# Research Simplified

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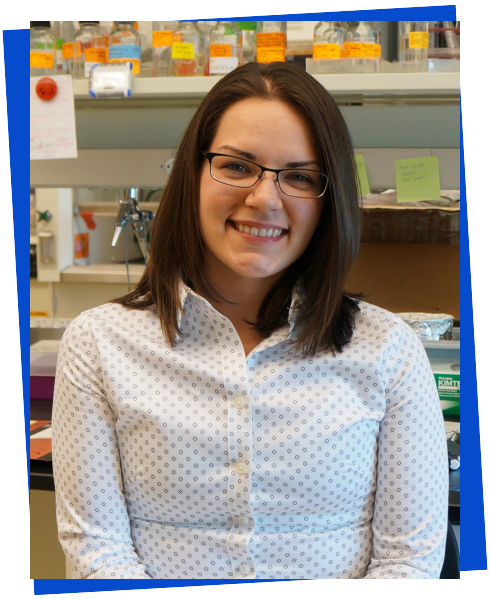
**Research Paper:** Regulation of KIF1A motility via polyglutamylation of tubulin C-terminal tails [read here]

**Authors:** Dominique V Lessard, Oraya J Zinder, Takashi Hotta, Kristen J Verhey, Ryoma Ohi, Christopher L Berger

**Research Simplified by:** Dominique Lessard
*Dominique is a member of Dr. Christopher Berger's Laboratory at the University of Vermont. As a member of UVM's Molecular Physiology and Biophysics Department, Dominique combines physics and physiology at the nanoscale level to advance our understanding of basic KIF1A function. Dominique has been working on KIF1A research since May of 2016.*



## Neurons & Transportation

The human brain and nervous system are made up of many types of cells that all work together to create a complex network, responsible for many processes in our bodies. Neurons, a type of cell found in the brain, require lot of energy and cellular resources to stay healthy. It is critical that these resources are delivered inside of the neuron at the exact location and time in which they are needed in order to perform all the neurological tasks required of them. However, there is one major problem: often times these resources are made very far away from where they are needed. Because of this problem, our neurons must have a way to effectively transport resources to ensure they are delivered when and where they are needed within the neuron.

## KIF Proteins

A main player in this process are kinesin molecular motors, also known as KIF proteins. Kinesins/KIFs are responsible for attaching to cellular cargo (the resources needed by the neuron) and carrying it to the location in which it is needed. How does a kinesin/KIF transport this cargo? It can be helpful to draw an analogy to understand this process; in this case, let's picture a kinesin/KIF motor as a car. Like a car, a kinesin/KIF needs gasoline to start its engine and begin transport. For kinesin/KIF proteins the fuel is known as ATP; ATP is inside all of our neurons and is an essential source of energy for the cell. Once a car has gas available, the next step is to find a road on which it can drive on to reach the intended destination. In the context of the neuron, the cellular roadways that kinesin/KIF motors follow to get to a specific destination are called microtubules.

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## KIF1A – The Porsche of Motor Proteins

There are many types of kinesin/KIF proteins involved in cargo transport. KIF1A is a specific motor that is extremely effective at cargo transport. Like a Porsche or a Ferrari, it can drive for very long distances at very fast speeds on microtubules. Our neurons rely on the highly effective KIF1A for many different neurological functions. However, when KIF1A cannot function properly (i.e., a mutation that makes KIF1A less effective) KIF1A-mediated cargo transport can be interrupted, impaired, or halted all together. Due to the fact that KIF1A carries very important cellular cargo, it is assumed that impaired KIF1A cargo transport contributes to the debilitating neurological changes resulting from KIF1A mutations.

## What We Don't Know

In regard to our understanding of disease-causing KIF1A mutations, there is a major barrier. This barrier exists because we know very little about how KIF1A functions within the neuron in a healthy cellular state, let alone a diseased cellular state. Let's go back to the car metaphor: imagine you go to start your car one morning and it won't turn on. Most people would take it to a shop, and have a mechanic diagnose that your battery is dead, transmission is broken, etc. When it comes to KIF1A though, we are still trying to figure out the key components of the protein that make it function properly. So if you were to take a KIF1A protein to the mechanic, they would have very little information to start diagnosing the problem.

## What We've Learned

Our research goal is to broaden our knowledge of basic KIF1A function to help us understand the disease-state effects of KIF1A impairment. The main goal of this research project is to reveal mechanisms contributing to optimal KIF1A function that we did not know previously. In this paper there are three main findings:

1) We have identified a unique behavior (pausing) of KIF1A on the microtubule that aids in its highly effective cargo transport. This taught us that KIF1A transport on microtubules is different than most other kinesin/KIF motors, and that this behavior helps KIF1A transport cargo for long distances in the neuron.

2) We have linked this unique behavior to a specific part of the KIF1A motor called the "K-loop". This part of KIF1A comes in direct contact with the microtubules. This taught us that the K-loop must be present and unaltered for full KIF1A efficacy.

3) We have identified a key part of the microtubule, a flexible rod on the microtubule surface, that KIF1A relies on to operate at full efficacy. This taught us that specific characteristics of the microtubules can govern the way in which KIF1A is able to transport cargo.

***Questions or comments about this research? Email us at contact@KIF1A.ORG.***