

Maggie's NSF CAREER Advice

- Workshops/Resources:
 - Attend NSF Engineering CAREER Workshop → so much useful info plus you get to mock review proposals
 - Attend WVU's CAREER Workshop → meet teaching resource contacts and discuss your ideas
 - Use Grant Writer's Seminars & Workshops (GWSW) Book – NSF Version "Write Winning Grant Proposals"
 - Read WVU's bank of successful NSF CAREER Proposals – this is really helpful to see what strategies work!
- Finding your fit:
 - Study the Program page you will apply to and use buzz words from their goals in your title/abstract
 - Contact the Program Officer with your white paper to discuss fit (I did not do this but you should!)
 - Look up past funded CAREER awards from that program and read their abstracts – you get an idea of what topics have been funded previously and if your topic fits in the theme
- Budget:
 - Look up past funded CAREER awards from that program and see what the budget ranges are
 - Ask for what you need (you may be surprised – you may get what you ask for!) I got nearly \$700k
 - Ask for 1 full month of summer salary
 - Ask all of your educational collaborators for a budget and add it to your total
 - This is your CAREER Award so you should be the only investigator on it
 - However, you can pay an assessment person which is a huge plus – I did this – reviewers pointed it out
- PI's Long-term Goals:
 - I waited a long time into my Assistant Professorship to try my 2nd time for the CAREER – with more experience under my belt I felt more confident knowing who I was as a researcher and educator, what made me unique and how I could make an impact
 - Take a long time to think about what makes you, you - what have you done in research previously? What have you done in education? What are you passionate about / what are your goals? What will you learn from the CAREER project in research and education? How can you further build on your research and education goals after the NSF CAREER is finished? I presented concrete future research areas and concrete educational goals I would like to pursue even after the grant period was done
 - Also have a PI Accomplishments section to highlight your teaching and mentoring experience
- Research Plan:
 - Have enough preliminary data and papers from your lab to show feasibility and successful track record
 - Be creative with your topic choice – this was the first time I ever applied for a proposal on this topic!
 - I combined two separate project areas (MRI contrast agents with neutrophil-platelet biology) which were based on my PhD and postdoctoral trainings respectively and I hit gold – this area is so unexplored!!
 - NSF is all about generation of new knowledge – not applications or products - so I focused my project not on the nanoparticles themselves but on how nanoparticle design impacts cell-cell interactions
 - It is better to dive deeper into 1 idea with your objectives rather than trying to tackle 3 different ideas
 - Also NSF does not support animal work or disease so I addressed this with: 1) proposing cell studies, microfluidic studies and a 'proof-of-principle' small scale animal model in the last aim and 2) using healthy cells and also mimicking inflammation with lipopolysaccharide (closest I got to 'disease')
- Education Plan:
 - Ideally base each part of your plan on something you have done before to give it feasibility
 - Use built-in WVU or WV programs that you can add innovation to → helps make execution manageable
 - Make sure education plan impact is wider than WVU – ideally throughout the state or even further!
 - Have specific details on what you will actually do and pick unique things that will get reviewers excited
 - Be truly excited about the education plan you propose as you will spend 5 years doing it!
 - Make sure to devote 3 pages to education and 1 page to broader impacts/prior NSF support
 - Cite some education literature to show you have done your homework towards your target population
 - Include concrete numbers on the number of people you will target/impact with your education plan
 - Definitely include specific assessment info for each objective; having an assessment person helps!
- Integration of Research and Education:
 - I did not have room for a separate stand-alone section for this
 - Instead, in each education aim, I underlined the sentences that spoke to the integration with research
 - My integration was how the research plan informed the education plan – not really vice versa
- Letters:
 - You need a STRONG and specific chair's support letter – needs to speak to details in your research and education plans, your past success, future promise, etc
 - Don't forget to get the stock 1 line support letters from all of your educational collaborators
- Getting advice from others:
 - Have educational collaborators and research collaborators give you feedback on your plans
 - Use WVU's grant review resources if possible (TIG, HSC mock study section, HSC tweak my aims, etc)

CAREER: Impact of MRI contrast agent design on nanoscale interactions with neutrophils and platelets

Award # 2339015

https://www.nsf.gov/awardsearch/showAward?AWD_ID=2339015&HistoricalAwards=false

PROJECT SUMMARY

OVERVIEW

Understanding how nanoparticle characteristics mediate their interactions with blood cells in the body is crucial to promoting their safety and effectiveness. When developing new nanoparticle contrast agents for magnetic resonance imaging (MRI), most studies have focused on the off-target effects of macrophages due to their key role in scavenging nanocarriers in the body. Despite the abundance of neutrophils and platelets in the circulation, these blood cells are often ignored in MRI contrast agent design. Upon activation, neutrophils and platelets can stick together to form cellular aggregates that can block blood flow, just as a clump of hair clogs a drainpipe. This CAREER proposal will generate new knowledge on how the physical characteristics of MRI nanoparticle contrast agents (their metal content, surface coating, and size) impact interactions with neutrophils and platelets. Dr. Bennewitz will investigate how contrast agent design mediates nanoparticle cell uptake and transport, activation of neutrophils and platelets, and their downstream cell-cell interactions in static and dynamic systems. This project will lead to the creation of safer and more effective MRI contrast agents by smarter design strategies to minimize off-target effects. The integrated education plan will target underserved students from rural, low-income and to-be first generation college households in West Virginia (WV), who are at-risk for not advancing their education. Collectively, the education plan will spark interest in STEM for all age groups from toddlers to high school students in WV. By combining hands-on research, experiential learning, creative integration of art and science, and exposure to real world applications in imaging, biomaterials and nanotechnology, these outreach activities will inspire the next generation of young scientists and engineers.

INTELLECTUAL MERIT

There is a critical need to elucidate how nanoparticle MRI contrast agents interact with neutrophils and platelets to maximize safety. Activated neutrophils and platelets can form neutrophil-platelet aggregates that trigger downstream damage including release of web-like DNA structures called neutrophil extracellular traps (NETs). NETs provoke endothelial injury, platelet activation, and neutrophil recruitment to promote vessel blockage. Dr. Bennewitz's group has shown that nanoparticle contrast agent coating and metal content modulates neutrophil function via differential release of NETs, reactive oxygen species, and cytokines. This CAREER proposal aims to determine how the physical characteristics of MRI nanoparticle contrast agents mediate interactions with neutrophils and platelets in complementary systems including static *in vitro* assays, a microfluidic platform, and a proof-of-principle preclinical mouse model. The central hypothesis is that the physical properties of MRI nanoparticle contrast agents modulate neutrophil and platelet nanoparticle transport, cell activation, neutrophil-platelet aggregate formation, NET release, and thrombosis. The central hypothesis will be tested with the following research objectives: (1) Investigate MRI nanoparticle uptake and transport in neutrophils and platelets (2) Evaluate MRI nanoparticle-mediated neutrophil and platelet activation, aggregation, and NET release under static conditions and (3) Determine MRI nanoparticle-mediated neutrophil-platelet aggregation, NET release, and thrombosis under dynamic flow conditions. This proposal will be transformative, as Dr. Bennewitz will be the first to determine how manganese oxide nanoparticles and conventional gadolinium chelate contrast agents impact neutrophil-platelet crosstalk, NET formation, and thrombosis *in vitro* and *in vivo*.

BROADER IMPACTS

The educational objectives of this CAREER proposal are to: (1) Host 10 rural, low-income WV high school students in hands-on summer research through the Upward Bound Program. Students will be exposed to nanoparticle synthesis and downstream incubation studies with neutrophils and platelets in static and dynamic systems. (2) Create and disseminate the first Biomedical Engineering module to 4,000 middle and high school students state-wide via the WV Science Public Outreach Team. Two hands-on activities will be integrated into the presentation to spark student interest in fluorescence imaging and polymer stimulus driven delivery, two key research concepts of this proposal. (3) Design and lead an interactive science meets art activity focused on fluorescent painting under blacklights for children age 10 and under at the Spark! Imagination and Science Center. The education plan will cultivate interest in STEM education and careers for underserved WV students and the public. In parallel, undergraduate and graduate students will gain valuable mentoring and teaching experience via their integral role in creating and disseminating the outreach activities to bolster their confidence, leadership, and retention in STEM.