NIH Award from the National Institute of General Medical Sciences

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- **Project:** Intermediate Filament Cell Surface Interactions
- **Start Date:** September 30, 2009
- **Total Award Amount:** $444,919

**How the results of this project will benefit society:**
Intermediate Filaments (IF) are structural proteins that are involved in determining cell shape, cell movement, mechanical integrity, and nuclear architecture. However, their specific functions remain unknown. We propose basic studies aimed at understanding their specific functions in the movement and mechanical properties of cells. These basic studies of the structure and function of IF not only will provide insights into understanding their normal functions, but also in determining their defective functions in the many diseases attributed to mutations in the genes encoding the different types of IF proteins.

**The problem the project is trying to solve:**
We propose to study the role of intermediate filaments (IF) in cell shape and motility. Our overarching hypothesis is that alterations in the assembly states and mechanical properties of cytoskeletal IF, specifically the type III IF composed of vimentin, play important roles in regulating the locomotory behavior of mesenchymal cells such as fibroblasts. These studies are important as IF are major elements of the cytoskeletal system of mammalian cells and yet their specific functions in cell motility remain unknown. Our specific aims are to determine the functions of vimentin IF in the formation of the lamellipodium/lamella that plays a major role in cell locomotion.

**How this project will work:**
Specifically we will study the changes in the assembly states and mechanical properties of vimentin IF that accompany the formation of lamellipodia. We will also determine the role that phosphorylation plays in the changes in vimentin organization that accompany the formation of lamellipodia and the initiation of cell motility. Live cell imaging of vimentin IF will involve the use of quantitative fluorescence speckle microscopy (qFSM) in order to begin to determine the nature of IF assembly, subunit exchange and their movements within cells. Other experiments are aimed at determining the changes in the mechanical properties of vimentin IF that accompany cell motility.

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