence. As faculty, it is incumbent upon us to recognize the students 'entry level' talents and guide them in academic and professional growth so that they may achieve their potential.

Professional Medical Education

● One of my most rewarding and critical jobs at OUHSC is teaching medical students. From my arrival at OUHSC in 2006 until achieving tenure in 2012, I steadily built and then sustained a medical teaching portfolio. My evaluations were good, albeit with room for improvement. This section focuses on the post-tenure period and the steps taken to further enhance the effectiveness of my medical school teaching.

● My teaching has evolved within the context of larger (and much needed) changes implemented by the Course Director (Dr. [redacted]). The curriculum was changed such that we now teach basic immunology to first year students rather than second year students. The individual teaching assignments have been modified such that the students have fewer instructors with each teaching a cohesive block in the course. I am primarily responsible for teaching the generation and operation of B cell immunity in health and disease. Our faculty, under Dr. [redacted] leadership has also over-hauled our lectures to include: more pre-recorded (and thus flipped) elements; clinical vignettes to make the basic science more relatable to the clinic; incorporation of audience response questions during class time to facilitate better interaction with students and confirm knowledge and understanding of key concepts; and review sessions to reinforce key concepts and answer specific questions. Our faculty, myself included, have taken classes on writing multiple choice questions with an emphasis on USMLE questions, and have had peer assessment of our lectures conducted. Consequently, the Step 1 USMLE scores for immunology have steadily risen over the past several years.

● I have worked to enable my teaching philosophy (extract the best possible performance from every student regardless of initial ability). In each of my lectures, I provide contact email addresses and tell the students at the beginning of the lecture to please contact me with questions, regardless of the day or time, especially as a test is approaching. I also emphasize that no one need struggle and that our faculty are there to help if difficulties are encountered. This allows students having difficulty to approach me confidentially and highly able students to explore nuances in immunology that cannot be covered in class. I also stay present after my lectures and make myself available in the break between double lectures to answer questions. This allows me to gauge understanding of concepts and if I feel something might not have come across clearly, I will clarify with the class immediately.

Course Code	Course Title	Role	Topics Taught	Years	Students /Class	Contact Hr
MMI 8300	Medical Microbiology Immunology	Instructor	Hypersensitivity POPS	2007 - 2010	20	2
			Tetanus POPS	"		2
			HIV POPS	2008 - 2010		2
			Hypersensitivity	2008 - 2009	165	1
			Immunodeficiency	"		1
MID 5155	Etiology and pathogenesis of disease	Instructor	Hypersensitivity	2010 - 2011	165	1
			Immunodeficiency	"		1
			Review Session	"		1
INDT 8116	Disease, Diagnosis, Therapy	Instructor	Antigen Recognition	2010	165	1
			Humoral Immunity	"		1
			Review Session	"		1
INDT 8156	Blood, Hematopoiesis, Lymphatics	Instructor	Immunodeficiency	2011	165	2
INDT 8132	**Muscular, Skeletal, Integument**	**Instructor**	**Antigen Recognition**	**2012 - 2018**	**165**	**2**
			Humoral Immunity	**"**		**2**
			Hypersensitivity	**"**		**1**
			Immunodeficiency	2012 - 2014		2

Table 1. Summary of Medical School Teaching. Bold font indicates current assignments.

Feedback, Evaluations and Improvements:

● I have already detailed the improvements I have made to my medical school teaching over the past several years including workshops on teaching and writing exam questions, including audience response questions in lectures, and using review sessions to reinforce important concepts. However, a critical aspect of improving ones teaching lies in responding appropriately to student evaluations. The comments from the medical students have been largely positive emphasizing that I take the time to carefully explain the material and are available to answer questions subsequently or in review sessions. I have also consistently received evaluation scores above 5.0 every year. There are some students that struggle with my [redacted] and vocal projection, although some individuals have mentioned that this is exacerbated by: English being their second language; the AV equipment, or watching a video of the lecture at 1.5x speed. Although, this has never come up as an issue with my graduate teaching, I will continue to strive to improve my vocal projection in the BSEB lecture hall. A remaining challenge is also to better incorporate the needs of the more able students who demand more information than is given in class. I will work to better sign-post additional material that they can consult if they wish, while being careful not to detract from core course material.

Graduate education

● As a biomedical researcher, I feel that training the next generation of researchers is critically important. In particular, this is essential for preserving the competitive edge that the US has internationally in science and medicine, and in facilitating future medical student training and translational research. My philosophy for training graduate students is similar to that of medical students, namely in extracting the best possible scientific and academic performance from each and every student. For these reasons, I have been very active in the following areas:

○ Teaching first year GPiBS students and second year Microbiology and Immunology students

○ Directing our first year Basic Immunology and Immunity in Disease Courses

○ Directing our second year Advanced Immunology course

○ Participating in departmental learning activities (Immunology Journal Club, student seminars)

○ Participating in campus-wide student activities (judging at GREAT conference, meeting incoming students at departmental receptions)

○ Serving on student committees (Microbiology and Immunology and other departments)

○ Taking laboratory rotation students

○Taking graduate students into my lab for PhD studies

<u>Classroom teaching:</u>

● In GPiBS, the basic science courses are typically didactic in nature, and although they impart essential material, do not represent the primary manner in which biomedical scientists learn throughout their professional career. I therefore developed an exercise in my GPiBS Immunology class (2011/12). In brief, I incorporated an active learning-based session at the end of my cell signaling lectures to help the students understand better how signaling in the immune system is examined experimentally. The students were asked to divide into small groups and were presented with a hypothesis. I then assigned each of four groups a different experimental system, spanning in vitro, ex vivo and in vivo approaches using mouse-derived and primary human material. After a discussion period, a spokesperson for the group would join me at the marker board and together with the class we would discuss and note the approaches to be taken. Each group would therefore get to learn from the others. During this process, the students learned how to approach scientific questions experimentally. This method also nicely adhered to my teaching philosophy because each student was able to contribute something to the discussion. Student evaluations were positive regarding this aspect of the class and now that I am the Course Director (since late 2017), I will work with the other instructors to ensure inclusion of experimental design in other parts of the course.

● My classroom teaching undergoes an important transition from first year to second year students. I directed the Microbiology and Immunology Advanced Immunology course from 2008-2013. This course is student led, paper-driven and interactive. Each student has to present primary research papers (provided by the instructor) to their student peers. Participation is actively encouraged and the instructor typically guides rather than drives the discussion. Students are graded on their presentations as well as their participation. This is in addition to more traditional methods of testing (written exam and oral exam). The oral examination is regarded as a dry run for the oral portion of the qualifying exam because the students have little or no experience with this important aspect of scientific communication. The oral exam practice nicely complements teaching initiatives in the Advanced Pathogenesis course where the students devise a hypothesis and a means of testing it as a take home exercise. Collectively,

the two departmental courses provide the students with experience required to develop many skills essential to performing as an academic researcher. I point out that this course was devised over 30 years ago by Dr. [redacted] and was subject to many refinements before I assumed the directorship. My contribution to improving the course was in three areas: a revised syllabus that more clearly outlines responsibilities and expectations for faculty and students; a brief introductory class whereby the course director explains how to present a research paper; and a take-home assignment whereby students write a Nature journal styled article ('News and Views'). Dr. [redacted], the current course director has maintained these elements in the course.

a. Graduate Teaching

Course Code	**Course Title**	**Role**	**Topics Taught**	**Years**	**Students / Class**	**Contact Hr**
BMSC 5221	GPiBS Journal Club	Instructor	Immunology, Vaccines	2007, 2016	6-8	4
BMSC 6032	**Basic Immunology** *(formerly GPiBs Immunology)*	Instructor **Course Director**	Signaling **Scheduling, Exams, Grading**	2008 - 17 **2018 -**	5 - 20	3 **38 (2)***
BMSB 6111	**Immunity in Disease** *(formerly GPiBS Immunity in Disease)*	**Instructor** **Course Director**	**Extrinsic regulation** **Hypersensitivity** **Scheduling, Exams, Grading**	**2008 -** **2010 -** **2018 -**	**5 - 20**	**1.5** **1.5** **19 (2)***
MI 6843	**Advanced Immunology**	**Instructor** **Examiner** Course Director	**Humoral Immunity** **Oral exam panel** Scheduling, Exams, Grading	**2007 -** **2007 -** 2008 - 2013	**4 - 12**	**3** **2 – 6** 48 (12)*

b. Other Teaching

Course Code	**Course Title**	**Role**	**Topics Taught**	**Years**	**Students per Class**	**Contact Hr**
MID 7135	Dental Microbiology, Immunology	Instructor	Antigen Recognition Immunodeficiency Hypersensitivity	2008 - 2013 2008 - 2013 2013	50	2 1 1
n/a	Headlands Summer Program	Instructor	Vaccines	2007	20	1

Table 2a and 2b. Summary of Graduate Teaching. My graduate education efforts have focused largely on classroom teaching and administration. Contact hours in parenthesis estimate my contact hours relative to the entirety of the course. I currently have 16 contact hours per year in direct instruction and have responsibility for directing two courses with a combined 57 contact hours per year. Asterisks (*) indicate contact hours under my direction versus the direct contact hours as a result of me teaching in those courses. Current activities are shown in bold font.

Student Committees

● As is evident from the full list in my CV, I have and continue to serve on several student committees. This is an important aspect of graduate education because committee members can provide insights that complement the guidance being provided by the primary mentor. Furthermore, when students receive similar guidance from more than one source, they tend to recognize its importance. *Thus far, I have served on 39 student committees*. Of the students who have graduated thus far, all have to secured a post-doctoral or PhD-level position, unless rejoining the MD/PhD program.

Teaching in the Laboratory

● Every day presents an opportunity for teaching in the laboratory. Most of my efforts are focused on graduate students. I have mentored three graduate students. Two have graduated with PhD's and one with a MS degree. I currently have a full time 3rd year graduate student ([redacted]) in my laboratory. Several students have rotated through my laboratory as well as summer students. I have also mentored four post-doctoral fellows. In this context, it is relatively easy to adhere to my teaching philosophy of extracting the best performance from each trainee. Whether it is summer, rotation or graduate students or post-docs, I practice an open door policy. I view my primary responsibility to maintain and further develop an environment in which they can thrive. This requires maintaining sufficient funding, equipment and resources and being on constant look-out for career opportunities. I conduct regular lab meetings with the entire lab (every 2 weeks on average) as well as weekly or bi-weekly one-on-one meetings with individuals in my lab. This allows me to tailor my training to their specific needs and abilities and gives them plenty of opportunity to voice concerns or seek further help in confidence. During these meetings which typically last around 1 hour, we review goals set at the previous meeting, discuss new data, design new experiments and set goals for the next meeting. As the student grows in confidence and experience, they eventually direct the meeting to a greater extent than I do. My laboratory currently consists of four individuals (myself, one Staff Scientist, one Research Associate, and one Graduate Research Assistant). The range of expertise and skills on hand facilitates training of new students and I intend to recruit another graduate student from the incoming class or from next year's class.

A full list of the students who have trained in my laboratory at various levels is included in my CV.

○ Graduate Student Achievements

Students in my laboratory have typically attained a high level of achievement during their graduate career, which is attributable to their commitment and the excellent environment at OUHSC and in our department. I feel that our laboratory and my mentoring approach have facilitated these achievements and the following highlights the more significant accomplishments:

[redacted], PhD, graduated in 2012 with six peer-reviewed publications. Three of those were first author articles. During her time in my laboratory she presented her work at the American Association of Immunologists (AAI) conference. I presented her work at a Keystone Conference and at a large European Federation of Immunology Societies (EFIS) conference as an invited talk. Her work has been the basis for several of our funding applications since 2012 and my current RO1 developed from her primary thesis topic. Hemangi worked in the biotech industry for 5 years and recently joined my laboratory as a Staff Scientist to help boost our efforts on human subjects' research and B cell repertoire analysis. She is currently day-to-day directing and managing our PHF-funded project.

[redacted] PhD graduated in 2015 as the Robert A. Patnode Award winner for outstanding graduate research in our department. She was the recipient of a national-level competitive fellowship from the AAI and published 6 papers from her work with me (three as first author). [redacted] also presented her work as an invited speaker at the AAI conference. Her work formed the basis for our continuing research, including my current NIH R21 award.

○ Mentoring Junior Faculty

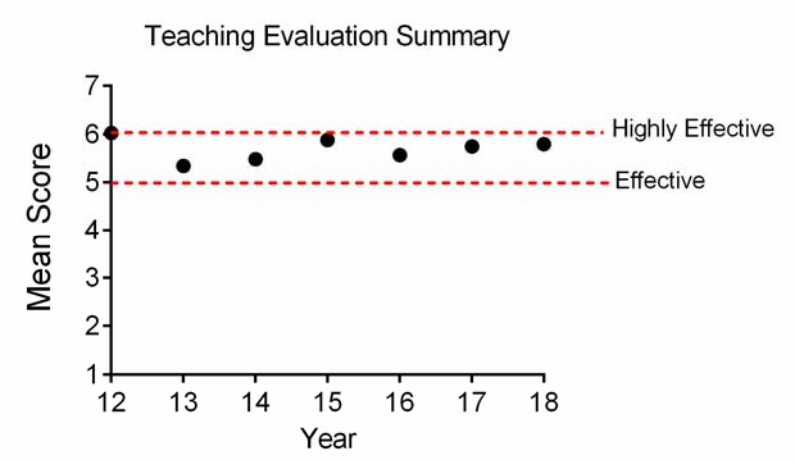
Commensurate with my growing experience I have spent additional effort on mentoring junior faculty. Just as I was fortunate to receive outstanding mentorship from several senior colleagues at OUHSC, it is important to try and communicate what I have learned to our junior faculty. I have served formally (Dr. [redacted]) and informally (Dr. [redacted]) from 2012 to the present. These activities are listed in my CV.

Evaluations on Medical Education

Summary of Score Distributions for the 11/12 through 17/18 academic years:

"[redacted] PhD was an effective teacher"

		Academic Year					
Answer Options	**11/12**	**12/13**	**13/14**	**14/15**	**15/16**	**16/17**	**17/18**
1- Strongly Disagree	0	1	1	0	4	3	0
2- Moderately Disagree	0	4	3	0	1	2	3
3- Slightly Disagree	0	4	8	2	7	5	1
4- Neither Agree or Disagree	5	16	7	10	4	3	4
5- Slightly Agree	22	20	24	14	16	20	26
6- Moderately Agree	38	33	29	43	41	31	36
7- Strongly Agree	35	21	28	30	27	37	30
Mean	***6.03***	***5.35***	***5.49***	***5.89***	***5.57***	***5.75***	***5.80***



[redacted] [redacted]

Selected Comments from Medical Students:

● **11/12** (i) Dr. [redacted] is always a pleasure in class. His presentations are always very professional. I really appreciated his notes on the power point and found them to be very helpful. (ii) As he gave more lectures, he got better each time. Hypersensitivities was the best one.

● **13/14** (i) Dr. [redacted] is a great lecturer. I really enjoyed learning from him. He seems very willing to answer questions, and he seems to know everything about immunology! (ii) Very concise and knowledgeable lecturer. I'd really enjoy his lectures more if he could speak a little louder however. He is a little soft spoken so even if his mic is working (which isn't always the case) I find myself straining to hear him. (iii) Dr. [redacted] was very straightforward with the material and always tried to make sure the class was following.

● **14/15** (i) Dr. [redacted] was a great lecturer (and not just because he has an awesome accent). He made it clear during his presentations what he was presenting and what we were learning. The test questions that were asked on his material were easily understood and answered based on his lectures and explanation of objectives and material. He was really funny too, I wish he would come lecture for us more often. (ii) Dr. [redacted] is an excellent instructor. If I could make one suggestion to him, it would be to place the mic a little closer to his mouth (or speak a little louder). It is often difficult to hear some of the things he says when re-watching the lectures. (iii) Love Dr. [redacted]. Clear and concise lecturing. Very open to questions and takes time to explain concepts in detail.

● **15/16** (i) I enjoyed your lecture and thought it was well organized, however I had difficulty hearing you at times. (ii) Very good and knowledgeable. (iii) He was a good professor! I liked his lectures. (iv) Other than the technical difficulties, I enjoyed Dr. [redacted] lectures. He went at a good pace. I do however think he assumed a little too much of the students and lost some. (v) Dr. [redacted] did a great job lecturing and his PPTs were easy to follow.

● **16/17** (i) Seems to really care about our success. If the lecture notes on his slides (underneath them) could be more organized and flow better, I would really appreciate it!

●**17/18** (i) No issues whatsoever. Keep doing what you do. (ii) Much better as lecturer than prerecorded slides. (iii) The voice-overs were very helpful. Thank you for putting it in written form as well. (iv) Sometimes a little too soft spoken so he is hard to hear, but great presentation of the material and great notes under the slides.

Evaluations on Graduate Education

I assumed directorship of the first year courses in Basic Immunology (MI6032) and Immunity in Disease (MI6111) in late 2017. The following information is therefore reflective of one year only and a class of 5 students. Results have been extracted from anonymous online surveys which have to be completed before final grades are given.

● Basic Immunology Spring 2018 Evaluation (MI6032)

Using the score range 1-7, with 7 being the most effective, for sixteen in class instruction periods with twelve different instructors, the *average* score was **6.51** (range 5.6 – 7.0).

In response to questions on the course:

The course was well organized	5.4
The course objectives were clear	6.4
The exams were reflective of the course objectives	6.0
Please rate the overall quality of the course	**6.4**

Specific Feedback

Very little written feedback was provided, with the only comment being a request to put T cell and B cell material together in the same block to improve flow. This will be organized if lecturer availability allows it. Organization has some room for improvement, particularly the process for obtaining and returning graded homework assignments to the students. I will work to simplify the process, which was our main logistical challenge this year.

● Immunity in Disease Spring 2018 Evaluation (MI6111)

Using the score range 1-7, with 7 being the most effective, for sixteen in class instruction periods with twelve different instructors, the *average* score was **6.84** (range 6.5 – 7.0).

In response to questions on the course:

The course was well organized	7.0
The course objectives were clear	7.0
The exams were reflective of the course objectives	7.0
Please rate the overall quality of the course	**7.0**

Specific Feedback (names of other faculty redacted)

There was a high level of enthusiasm for this course as indicated by the comments.

● He made the lecture very engaging and gave us several examples of therapeutics for specific CNA disorders and covered general topics that we would potentially hear.

● He is always fun to talk to and I really enjoyed hearing him give us a lecture. He covered the topic very well, especially considering how broad the topic is, and made sure we understood what was going on.

● *Dr. [redacted] is a fantastic lecturer and I especially enjoyed that he exposed us to the flipped format that we will be encountering in the next semester of courses. Having the recorded powerpoint was also useful when studying.*

● Dr. ******* is a lot of fun to have as an instructor. He is very engaging and explains the material in such a way that it is very easy to understand while it is actually a very complicated topic.

● Dr. ******* lecture was very well organized and I think she gave us a very comprehensive overview of autoimmunity, which is a huge topic.

● I don't have an interest in cancer but I really enjoyed Dr. ******** lecture. I liked how we got an overview of how the immune system interacts with cancer as well as the ways of combating cancer and how they work within the immune system, such as CAR T cells and checkpoint inhibitors. The clear application of what we learned in the first two immunology blocks was exciting to me.

[redacted] [redacted]

RESEARCH NARRATIVE

Introduction

My position at OUHSC entails **65 - 70%** of my time and effort being spent on research activities. I have built a vigorous research program that is well-funded and aligned with the infectious disease, immunology, and cancer components of the OUHSC Strategic Plan. This is evidenced through my publications, a number of which involved collaboration with investigators in my own department and across campus. My laboratory built and then sustained a direct cost income from federal and other sources that is typically in the range of $500K per year in direct costs. I have also maintained a laboratory of 5 - 8 individuals for the past 12 years consisting of summer students, graduate students, post-doctoral fellows, research assistants, research associates, staff scientists, and research faculty.

Summary of Prior Research Trajectory and Accomplishments

In my 12 years at OUHSC I have secured over $8,000,000 in extramural funding (including direct costs), with funding primarily from federal sources (NIH and Department of Defense). I have also received funding from several local and regional funding organizations (OCAST and PHF). I currently hold two NIH grants (RO1 and R21) and two PHF Team Science Grants (one as lead PI). During my time at OUHSC, I have consistently published 2-4 peer-reviewed articles per year with more than half of those articles being on primary research directly from our laboratory. My long-term research interest is on the adaptive immune response to bacterial infection and bacterial toxins. My work has been concerned with the effects on and mechanisms by which Natural Killer T (NKT cells) influence the B cell-driven antibody-producing arm of the adaptive immune system.

The interactions between NKT cells and B cells that form the core of our research continue to impact the fields of B cell and NKT cells research. However, our work is having an impact beyond that of antibody production. In 2009, we published a paper in *Blood* demonstrating that interaction between the CD1d molecule expressed by B cells and the T cell antigen receptor (TCR) expressed by NKT cells was necessary for NKT cells to enhance antibody responses by B cells. This work helped me secure my first RO1 which resulted in 12 publications, mainly by my graduate students (please refer to teaching narrative). The B cell CD1d / NKT interaction has since been discovered by other laboratories to have implications for the immune dysregulation found in Systemic Lupus Erythematosus (SLE), in blood group antigen recognition, and in progression of Chronic Lymphocytic Leukemia (CLL). In other words, we discovered a molecular interaction between two immune cell types that influences the course of several diseases.

My early work at OUHSC focused on the mechanisms by which NKT cells interacted with B cells to enhance antibody production. We started initially by testing the immune response to model antigens (my first RO1), to anthrax toxins (my DTRA grant), and then to *C. difficile* toxins (included in my current and second RO1). A long-standing collaboration with the Ballard laboratory has been instrumental in our move beyond model antigens to bacterial toxins and the pathogens that produce them. As a result of our studies, we have discovered that NKT cells affect memory B cells and plasma cells. Memory B cells and plasma cells are the two major effectors of long-lived antibody responses following infection of vaccination. As detailed in my CV, we have published extensively on this topic.

[redacted] [redacted]

Summary of Current Research and Future Directions

In recent years we have to a significant extent re-directed our research focus by incorporation of studies on the immune response to *Clostrioides difficile* (*C. difficile*). This is in recognition of the fact that individuals with this debilitating enteric infectious disease are often re-infected and suffer from several recurrent infections before ultimately succumbing. Consequently, over 30,000 people die in the US each year from *C. difficile*-associated complications and the financial burden on the healthcare system keeps increasing. Recurrent infection demonstrates that a primary infection does not adequately immunize the host against a second infection. Our goal is to try and understand this phenomenon such that better vaccines and/or therapies for *C. difficile* can be devised. We are attacking this question from different angles supported by 3 active grants and seeking additional funding to address newer questions. Some of the research is NKT cell-related, while some considers B cell responses in a broader context. Our current and planned research is therefore well-aligned with the OUHSC Strategic Plan which prioritizes research in immunology and infectious disease.

Influence of NKT cells on immune response to *C. difficile* carbohydrates

We have typically focused our work on secreted bacterial toxins (and continue to do so with *C. difficile*), but it is also accepted in the field that understanding the immune response to bacterial cell wall antigens offers strong possibilities for developing vaccines that limit colonization and/or bacteremia. To this end, we have been examining whether NKT cell activation represents a pathway for stimulating protective immunity to *C. difficile* following immunization with a carbohydrate antigen known as PSII (polysaccharide II). Using in vivo mouse immunization and challenge studies, we have observed that NKT cell-activating glycolipid adjuvants boost protective antibody responses directed against PSII and limit bacteremia and pathology.

This work is currently supported by NIH grant R21 AI125708 and is listed in my CV.

We have also filed a provisional patent on this work and anticipate publication of two manuscripts by late 2018 or early 2019. Elements of this work will be included in future grant applications and experiments to incorporate the carbohydrate into a toxin-based vaccine are planned.

Mechanisms of action of a combination of two vaccine adjuvants

One of our projects involves the examination of the immunological consequences of combining two established vaccine adjuvants. This is because there is no known adjuvant that adequately provides the breadth of immune response whereby good cellular (T cell) and humoral (B cell) immunity if achieved. The most widely used vaccine adjuvant in humans is Aluminum-based (Alum) and is potent with regard to T helper 2-driven humoral immunity. This is good for achieving most antibody responses, but fails to stimulate good T helper 1 responses or good T cell immunity. The NKT-activating glycolipid adjuvant α-galactosylceramide (α-GC) is a potent NKT activator and stimulates a mixed Th1/Th2 response. We reported in 2012 that some NKT cells respond to Alum, and it is well-established that others respond to α-GC. Our goal in this project is to examine the immune response to combinations of Alum and α-GC in immunized mice and in peripheral blood samples obtained from human volunteers. Our working hypothesis is that there is a coordinated action of two types of NKT cell that allow full expression of the immune response to the Alum/α-GC adjuvant combination. If successful, we will provide a

foundation for incorporation of α-GC into Alum-containing vaccines and perhaps add a much needed Th1 component to the response.

This work is currently supported by NIH grant RO1 AI134719 and is listed in my CV.

Murine B cell Memory to *C. difficile* infection

We are analyzing the immune response to *C. difficile* infection in mice to determine if it can be used to model recurrent infection in humans. Thus far, we have observed that a primary infection did not protect or limit a secondary infection, confirming that infection was non-immunizing. We have shown a failure to induce toxin-specific antibody responses following a primary infection and it is known that anti-toxin antibodies curtail pathology in infected animals. In contrast, immunization stimulates an excellent primary and memory antibody response that encodes toxin-neutralizing antibody. However, infection did not stimulate the memory compartment in pre-immunized animals and protection was conferred by the pool of antibody that existed before the infection. Furthermore, immunization blocked pathology but had no effect on bacteremia. Our observations thus far have several implications for understanding the immune response to infection and immunization, and highlight limitations of current vaccine approaches. For example, if infection does not stimulate the memory compartment, then booster vaccines may be needed every year to maintain antibody-mediated protection. If immunizing against toxin limits disease but not bacteremia, then current vaccination approaches could create a population of infectious but asymptomatic individuals. Our next grant proposal will seek to address these issues fully.

We are currently seeking NIH funding for this project:

Project Title:	Humoral immunity to *C. difficile* infection
PI:	[redacted]
Effort:	30%
Funding Agency:	NIH
Grant Number:	TBD
Direct Costs:	TBD
Project Dates:	07/01/19 – 06/30/24 (submission planned for 10/05/18)
Project Goals:	To determine the mechanisms of action underpinning B cell memory and Plasma Cell responses to *C. difficile* and its antigens.
Mentoring:	Graduate Student ([redacted]) Staff Scientist / Project Manager ([redacted])

Human B cell Memory to *C. difficile* infection

Despite the large number of publications on human antibody responses to *C. difficile*, virtually nothing is known about B cell memory to this pathogen and what type of antibody those cells encode (neutralizing versus non-neutralizing or toxin-specific versus toxin non-specific). We have therefore established a consortium of investigators to single cell-sort memory B cells from human volunteers with a history of *C. difficile* infection. The sorted B cells are then barcoded and their antibody genes sequenced at the single cell level. The sequences can be used to produce monoclonal antibodies for testing. Working with the Ballard, Webb, Wren, and James groups we produced our first antibodies from a volunteer and observed that while they

are toxin-specific, they do not neutralize the toxin. This could be one reason why infection does not protect against subsequent infections.

This work is currently supported by a Presbyterian Health Foundation (PHF Team Science Grant) and is listed in my CV.

Our goal is to use the PHF funds to develop a multi-PI national level grant to expand on these studies. If successful, this will complete my plan to fully develop a translational component to our research on *C. difficile*.

Zika Virus Research

I am in the early stages of collaboration with OUHSC researchers (Drs. Papin, Myers, and Parks) on the immune response to Zika virus (ZIV). Antibodies reactive to West Nile Virus (WNV) can cross-react with ZIV. Using unique resources at OUHSC including the baboon colony, we have secured a Presbyterian Health Foundation (PHF) Team Science Award to develop research on the effects of prior infection with WNV to the immune response and pathogenesis associated with ZIV infection.

This work is also supported by a Presbyterian Health Foundation (PHF Team Science Grant) and is listed in my CV.

Cancer Research

I have collaborated with numerous colleagues at OUHSC, particularly Stephenson Cancer Center (SCC) members. Several publications have arisen from these efforts which are listed in my CV.

Rao Laboratory, OUHSC/ SCC I have provided assistance on the influence of Natural Killer (NK) cells and NKT cells on murine pancreatic and colon tumor models which has led to three peer-reviewed publications.

Chen Laboratory, University of Central Oklahoma (UCO) I have provided assistance on the immunological aspects of Dr. [redacted] investigations on a new mode of therapy for solid tumors which involves using laser therapy to break immunological tolerance to tumors. Some of Dr. [redacted] initial work (as an RO1-funded PI at UCO) was recently accepted by the high impact (10.2) *Clinical Cancer Research* journal (listed in CV). I was a co-author on that study, as was Dr. [redacted] of the SCC.

Saban Laboratory, OUHSC / OU Cancer Institute (pre-SCC) I provided assistance on the immunological aspects of Dr. [redacted] investigation on Bacillus Camille Guerin (BCG) therapy of bladder cancer which was published in the BMC Cancer journal.

Kelly Laboratory, Dartmouth College and Medical School I provided assistance by examining NKT cell contributions to a lymphoma cancer model which was published in the high impact factor journal Blood (10.4 in 2008):

Expert Opinion Requests My expertise on NKT cells has been sought by the journal Blood (please refer to service portfolio). Amongst my assignments was my review of an article linking NKT cells to progression of Chronic Lymphocytic Leukemia (CLL). I was then asked to write an

expert commentary to accompany the published article. This provides evidence of the increasing recognition of my research program:

● I have therefore established a track record of collaboration with cancer researchers applying immunology to their research. This facilitates high impact publications and funding by other investigators including SCC members and aligns with the OUHSC Strategic Plan. This may become more evident in the coming years as immunotherapy is rapidly changing cancer research and treatment.

Closing Remarks

In my time at OUHSC, I have secured a significant level of federal funding in order to build and sustained a vigorous research program at OUHSC. This is despite a challenging funding climate and no longer being eligible for new investigator status at the NIH. My research goals are closely aligned with the Infectious Disease/Immunology component of the OUHSC strategic plan and my ongoing projects allow for both local and national collaborations with internationally-renowned investigators. Over the next few years, my intention is to further consolidate these efforts and to begin fulfilling my role as a full Professor at OUHSC. To achieve this goal it will be necessary to continue to secure federal funding, and to further increase national and international recognition for my research program. The environment at OUHSC makes these goals highly possible.

[redacted]

SERVICE NARRATIVE

Service Philosophy

In order for biomedical research and medicine to thrive at the institutional, regional, national and international level, it is critically important that faculty members share their expertise. We are fortunate at OUHSC to have an administration that follows the principles of shared governance whereby faculty members make contributions to all aspects of college life. In my time at OUHSC, I have contributed to this shared governance and therefore contributed to the institutional mission. I have also provided expertise at a regional, national and international level because I feel it is important to look beyond my own laboratory and OUHSC and contribute what I can to the global scientific and medical endeavor. My position at OUHSC until 2016 entailed 10-12% of my time and effort being spent on service activities, but 15% is a better estimate of my scheduled activities until 2022. My contributions and leadership positions listed in my CV.

Professional Service

● Department

I have provided service to the Department of Microbiology and Immunology since my arrival in 2006 and my responsibilities have increased since being award tenure in 2012. I have served on three faculty search committees and am currently serving a chair of our current search. Each of our prior searches resulted in successful recruitment of faculty who achieved national-level funding for their research. I have also served as a seminar coordinator for the department, on departmental review committees and have chaired the department Awards Committee which is charged with identifying the strongest applicants from our student body for the various scholarship and recognition awards that our department offers. I have also hosted at least one external seminar speaker every year since my arrival in 2006 which has given me the opportunity to introduce my collaborators and experts in my field to my department colleagues and to raise the profile of our department.

● College of Medicine and Graduate College

A full list of my service to the College of Medicine and the Graduate College is provided in my CV. My most significant contribution is three years' service as a member and as a chair of the GPiBS Admissions committee which is charged with identifying the strongest candidates for our graduate program. In several years, I have also reviewed grants submitted by junior faculty to the College of Medicine Alumni Association.

[redacted]

● OUHSC Campus and University

A full list of my service to the OUHSC Campus and University is provided in my CV. It is difficult to select what I view as the most important and/or rewarding service commitments at the institutional level as I have had the privilege of working with excellent colleagues in several capacities. Arguably my Member and Chair positions on the GPiBS Admissions Committee and my Chair position on the rodent oversight Committee were both highly important and rewarding as I felt that I was making substantial contributions to the research enterprise at OUHSC. Since achieving tenure in 2012, and commensurate with my experience, I have provided service on a variety of committees at OUHSC, always having at least one significant administrative responsibility. [redacted]

● Local/Regional Service

My most important regional service has involved review of grant applications submitted to the INBRE program directed by Dr. [redacted]. This is critical to the mission of OUHSC and for biomedical research in Oklahoma. The INBRE funding mechanisms allow training of students and provide a stepping stone for junior investigators to seek national level funding. For the past 11 years, I have reviewed small grants, collaborative grants and equipment grants from regional institutions. I have also reviewed junior investigator grants submitted by OUHSC and OMRF faculty and currently serve as a junior faculty mentor for the INBRE program. These endeavors are particularly important because amongst the many benefits, the INBRE program builds research infrastructure in Oklahoma and boosts the number of nationally competitive researchers at OUHSC and OMRF.

● National Service

○ I have provided significant service to national level learned societies.

Although it is a small contribution, I have also been happy to assist with AAI's ongoing efforts to address gender disparity issues in science by assisting the Status of Women committee with their Round Table discussions at the annual conference. I attended the Immunology 2017 and 2018, American Association of Immunologists (AAI) Annual Conference, Washington D.C., May 2017 and Austin, Texas, May 2018 respectively and lead round table discussions on grant writing for junior investigators.

In 2016, it was an honor to be selected by the American Association of Immunologists (AAI) President Dr. [redacted], to join the AAI Program Committee. During my 3 year tenure on the Program Committee (2016-2019), I have the privilege of contributing to the scientific direction of the annual conference for the world's largest immunology society representing over 8,000 members.

○ I have provided significant service to the national level peer review effort.

As listed in my CV, I have reviewed for approximately 30 different journals in the life sciences, and have served as an Associate Editor or Editorial Board member on two of them. My most significant service was two terms (4 years) as an Associate Editor with the Journal of Immunology, the flagship journal of the American Association of Immunologists. Consequently, although I have reviewed frequently for the Journal of Immunology since 2000, the scope has continually broadened to include the top-tier journals (PNAS, Nature Medicine).

I have also served as an ad hoc member of NIH study sections on average once per year since 2009. During that time I gained valuable experience which positioned me for full membership on a standing study section. This year I was invited to serve for 4 years (3 times per year) as a Permanent Member of the Vaccines against Microbial Diseases (VMD) study section. I feel this is recognition of my peer review skills by the NIH and have accepted the position.

I have therefore steadily built a record of national service over the past 12 years and these efforts have increased significantly since achieving tenure in 2012. I believe my AAI and VMD appointments represent national level recognition of our work and my expertise and allow me to advocate for immunology research in Oklahoma.

● International Service

As listed in my CV, I have periodically reviewed grants for several international funding agencies, which was an earlier sign of recognition of our research program. For confidentiality reasons, I cannot discuss individual applications, but those requests are often in part because the investigator has based cited our published work in the development of their own project idea. It was also my privilege to conduct a thesis defense at Trinity College in Dublin, Ireland, which again is a sign of international recognition of our work.