When my older brother attempted to take his own life, my family gave me one sentence as a weak explanation for *why*: "Sarah, it's an issue with his brain – a chemical imbalance." Although I was only twelve, this moment set the course for my future study of neuroscience. I craved an understanding of how chemical changes in my brother's brain could ultimately impact his thoughts and feelings. By the time I began college, this curiosity had led me to the vast, beautiful, and frustrating unknowns of neuroscience. My subsequent explorations into molecular neuroscience solidified my intentions to pursue a Ph.D. and dedicate my career to illuminating the brain's underlying molecular mechanisms.

At the University of North Carolina, my surface-level fascination with the brain evolved into a deeper intellectual interest in synapse regulation. In Dr. Patricia Maness's lab, I characterized two neuronal cell adhesion molecules, which we hypothesized might have a role in regulating synapse remodeling. I was particularly intrigued by the homology between these two receptors, and I sought to uncover similarities in their signaling pathways. To test these theories, I pioneered our lab's analysis of neuronal morphology and synaptic biochemistry using knockout mice. The challenge of designing the most efficient and simple experiments to answer multifaceted questions enthralled me. With practice, I learned effective ways to deconstruct research questions into digestible experiments. My biochemical investigations demonstrated little signaling overlap between the two receptors and raised the exciting possibility that different cell adhesion molecules might selectively eliminate individual synapses. My discovery of these receptors' functions and their exclusive signaling pathways led to two publications and a manuscript that is currently under review.

After working in an academic lab, I was curious to see how basic research is translated into helpful therapies for people like my brother. To explore this translational side of drug development, I interned at Vertex Pharmaceuticals in the Drug Metabolism and Pharmacokinetics Department. I implemented micro-infusion pumps to streamline rodent dosing regimens to be more accurate and reproducible while also decreasing the number of animals needed to test each compound. I had the opportunity to present my research to Vertex's Research and Development Executive Leadership, and my project was later integrated into the global preclinical pipeline. While I remain fascinated by therapy development, I discovered at Vertex how much these therapies depend on advances in basic scientific research. I was motivated by this experience and sought an opportunity to investigate the molecular mechanisms of psychiatric disorders with Dr. Morgan Sheng at the Broad Institute.

Working with Dr. Morgan Sheng has been my most formative experience as a young scientist. Under Dr. Sheng's mentorship, my thinking about scientific questions has been fundamentally expanded and restructured, leading me to approach research with creativity and originality. I am fortunate to also have the responsibility and intellectual autonomy to guide my projects in Dr. Sheng's lab. My research investigates how overactivation of the immune system through the complement cascade might lead to neuronal damage and synapse loss.

My main project aims to identify neuronal activators of the complement cascade. The complement cascade is a system of innate immunity that, in addition to its canonical role in pathogen defense, regulates the microglial engulfment of synapses. In my first year, I identified and characterized a novel binding partner of Clq, the initiator protein of the complement cascade. Currently, I am using snRNA-seq and immunohistochemistry on knockout mouse models of this binding partner to further investigate transcriptional and cellular changes in neurons and microglia. With a manuscript in preparation, my research will be the first to identify a binding partner of Clq in the brain that modulates complement activity and alters microglia engulfment of synapses. More broadly, my research provides insight into possible mechanisms of synapse loss in neurodegenerative diseases and psychiatric disorders. I recently presented these data to the 100+ scientists at the Stanley Center for Psychiatric Research, which sparked new collaborations for our lab and was a valuable opportunity for me to share my research with the larger scientific community. Through my comprehensive training in the Sheng Lab, I have cultivated my ability to think critically and communicate effectively, and I feel well-prepared for graduate education. I have cherished the opportunity to apply my formal background in biochemistry to research at the nexus of immunology and neuroscience, and I plan to pursue similar interdisciplinary projects in graduate school.

I believe that joining the University of California Berkeley's Molecular and Cellular Biology program would allow me to develop the research experience and intellectual framework necessary to conduct cutting-edge and high-quality research. Specifically, I would be honored to work with Dr. Kaoru Saijo to continue investigating the molecular mechanisms of microglia in neurodegeneration. Additionally, I would appreciate working with Dr. Helen Bateup on neuronal mTOR signaling in neurodevelopmental disorders. I am also fascinated by the investigations of Dr. John Flannery; Dr. Flannery's research into gene therapies for retinal diseases is new to me but excites my interest in developing innovative therapeutics. In addition to a wealth of researchers who fit my current research interests, the MCB program provides an exceptional and highly interdisciplinary training environment, where I could expand and integrate my knowledge of neurobiology with other disciplines, such as immunology and biochemistry.

I am enthusiastic about the exploration, challenges, and growth that lie ahead for me in graduate school, and I hope these experiences will be at UC Berkeley. Ultimately, I aspire to lead my lab as an academic professor or principal investigator. My research interests will undoubtedly evolve with more training, but I remain committed to exploring basic science with the goal of advancing the therapeutic treatment of a range of mental disorders. Personally, I am indebted to the scientists who came before me and helped develop effective therapies for major depressive disorder; my brother, with the help of antidepressants, is now living a full and happy life. With training from UC Berkeley, I am confident that my research background, aptitude for learning, and ability to thrive working independently and collaboratively will allow me to significantly contribute to our molecular understanding of the brain.