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ESTABLISHING A SYSTEM FOR STRUCTURE-FUNCTION ANALYSIS OF THE NOVEL ROLE THAT NUP153 PLAYS IN NUCLEAR ASSEMBLY

Marianne Mercer (Katharine S. Ullman, PhD)
Department of Oncological Sciences

In mitosis, equal partitioning of DNA between daughter cells requires an integrated series of events. At the start of anaphase the chromatin separates and forms two chromatin discs. This chromatin is then targeted by nuclear membrane proteins and membrane to form the nuclear envelope. These membrane components come together to surround the chromatin as it decondenses. Continuous membrane addition allows further expansion of the newly formed nuclear envelope. This is a highly coordinated process, and the mechanisms are still not fully known. Many nucleoporins that form the nuclear pore complex have different functions in mitosis. Nup153 is known to have various roles in nuclear disassembly and reassembly, which are very different from its role in nuclear transport where it has been more extensively studied. Nup153 has a novel role in nuclear envelope formation. When Nup153 function is disrupted, Lamin B2, a component of the nuclear lamina, as well as membrane proteins of the nuclear envelope, mistarget. This indicates that Nup153 is responsible for the assembly of these components into recruitment the newly-forming nucleus.

In this study, a system in which to perform rescue experiments with structural mutants of Nup153 was designed as a strategy to elucidate its role in nuclear envelope reformation. DNA constructs encoding a panel of Nup153 structural mutants were cloned, either by modifying a previously made construct or by creating new mutations. These were then introduced into a mammalian cell line and selected in order to generate stable, constitutively expressing cell lines. Now, in rescue experiments, endogenous Nup153 can be depleted to test the ability of the mutant Nup153 to rescue the Lamin B2 mistargeting phenotype.