



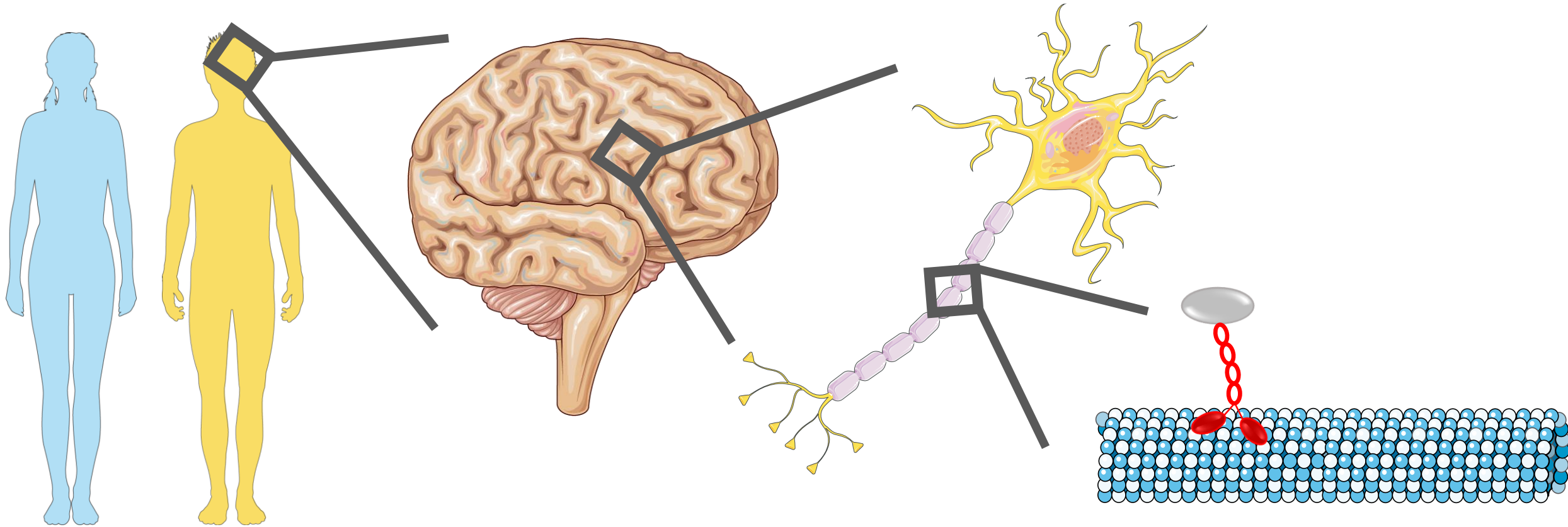
Uncovering KIF1A: A Basic Science Perspective

Speaker: Dominique Lessard, Berger Lab

August 16, 2019

Visit kif1a.org/2019Conference to watch a recording of this presentation.

Uncovering KIF1A: a basic science perspective.



August 16th, 2019
Dominique Lessard - University of Vermont
KAND Family & Scientific Engagement Conference

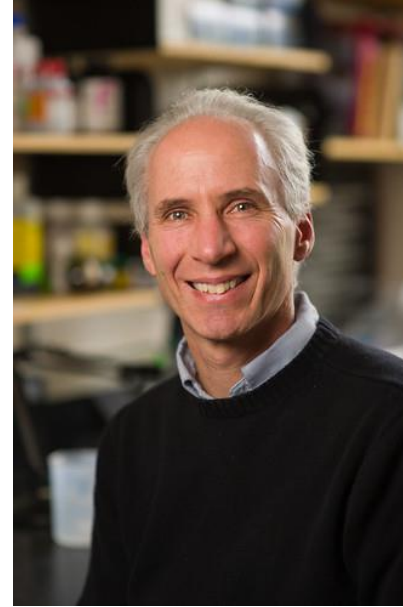
The Berger lab: Who are we?



University of Vermont | Burlington, VT
Larner College of Medicine
Molecular Physiology and Biophysics Department



How do certain processes within our bodies work at
a microscopic level?



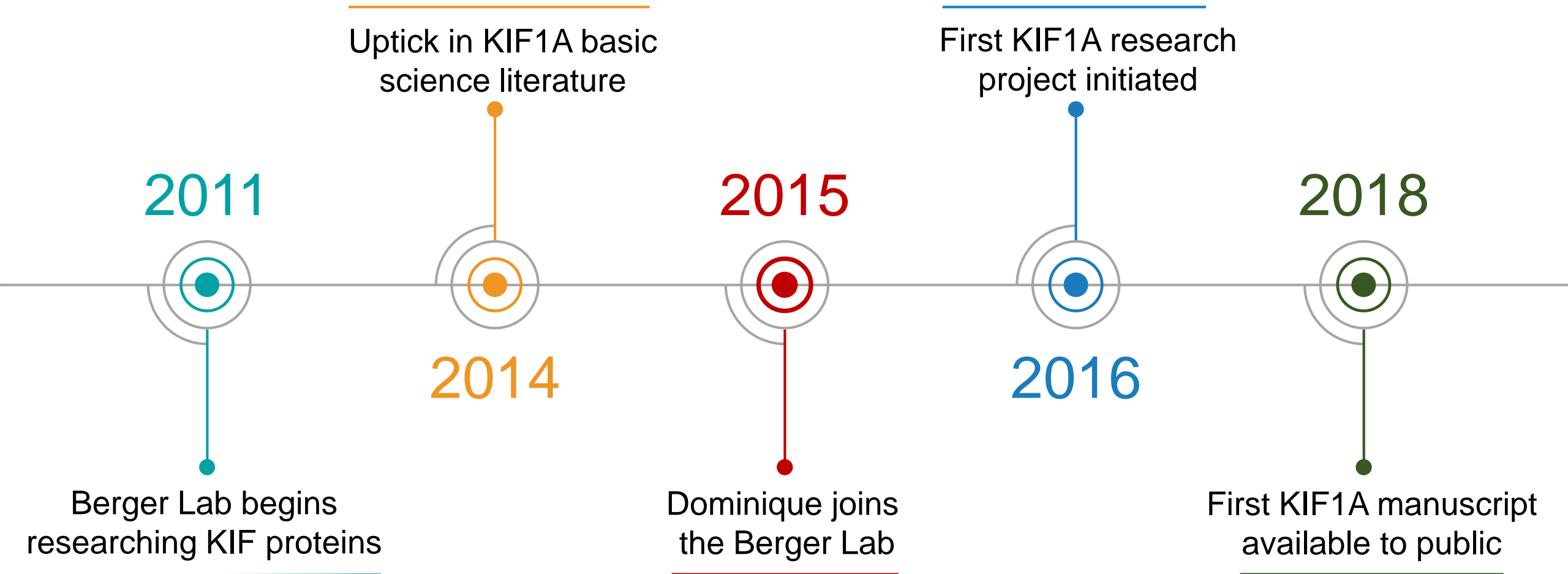
Christopher Berger, PhD

- 7 member team
- 3 KIF1A researchers
- Basic science lab

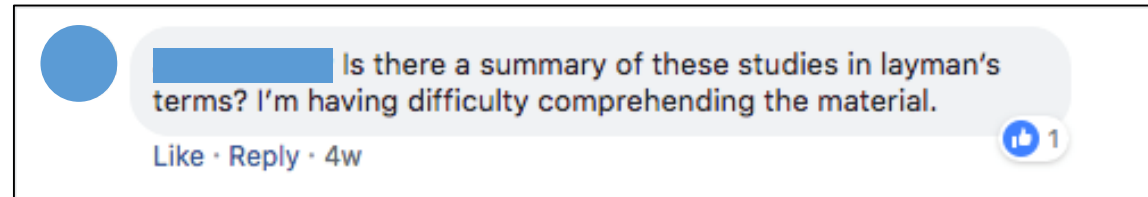
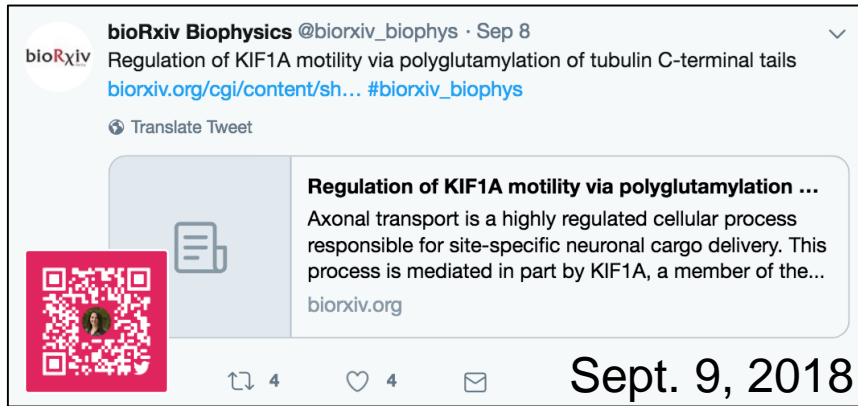
Basic science research

- Goal: Understand the fundamentals of certain natural phenomena
- Research findings become the foundation for other areas of research

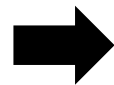
How did the Berger lab start researching KIF1A?



How did the Berger lab connect with KIF1A.org?



Luke Rosen



Luke Rosen, Founder
Kathryn Atchley, President
Shannon Scott DNP, Chief Science Officer



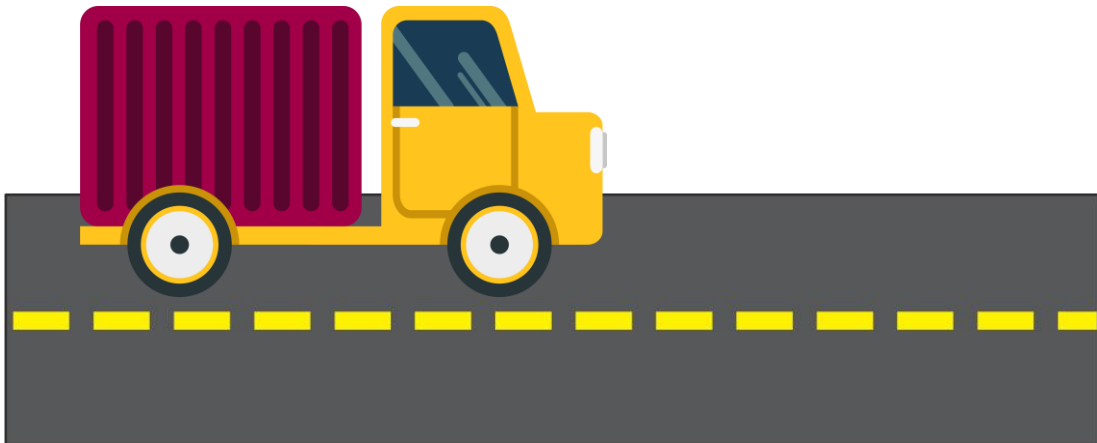
Wendy Chung, MD, PhD
Lia Boyle, MD, PhD student



COLUMBIA UNIVERSITY
MEDICAL CENTER

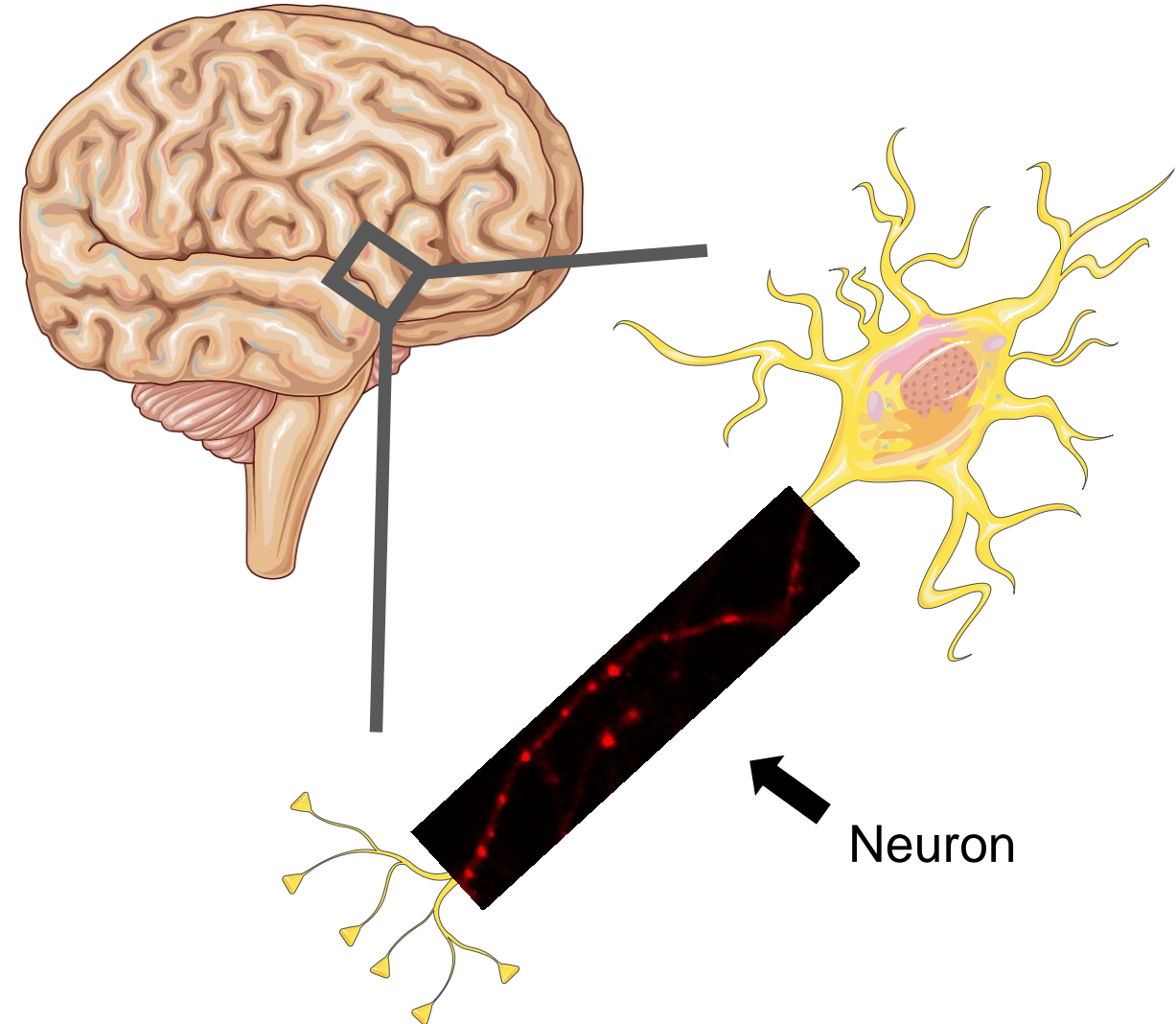
What is a KIF protein?

- KIF= Kinesin superFamily
- ~ 50 different KIF proteins in our bodies
- Motor protein
 - Use a cellular fuel source to transport cargo inside of our cells

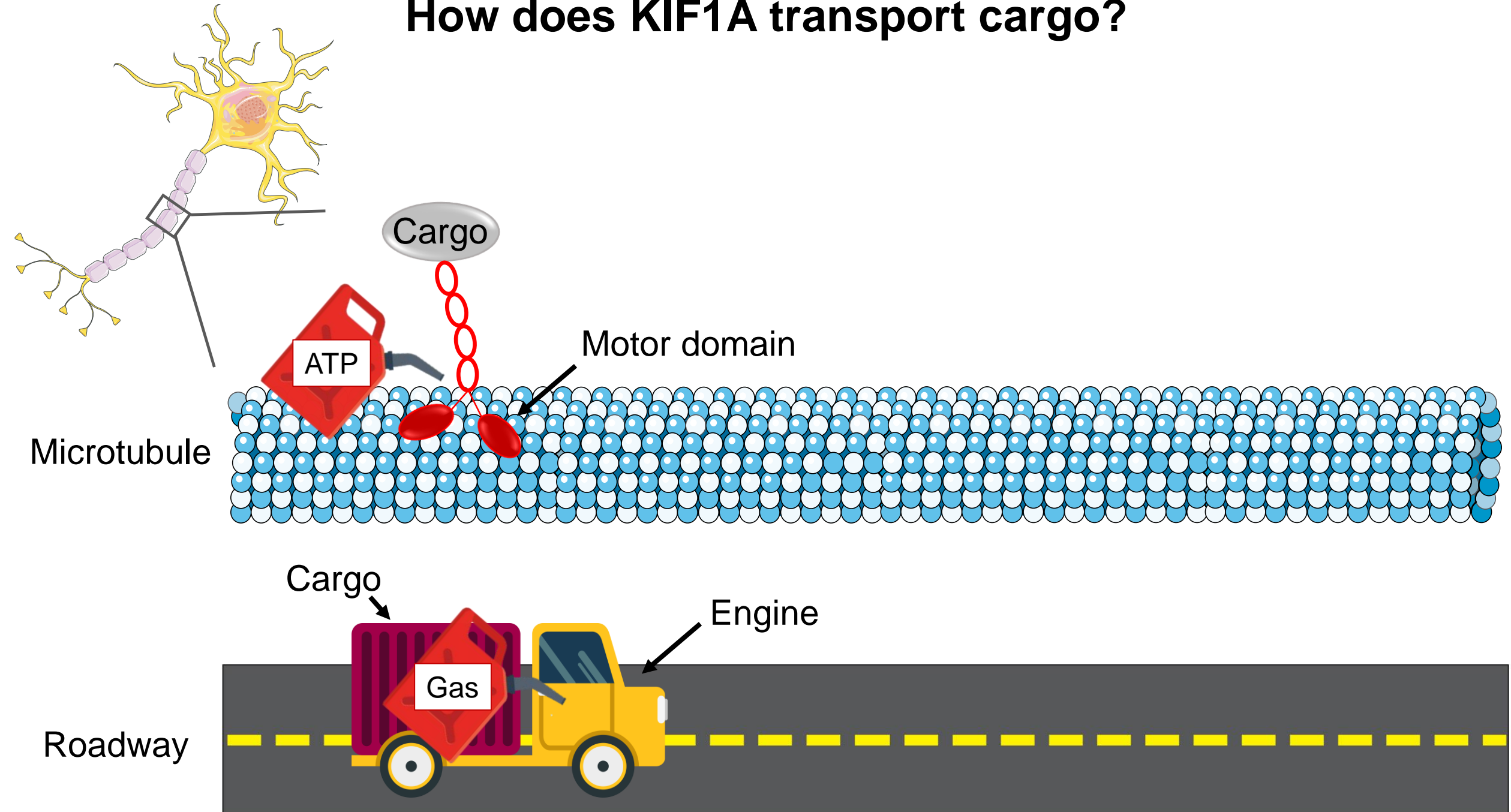


What is a KIF protein?

- KIF= Kinesin superFamily
- ~ 50 different KIF proteins in our bodies
- Motor protein
 - Use a cellular fuel source to transport cargo inside of our cells
- Organ/cell type specific
 - Ex) KIF1A is found in nerve cells (neurons)
- KIF specific behavior
 - Ex) KIF1A is an extremely efficient cargo transporter, compared to other KIFs

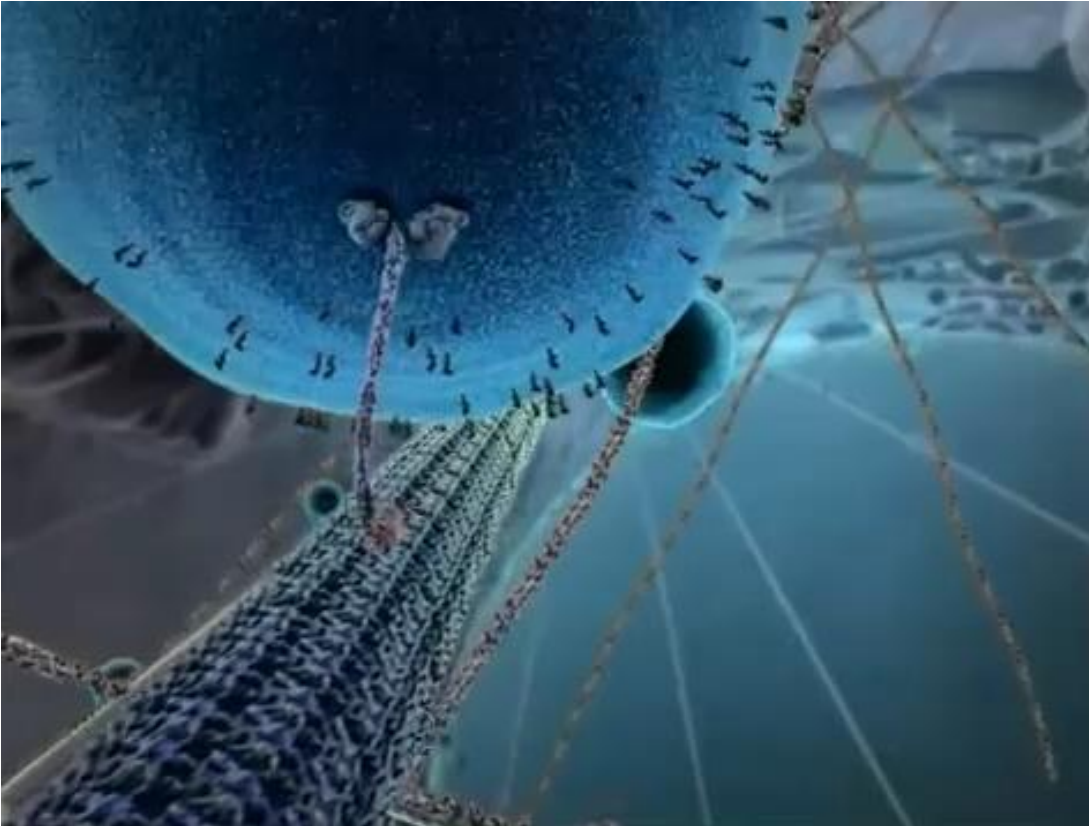


How does KIF1A transport cargo?



How does KIF1A transport cargo?

KIF1A + ATP (fuel source) = movement What we know about KIF1A movement:



- KIF1A walks along microtubules
- KIF1A carries/delivers cargo (vesicles) needed to keep nerve cells healthy
- KIF1A needs to be attached to cargo to move long distances
- KIF1A has a unique structure in the motor domain (engine) that allows it to move long distances

Big picture questions: what do we want to learn about KIF1A?

Problem: Very little is known about the specifics of KIF1A function!

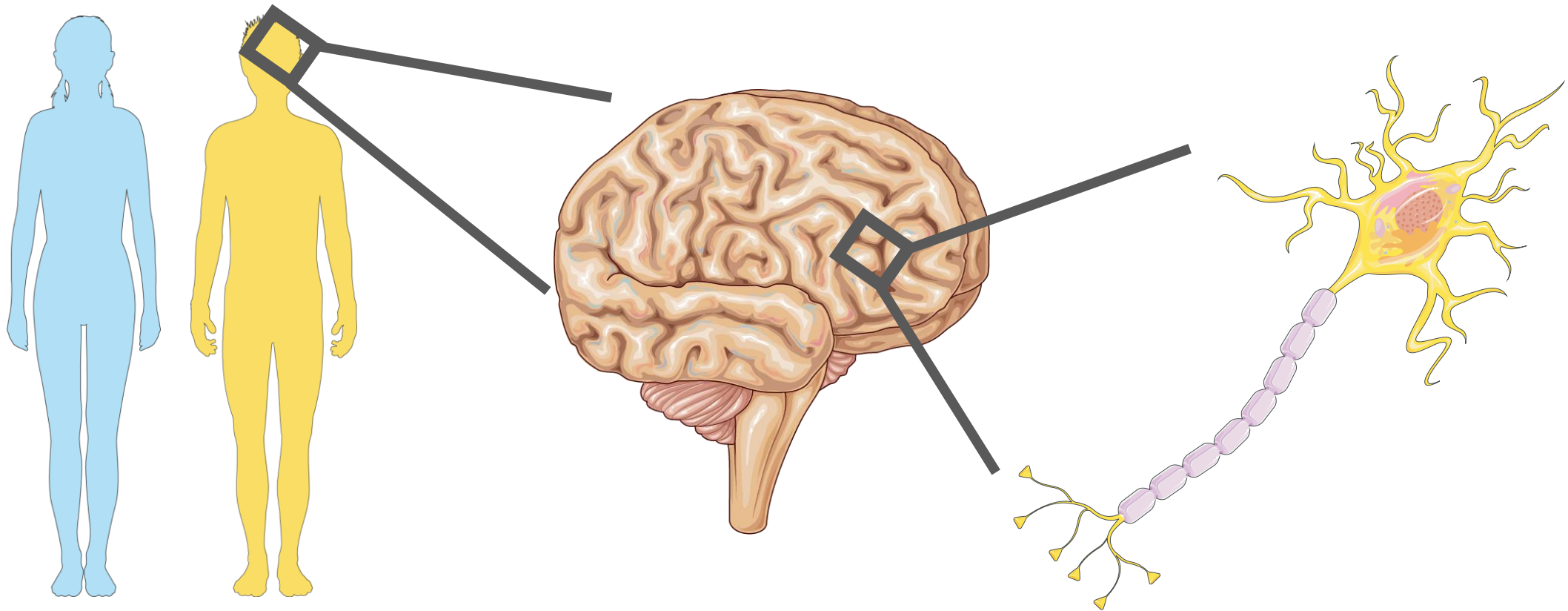
Research Aim: Uncover the fundamental character traits of KIF1A.

How does KIF1A walk along cellular roadways?

What are the unique behaviors of KIF1A?

How does KIF1A navigate on crowded roadways?

How does the Berger lab research KIF1A?

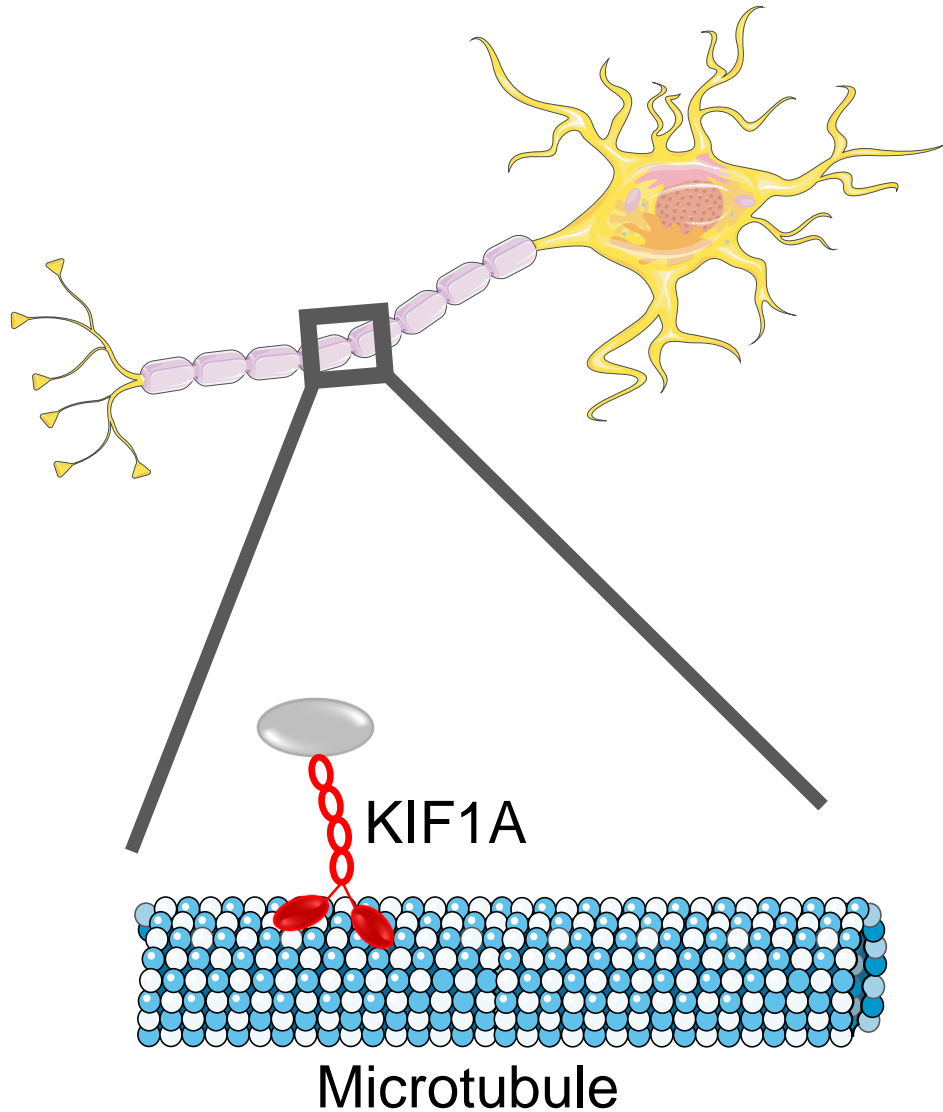


Organism level X

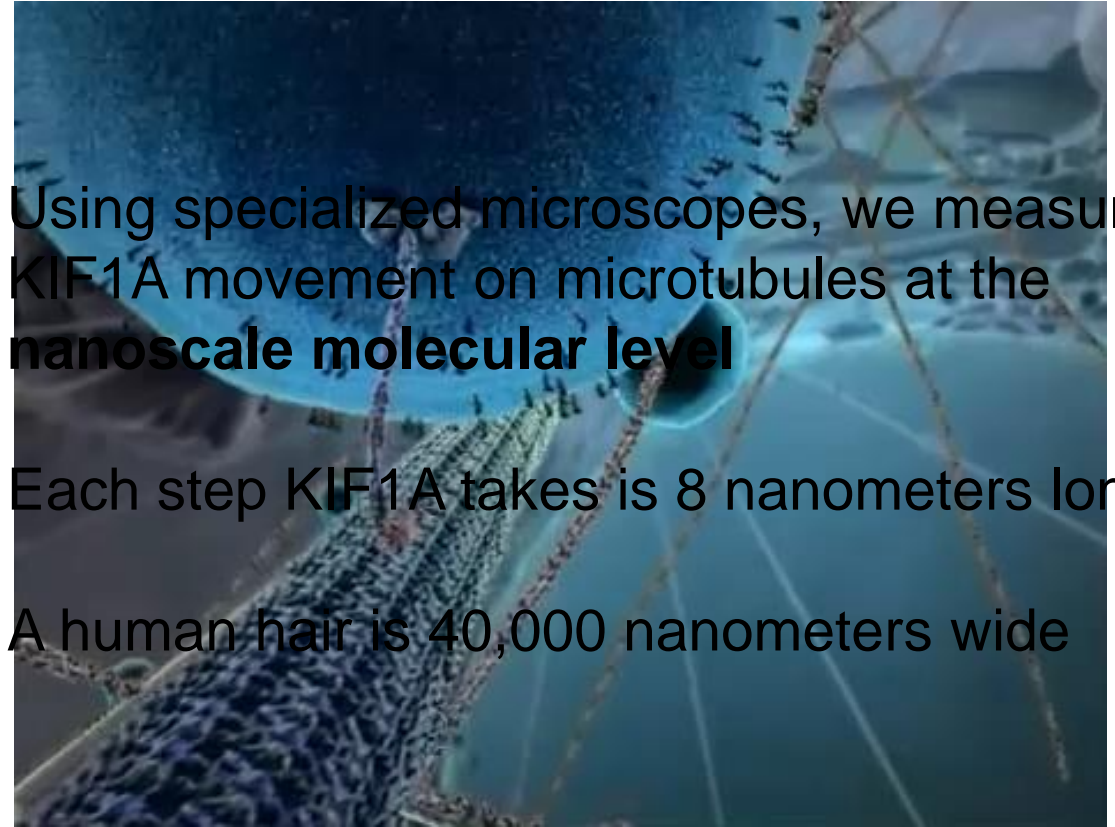
Tissue level X

Cellular level X

How does the Berger lab research KIF1A? At the nanoscale!



- Using specialized microscopes, we measure KIF1A movement on microtubules at the **nanoscale molecular level**
- Each step KIF1A takes is 8 nanometers long
- A human hair is 40,000 nanometers wide



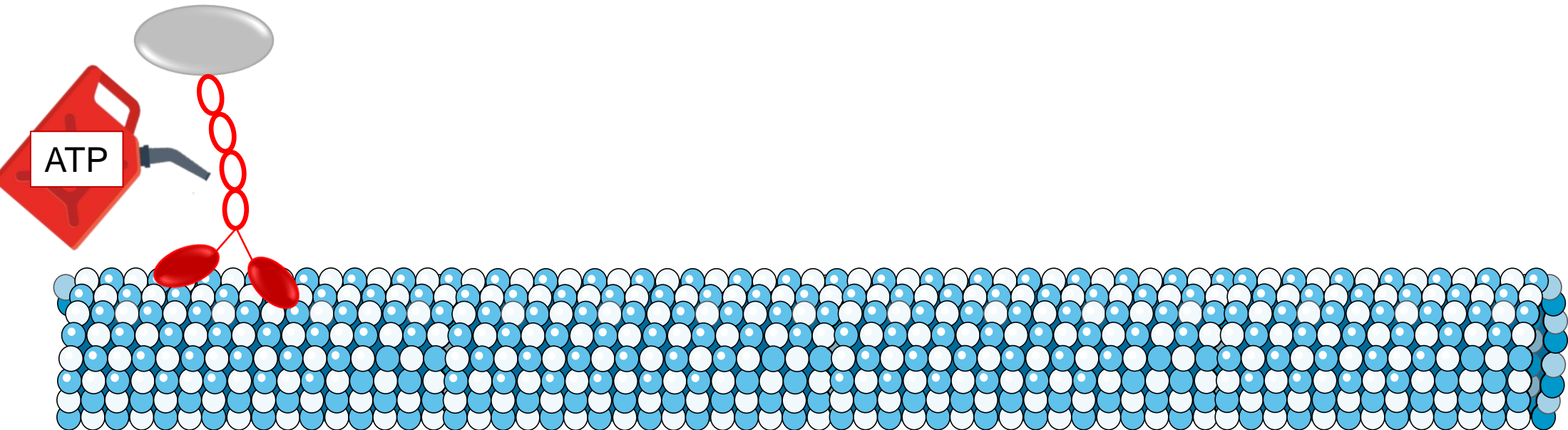
Red: Microtubule **Green dot:** KIF1A

How does KIF1A walk along cellular roadways?

What are the unique behaviors of KIF1A?

Recent findings: KIF1A pauses between sections of movement.

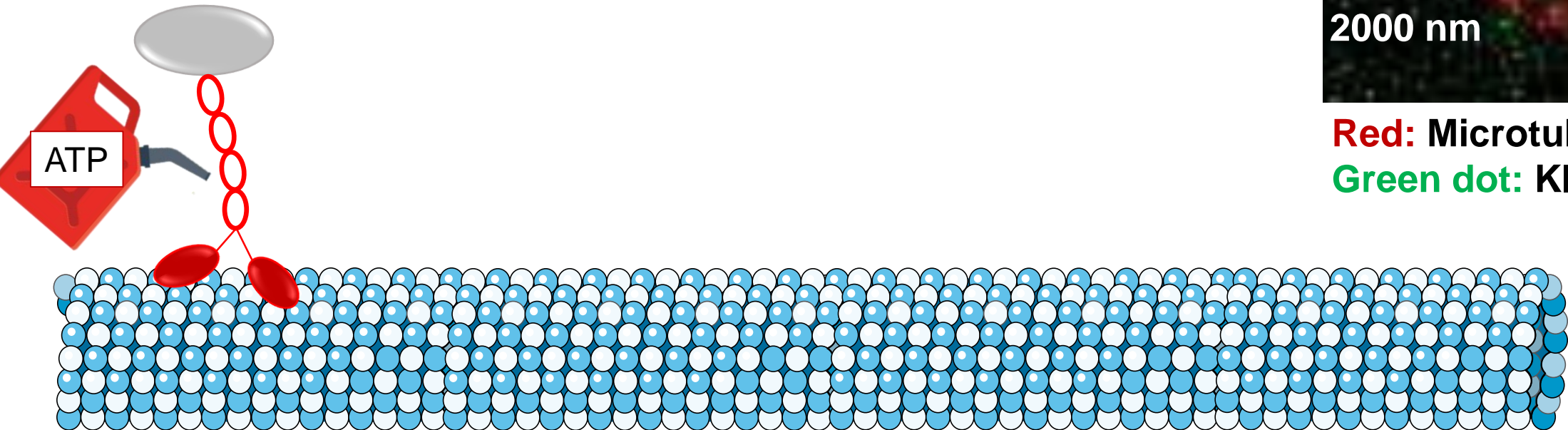
- Typically, we think of KIF proteins as constantly moving from point A to point B.



Recent findings: KIF1A exhibits unique pausing behavior.

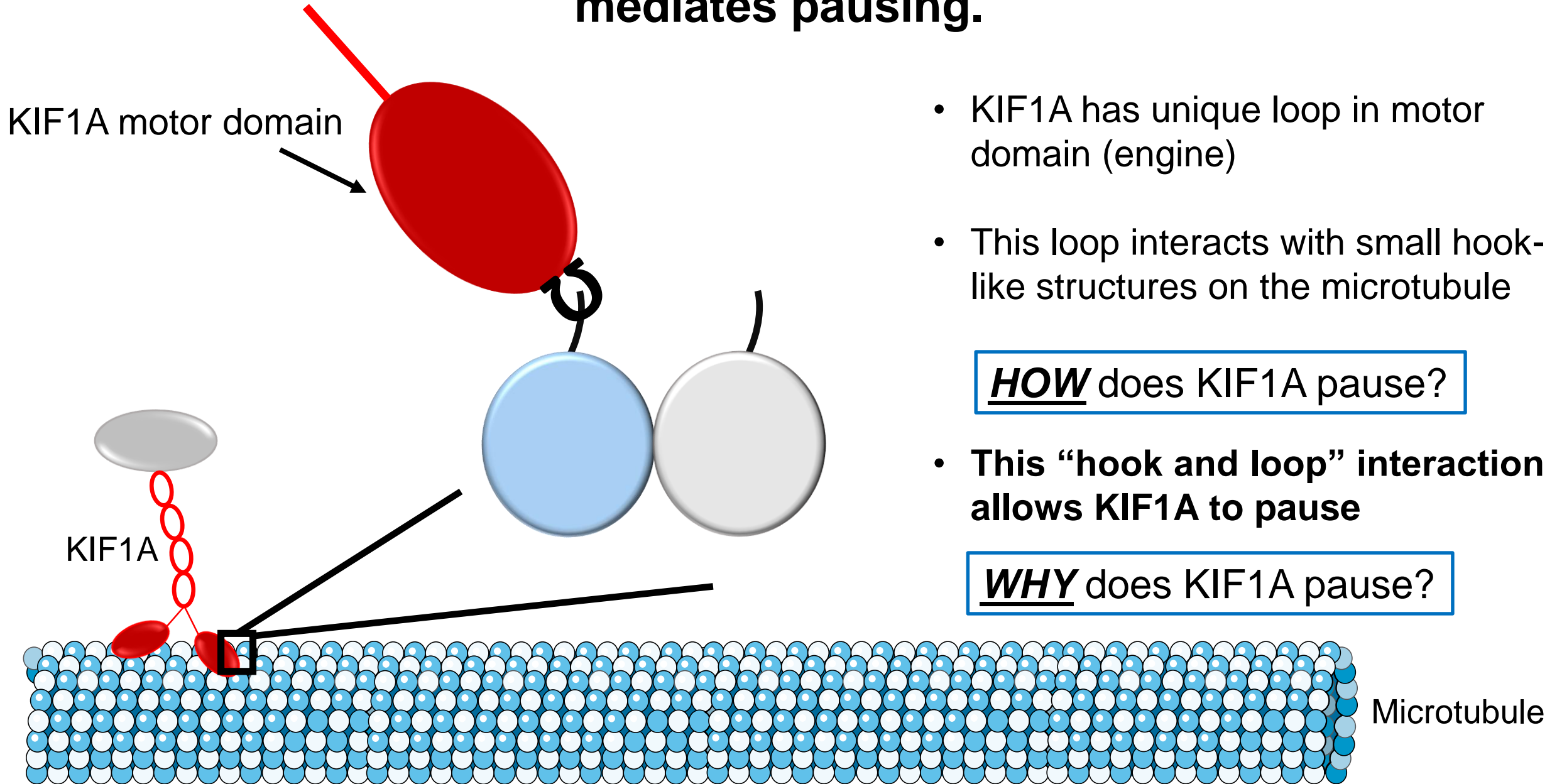
- KIF1A exhibits unique pausing behavior

HOW does KIF1A pause?

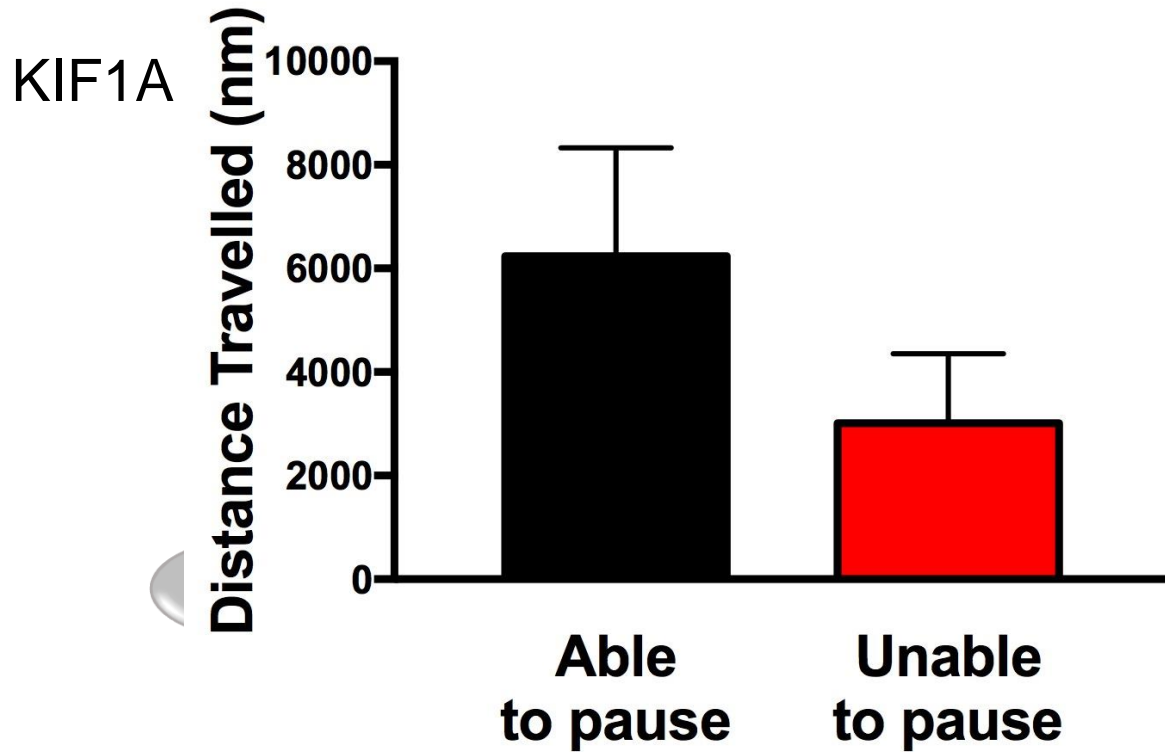


Red: Microtubule
Green dot: KIF1A

Recent findings: Unique interaction between KIF1A and microtubule mediates pausing.

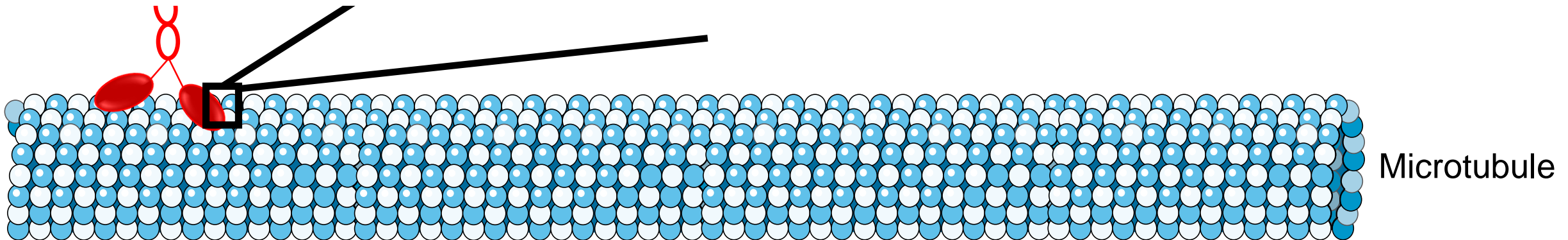


Recent findings: KIF1A needs to pause in order to walk long distances.

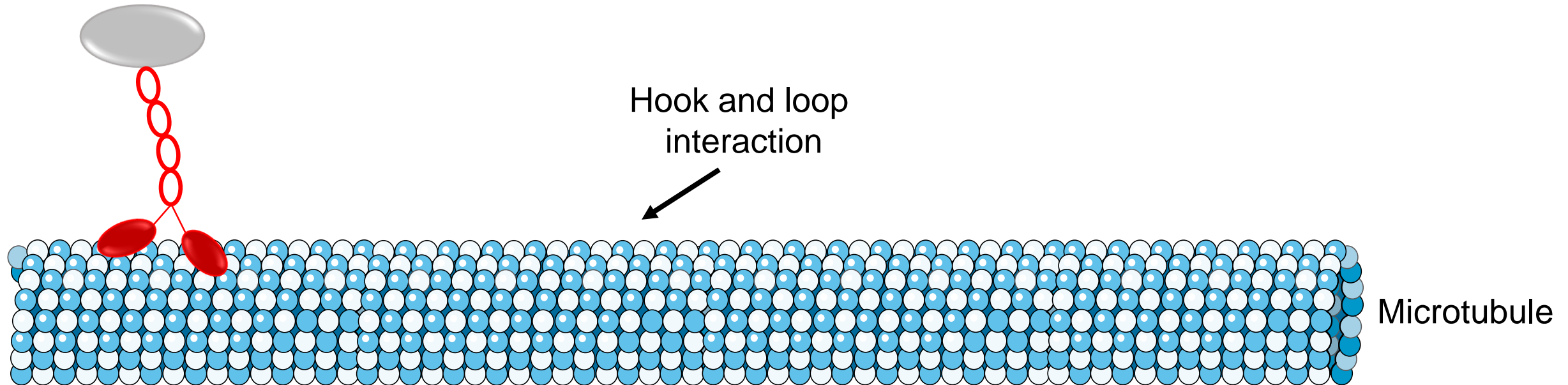


What happens if we disturb the system?

- Remove the hooks?
- Remove the loop?
- **No pausing**
- **Reduced distance travelled**



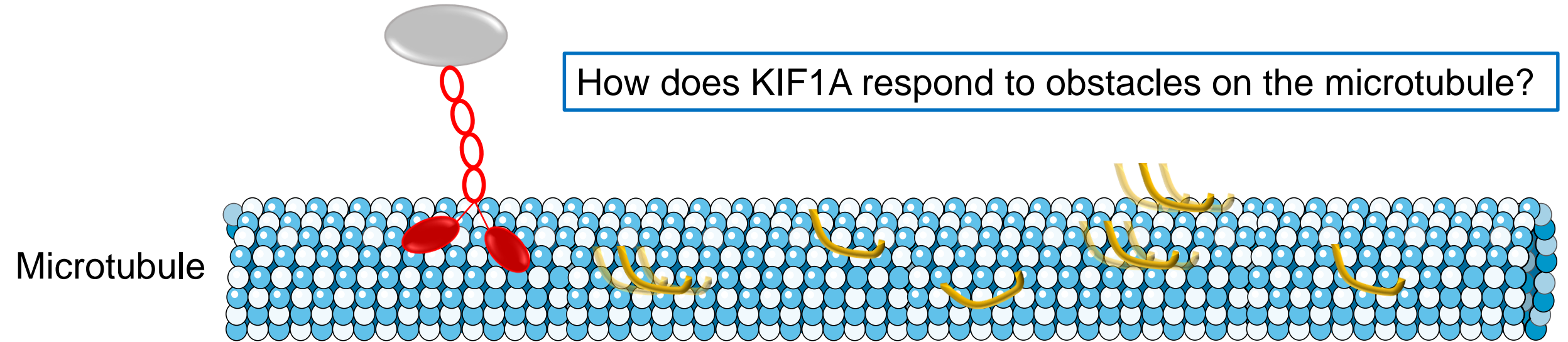
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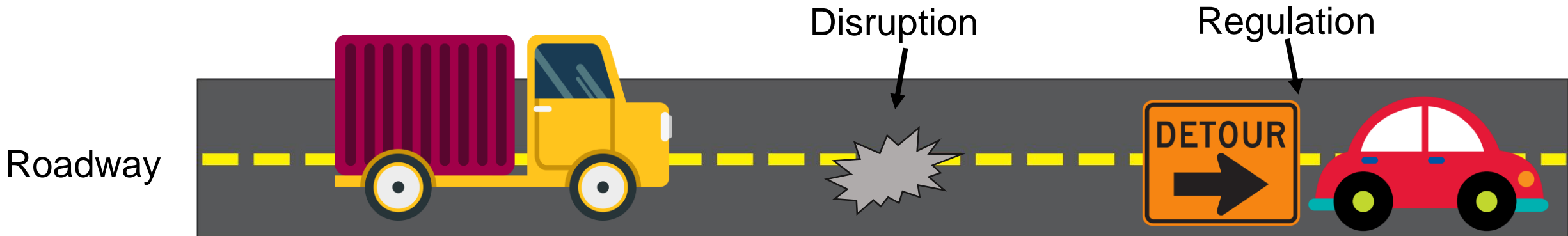
How does KIF1A navigate on crowded roadways?

KIF1A is confronted with many obstacles on microtubule roadways.

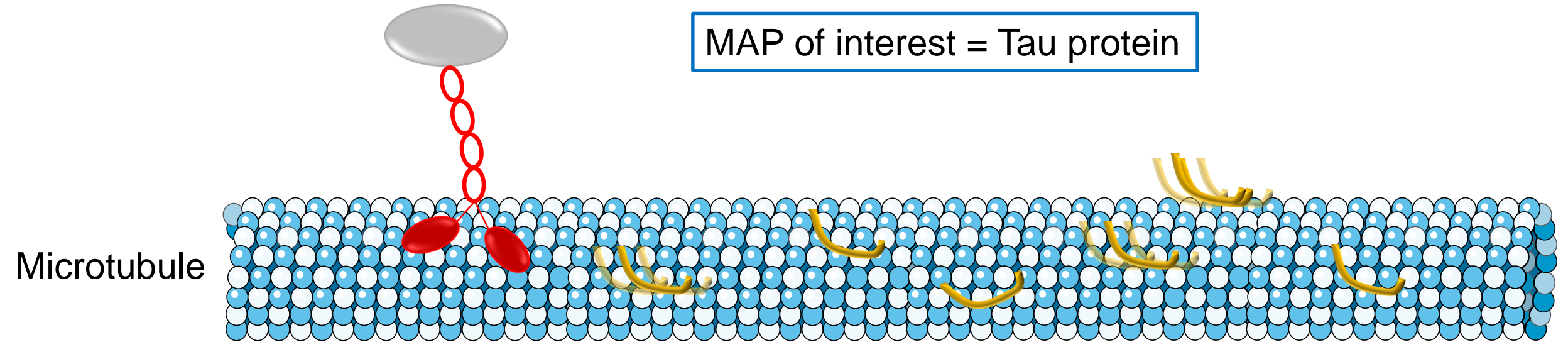
How does KIF1A respond to obstacles on the microtubule?



- Microtubule associated proteins (MAPs) sit on top of the microtubule surface

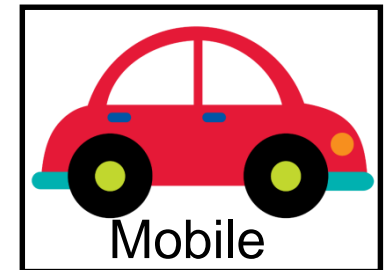
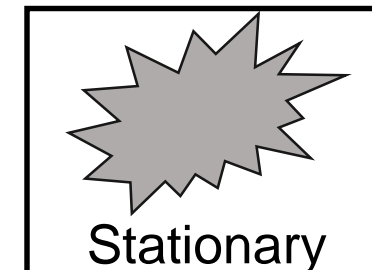


Question: How does KIF1A respond to Tau obstacles?

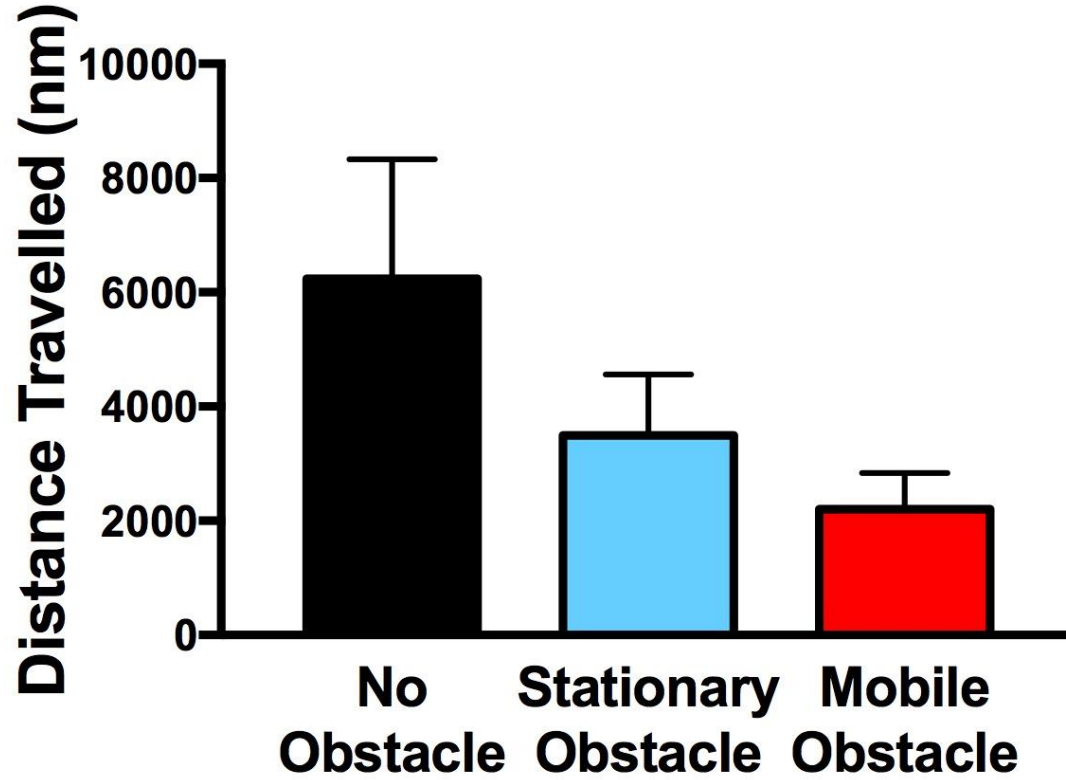


Why do we use Tau as an obstacle?

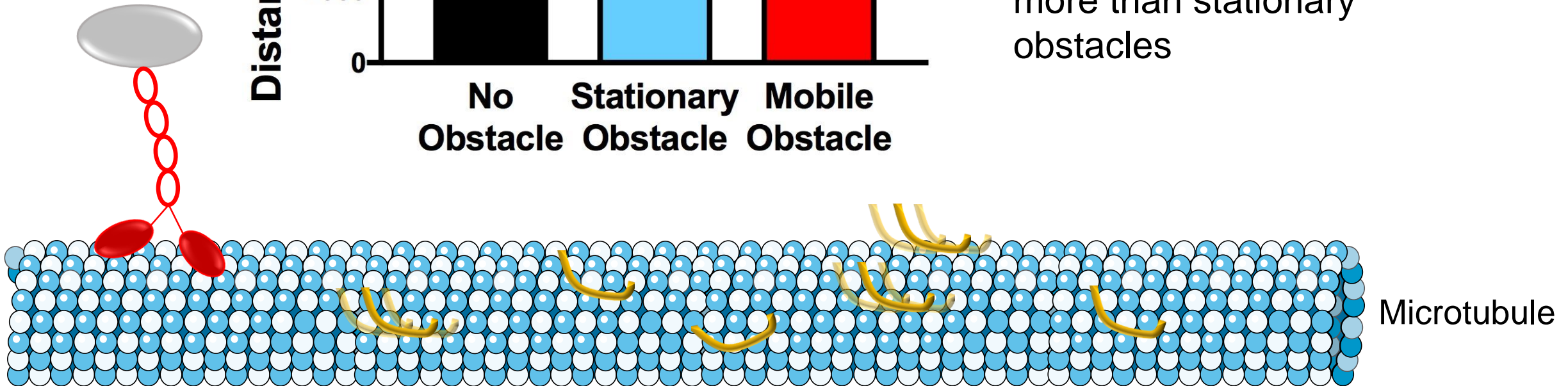
- Exists predominantly in nerve cells
- Has both stationary and mobile behavior
- Known to regulate other KIF proteins



Recent findings: KIF1A is regulated by Tau.



- Both stationary and mobile obstacles reduce the distance that KIF1A can travel
- Mobile obstacles reduce KIF1A's distance travelled more than stationary obstacles



Conclusions and ongoing projects: What did we learn and where will it take us?

Previous questions

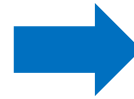
New knowledge

How does KIF1A behave?



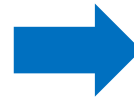
Unique pausing behavior.

How does KIF1A transport cargo over long distances?



Pauses facilitate long distance transport.

How does KIF1A respond to obstacles?



KIF1A is regulated by obstacles, specifically mobile obstacles.

Next big questions: what about KIF1A mutations?

How do mutations in KIF1A affect...

Pausing?

Cargo transport?

Obstacle navigation?

Thank you!!!



The University of Vermont
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- Finlay Pilcher, MS

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