

# Mechanical Changes of the Cell Nucleus in Disease and Aging

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## **Abstract:**

The sequencing of the human genome has provided a wealth of scientific information, but this information is limited by the poor understanding of the mechanisms that control gene expression. In addition to containing the code for the cell, the genome within the nucleus is a complex self-assembled polymeric structure with unique biophysical properties. We have developed numerous techniques including micromanipulation and micropatterning, multichannel registration particle tracking algorithms and fluorescence lifetime imaging to determine how these biophysical properties impact nuclear and cellular function. We are particularly interested in the role that force and cytokine treatment play in altering nuclear mechanics and gene expression in primary human cells. We have quantified nuclear stiffness in a broad spectrum of cell types: cells with less regulated gene expression patterns, including stem cells and cancer cells, have much softer nuclei whereas aged cells have stiffer nuclei. While the mechanisms directing stiffness are still being elucidated, we have quantified dramatic downstream impacts of nuclear stiffness on cellular migration. Recently we have investigated the interconnectedness of cell forces, and we are using the cell nucleus as a read-out for intracellular force generation within monolayers. With this new technique we have been able to determine spatial force variations within heterogeneous monolayer systems as a mimic for early disease models of epithelial and endothelial pathology. These results have broad implications in cell biology, cancer, atherosclerosis and for applications in cellular therapies.

## **Biography:**

Dr. Kris Noel Dahl, professor in the Department of Chemical Engineering at Carnegie Mellon University, holds appointments in Biomedical Engineering, Materials Science, Computational Biology, Molecular Biophysics and the Center for Ethics and Policy. Her group is interested in structure and mechanics of materials inside cells including the nucleus and cytoskeleton. Dahl received her BS degree from Carnegie Mellon in 1998, and Ph. D. degree in Chemical Engineering at University of Pennsylvania in 2004. She performed her postdoctoral fellowship in Cell Biology at Johns Hopkins University before joining Carnegie Mellon in 2007. She is a recipient of a Whitaker Fellowship and NIH Postdoctoral Fellowship for her training. She received an NSF CAREER award as well as a Young Investigator Award from the World Congress of Biomechanics. In 2020 she was elected to the American Institute for Medical and Biological Engineering (AIMBE) College of Fellows. She has published more than 50 peer reviewed papers and 10 review papers and book chapters. Currently, Dahl is the Co-Director of the Center for Mechanobiology and Genomics and the Co-PI: Biomechanics and Regenerative Medicine NIH-T32 Training Grant with the University of Pittsburgh.



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**Where: EEP 252**