**Title:** Functional Studies of Lambda Phage Assembly
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Viruses are responsible for a range of human infections which can cause colds, influenzas, and even cancer (Cue, 1997). The focus of the research performed is on double stranded DNA (dsDNA) viruses like the herpes virus, adenovirus, and cytomegalovirus. In this study, a model system is utilized with a bacteriophage serving as the model. The bacteriophage, Lambda, is a simpler version of a dsDNA virus that infects bacteria and as such poses less of a threat when working in the lab and is relatively easy to produce (Casjens, 2011). Although simple, it retains the mechanisms and structure of the more complex viruses mentioned previously. Many dsDNA viruses have DNA packaging motors that recognize viral DNA and translocate the DNA into the head of the virus, called a capsid, by producing tremendous force (Feiss, 2013). The proteins involved in this process, a large terminase subunit and a small terminase subunit, make up the packaging motor. These proteins work together to use an inchworm mechanism that hydrolyzes ATP to pack DNA into the capsid so densely that the head of the virus is nearly a solid (Nurmemmedov, 2011).

Although both have been successfully studied independently, it has been a challenge to study them together as a single unit (Rossmann, 2012). The mechanism by which these proteins operate is still poorly understood. To better understand these proteins and by extension viral assembly, DNA binding assays were performed, and structural studies will be carried out upon successful crystallization. Determining the structure via crystallography would allow for expanded research and the prospect of new ways to inhibit these viruses but the size and dynamic nature of the terminase protein makes crystallization difficult. It is hypothesized that as it is a DNA packaging motor, utilizing DNA to stabilize the protein will allow for crystallization. The

terminase enzyme was expressed and purified from E. *coli*. DNA binding assays were performed with non-denaturing PAGE to study how the protein binds DNA to initiate viral assembly and it was discovered that the protein binds non-specifically. Viral DNA was synthesized via PCR and will be combined with the terminase enzyme for crystal screening. The functional and structural studies presented will prove useful in understanding viral assembly in hopes of developing new therapeutic strategies. Current strategies include medications that act on polymerases, a replication enzyme. As the enzymes are interrupted, sloppy replication occurs and gives rise to mutation. Ideally, inhibition of the packaging motor will allow for a more targeted approach so as not to produce side effects, and to prevent viral assembly and mutation.

## References


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