Example of the "Letter of Intent"…all the answers provided are **fictitious**. Information regarding the application and actual assistantship/fellowship competition will be provided in a registration packet sent via email from UNMC Graduate Studies.

Name: Jane M. Doe

Program: UNMC Graduate Program
UNMC Campus zip: 9325

Title of Proposal: (State what you will identify/clarify with your project aims…usually there's a limit on characters, so keep it concise)
(Ex.) Mutating MRE11 causes telomeric instability and cancer cell death.

Chair of Supervisory Committee: John P. Smith

Members of Supervisory Committee: Johnny Quest, Yosemite Sam, Roger Rabbit

Study Section: (Example) List the top three sections that applies to your proposal
1) Biochemistry or Molecular Biology
2) Systems Biology
3) Genetics

Abstract: (Written statement of purpose…)
Background: Describe the main points of the background that an outside researcher would need to know to understand your proposal.

Telomeres are vital capping structures at chromosomal ends composed of DNA repeats (TTAGGG). Telomerase, a reverse transcriptase over-expressed in almost all cancer cells, synthesizes these repeats in opposition to the gradual shortening telomere after every cell division. Progressive telomere attrition causes cells to enter senescence, but telomerase expression conversely extends cellular lifespan. Therefore, drugs targeting telomerase are novel strategies in cancer therapy development.

In normal human cells, telomere associated protein MRE11 binds to the telomere by two DNA-binding domains. When bound, MRE11 recruits and optimizes the processivity of telomerase to synthesize telomeric repeats. The interaction between MRE11 and the telomerase complex is thought to involve a zinc-finger in C-terminal domain of MRE11. But their interaction has yet to be elucidated. **The goal of this project** is to validate our **hypothesis** that by mutating this zinc-finger domain, the interaction and recruitment of telomerase by MRE11 is disrupted in cancer cells, thereby resulting in telomere attrition and cancer cell death. To test our hypothesis, we propose the following **Specific Aims**: 1) use ChIP-on-ChIP analysis to purify the protein-DNA complexes to perform Mass Spectroscopy, Circular Dichromism, and X-ray Crystallography; 2) Define the role of MRE11 in regulating the processivity of telomerase by retroviral expression of wild-type and mutant MRE11 in cancer cell lines and later test telomere elongation by performing TRAP assay and telomeric instability by Western Blotting for DNA damage factors; 3) Visualize the disruption of telomerase recruitment by mutant MRE11 using Confoccal Microscopy. **The obtained results will provide insight on an alternative regulation of telomerase and the development of a telomere targeted cancer therapy.**