Significant Research Experience Essay Example

Prompt: Please describe your significant research experiences. (AMCAS MD/PhD Section)

What this essay does: *Opens with the research question, not with feelings about research. Names the PI, institution, techniques, and a specific experimental result that required troubleshooting. Covers two lab experiences with a clear narrative bridge between them. Includes a connective tissue sentence linking bench work to a clinical outcome. Closes with the clinician-scientist identity as a conclusion earned from evidence.*

Research in the Kim Lab at Northwestern University focuses on substrate specificity in the ubiquitin-proteasome system, specifically on how the E3 ubiquitin-protein ligase San1 recognizes and tags misfolded proteins for degradation in yeast. My work in this laboratory, which began in the spring of my freshman year and continued for three years under the supervision of Dr. Rachel Kim, addressed a subset of this question: whether the ubiquitin modification pathway could be synthetically reconstituted in E. coli, a prokaryotic organism in which ubiquitin does not naturally occur.

During my first year in the Kim Lab, I worked primarily in a supporting role, assisting graduate students with ongoing experiments and mastering foundational techniques including yeast and bacterial transformation, PCR and gel electrophoresis, site-directed mutagenesis, co-immunoprecipitation, and quantitative western blotting. This period was technically demanding in ways I had not anticipated. My first twenty western blots produced inconsistent band intensities that I eventually traced to variability in transfer membrane hydration time, a detail not covered in the lab protocol but one that Dr. Kim identified immediately when she reviewed my raw images. That experience established an approach to troubleshooting I have applied in every experiment since: when results are inconsistent, interrogate the protocol at the step level before assuming the biology is the problem.

In the spring of my sophomore year, Dr. Kim invited me to develop an independent project, which I proposed as a survival-based split-protein assay to detect ubiquitin pathway reconstitution in E. coli. The proposal, which I wrote with guidance from Dr. Kim and submitted to the Northwestern Undergraduate Research Grants program, was funded in full. The assay I designed exploited the fact that a reconstituted ubiquitin pathway in E. coli would modify a reporter protein fused to a bacterial toxin, allowing positive selection of cells in which the pathway was active. The most challenging phase of the project was optimizing co-expression plasmid ratios to prevent toxicity from overwhelming the selection before ubiquitin modification could occur, a process that required iterating through forty-eight plasmid ratio combinations over eight weeks of experiments.

The assay eventually worked. In conditions where all three components of the ubiquitin cascade were co-expressed, we observed a statistically significant increase in E. coli survival relative to controls, which western blotting confirmed was associated with ubiquitin-modified reporter protein. This result, which represents the first survival-based functional screen for ubiquitin pathway activity in a prokaryotic organism, was presented at the 2025 Northwestern Undergraduate Research Symposium and is currently under revision for submission to the Journal of Biological Chemistry.

The direct applicability of this work to disease is not abstract. Protein aggregation disorders including Huntington's disease, Parkinson's disease, and spinocerebellar ataxia involve failure of the ubiquitin-proteasome system to clear misfolded proteins from neurons. A high-throughput screen for E3 ligase substrate interactions, which my assay makes possible, could identify ligase-substrate pairs that are disrupted in disease states and represent novel therapeutic targets. Seeing a project move from a technical puzzle in a prokaryotic organism toward a potential clinical application has been the most motivating experience of my research career and the clearest reason I am pursuing an MD/PhD rather than a research-only path.

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