**Nicole Putnam, Ph.D., of Vanderbilt University**   
[**“The impact of innate immune recognition of Staphylococcus aureus on bone homeostasis and skeletal immunity”**](https://www.niaid.nih.gov/sites/default/files/nicoleputnamapplicationF31.pdf)

**Respective Contributions:**

###### RESPECTIVE CONTRIBUTIONS

**Concept**

Dr. Jim Cassat (sponsor) and I share an interest in understanding host-pathogen interactions that trigger changes in human cell biology. We began discussing ideas for thesis projects when I joined the laboratory in May 2015. We are both excited to define how bacteria stimulate host skeletal cells to induce dramatic changes in bone remodeling processes, which are normally under tight regulation.

###### Project Design

In order to best study skeletal changes in bone remodeling, Dr. Cassat and I began to design my project with the support of Dr. Julie Sterling (co-sponsor), Assistant Professor in Medicine, Clinical Pharmacology, and Cancer Biology, and faculty member in the Vanderbilt Center for Bone Biology. Earlier work done in the Cassat laboratory demonstrates that bacterial strains deficient in toxins to induce skeletal cell death are still able to induce considerable bone destruction and aberrant bone formation during murine osteomyelitis. Relevant literature in the field describes inflammation-induced changes in bone homeostasis driven by alterations in bone-forming osteoblasts and bone-resorbing osteoclasts. Therefore, Dr. Cassat, Dr. Sterling and I designed preliminary experiments to test the impact of bacteria on osteoclast differentiation *in vitro* and the impact of innate immune recognition on bacterial clearance and bone homeostasis*.* From these promising results outlined in the Research Strategy, we developed a plan to discover the mechanism by which skeletal cells sense and respond to bacteria leading to alterations in bone remodeling.

###### Fellowship Application

I designed the studies, optimized the experiments, and generated all of the preliminary data included in this application. From these data, I have developed a series of hypotheses and formulated specific aims to test these hypotheses. I have documented these through writing of the Research Strategy of this F31 proposal, and then addressed feedback from Drs. Cassat and Sterling on this proposal.

###### Future Contributions

I will design and perform all of the experiments proposed in the Research Strategy, with some contributions from others. The advanced surgical techniques for the *in vivo* osteomyelitis model require Dr. Cassat, however, I will follow up with animal care and monitoring, as well as end point harvest and analysis. Additionally, Josh Johnson (see letter of support), who has years of experience in bone histology and is the manager of the Bone Histology core, will embed and section my samples. I will perform all staining of histological sections, all data interpretation from experiments, and statistical analyses with input from Drs. Cassat and Sterling.

Committee meetings will be held biannually, chaired by Dr. Eric Skaar (see letter of reference), and attended by my co-sponsor Dr. Julie Sterling, as well as Drs. Jeff Rathmell, Dan Moore, and Isaac Thomsen (see letters of reference). These meetings will provide the opportunity for my committee members to give feedback on my proposed experiments and data analysis, which will further enhance the quality of this proposed Research Strategy.

**Nico Contreras, University of Arizona**

[**“The Immunological Consequences of Mouse Cytomegalovirus on Adipose Tissue”**](https://www.niaid.nih.gov/sites/default/files/F31-sample-application_nico_contreras.pdf)

**Respective Contributions:**

#### Respective Contributions:

The mentor plan was designed in collaboration by the Supervisor (Nikolich-Zugich) and Principal Investigator (PI, Contreras) based upon curriculum completed prior to joining the laboratory and work occurring within the laboratory. The research strategy and proposal was drafted and submitted to the PI’s qualifying exam committee. Minor edits based upon feedback of the committee were made.

**Samantha Lynne Schwartz, Emory University**

[**“Regulation of 2'-5'-Oligoadenylate Synthetase 1 (OAS1) by dsRNA”**](http://www.niaid.nih.gov/sites/default/files/F31-Sample-Application_Samantha-Schwartz.pdf)

**Respective Contributions:**

### RESPECTIVE CONTRIBUTIONS

The project described in this proposal is founded on an initial observation made by a previous Conn Lab graduate student, Dr. Virginia Vachon. Specifically, she found that single point mutations within each OAS1 activation consensus sequence in the double-stranded RNA duplex used in previous structural studies had starkly different impacts on the ability of the RNA to activate OAS1. After I joined Dr. Conn’s lab for my thesis work, we discussed this observation and together outlined a set of experimental approaches that could tease out the molecular basis for how RNAs with similar affinity could have such different capacities to activate OAS1.

Following these discussions in early summer 2016, I began developing a form of this proposal in the IBS 522r Hypothesis Design and Scientific Writing course taken as part of the Biochemistry, Cell, and Developmental Biology (BCDB) Program core curriculum. This course is co-directed by Drs. Conn, Anita Corbett, and Joanna Goldberg. The course includes all second year BCDB and Microbiology and Molecular Genetics (MMG) Program students, as well as other MD/PhD students enrolled in various graduate programs at Emory. This course taught us how to think critically and to communicate our science. As part of the course, I prepared an NRSA-format research proposal in a step-wise manner with weekly assignments to outline, write, and re-write each section of the proposal. As a result, I received feedback on my developing proposal from a large number of individuals. For each week’s assignment, Dr. Conn worked closely with me, typically through an initial discussion of ideas and then written comments on a draft version of the section to be submitted. During the entire process, Dr. Conn assisted by critically evaluating my writing and ideas and always followed up with helpful advice and suggestions. I worked very closely with my “class mentor,” Dr. Corbett, who would provide written comments on each week’s assignment to offer an additional perspective to help guide me as I developed, wrote, and re-wrote the various sections of my fellowship. In several of the classes, I also received feedback from classmates through a presentation of aims and a model figure and other in-class exercises. Once the complete proposal was compiled, I received additional comments from a senior BCDB student (Mr. Ed Quach) before finally “submitting” my proposal for review by two faculty members (all mentors of students in the class are required to review two “grants” of other students in the class). Comments from these anonymous reviews were also provided to me before I prepared the current proposal. Finally, I also received comments from Dr. Conn and my Co-sponsor, Dr. Lowen, on the version of my proposal that I ultimately submitted.

The preliminary data presented in this proposal was collected and analyzed by me unless otherwise specifically noted in the corresponding figure legend.

Moving forward, for the experiments described in this proposal, I will design, conduct, analyze, and interpret the results with assistance from Drs. Conn and Lowen. My sponsors will also assist me with correctly interpreting and presenting the results of my experiments, as well as advising me on experimental design for the next steps through both our regular scheduled meetings and informal discussions. Dr. Conn’s office is adjacent to the lab, and he is always available and eager to talk about experiments or data. Though I strive for independence in the execution of my experiments, his expertise and availability has been a tremendous asset to my training thus far. For preparation of manuscripts, I will construct a thorough outline prior to seeking assistance from Drs. Conn and Lowen so that we can further organize my thoughts and findings into a cohesive story. I will then write initial drafts with my sponsors’ guidance until I can piece together a well-written first draft independently. I will also seek feedback on my results and manuscripts from my thesis committee, other colleagues (e.g. Dr. Christine Dunham and her group, with whom we have joint lab meetings), and current Conn and Lowen lab members.