Research Proposal

Title: Potential Role of p53 in Hutchinson-Gilford Progeria Syndrome Pathology

Program of Study: Biology and Chemistry

Presentation Type: Print Poster

Mentor's and mentor email: No faculty sponsor

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Category: Theoretical Proposal

Abstract: Hutchinson-Gilford Progeria Syndrome (HGPS) is a rare aging disorder for which the scientific community has yet to develop a cure. The specific aim of this research proposal is to determine whether or not p53, a protein intimately associated with DNA damage repair, is inappropriately localized to the nuclear lamina and thus associated with progerin. If this is true, then future work could be done to investigate what other proteins involved in DNA damage response may be affected by the presence of progerin. HGPS is caused by a *de novo* point mutation of the LMNA gene that gives rise to a mutated version of the lamin A protein called progerin. Lamin A constitutes a large portion of the nuclear lamina, which provides structural support for the nucleus. The presence of progerin in a cell nucleus causes extensive cellular pathologies that ultimately lead to HGPS patients having an average lifespan of 13 years. HGPS mimics natural aging, but at an alarming rate, ultimately leading to premature death, typically due to heart failure. Most of the problems caused by progerin are a product of the mutated protein binding too tightly to proteins involved in cellular processes such as mitosis and apoptosis. As p53 is a protein well-documented to be involved in DNA damage response (DDR), its interaction with progerin is worth being investigated as an additional causal factor in decreased cell proliferation in HGPS patients. In order to increase the ability of an HGPS cell to perform DNA damage repair, one must first understand why the cell is unable to perform DDR in the first place. If p53 is found to be abnormally localized to the nuclear lamina in HGPS cells, it may be further investigated to confirm that it is binding with abnormal affinity to progerin. If p53 is binding too tightly to progerin, it may be the case that p53 is unable to perform normal functions as a result of this binding. Understanding exactly how this disease affects the body at the cellular level would give the scientific community a better look into how our bodies age over time and possibly open the door to extending life.