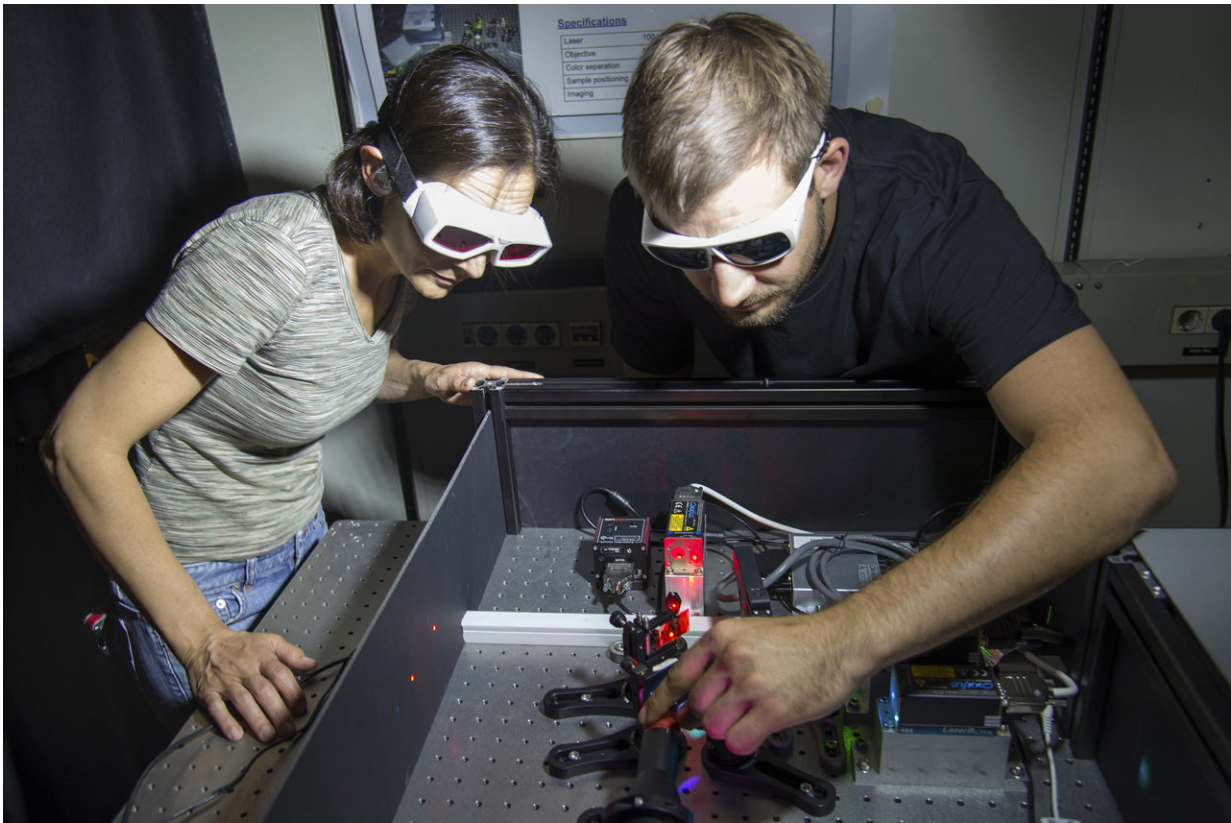


Research team reconstructs motor-cargo complex for ciliary transport

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Dr. Zeynep Oekten and co-author Willi L. Stepp at the fluorescence microscope they use to observe the motor proteins running along the microtubules (see video). Credit: Andreas Battenberg / TUM

Every living organism expresses fine cellular protrusions known as cilia.

Flagellates need them to move, roundworms to find food, and sperm to move towards the egg. Cilia form fine protective hairs in the lungs and play a crucial role in the differentiation of organs in embryos. A research team at the Technical University of Munich (TUM) has now reconstructed the protein complex responsible for transport within cilia, which plays a decisive role in their functioning.

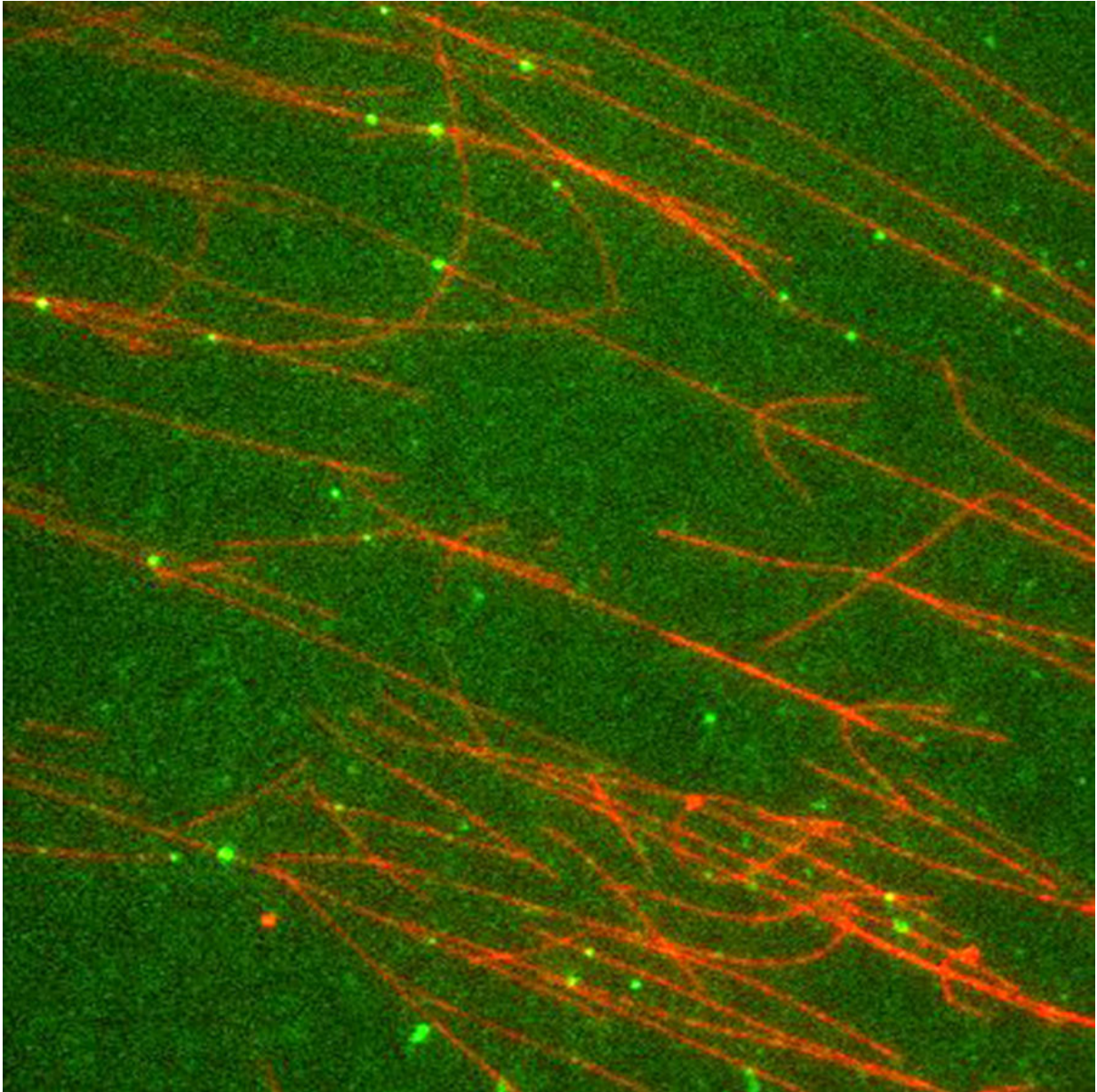
These excrescences of eukaryotic cells even ensure that the human heart ends up in the right place—cilia control the organ development of the growing fetus. "This multifunctionality is absolutely fascinating," says Dr. Zeynep Ökten, biophysicist in the Physics Department of the Technical University of Munich.

Only in recent years has the significance of cilia for signal transduction has been recognized. "To date, we know very little about which biochemical processes control the various functions. This makes understanding the basic mechanisms even more important," says the scientist.

The scientist holds a glass plate with thin, liquid-filled capillaries up to the light. There is not much to see—just a transparent liquid. Only under a [fluorescence microscope](#) does the movement of dye-marked compounds become visible as green dots, all striving in one direction. As if on a highway, the transport proteins migrate along the thin channels of the cilia. But just how these engines are started has remained a mystery until now. That is why Zeynep Ökten and her team decided to reconstruct the [protein](#) complex.

The [building blocks](#) of the [protein complex](#) stem from the model organism of the *Caenorhabditis elegans* nematode. It uses its cilia to find food and detect hazards. The biologists have already identified dozens of proteins that affect the function of nematode cilia.

"Here, the classical top-down approach reaches its limits because too many building blocks are involved," explains Ökten. "To understand the intra-flagellar transport, IFT for short, we thus took the opposite approach, studying individual proteins and their interactions from the bottom up."



Motor proteins (green dots) move along microtubules like trucks on a highway.

Credit: Georg Merck / TUM

The needle in a protein haystack

The work resembled the proverbial search for the needle in a haystack. A variety of molecular compounds came into question. After months of experimentation, the researchers stumbled upon a minimal combination of four proteins. As soon as these proteins fuse into a complex, they begin migrating through the capillaries of the sample carrier.

"When we saw the images of the fluorescence microscope, we immediately knew: Now we have found the parts of the puzzle that start the engine," recalls Ökten. "If just one of these components is missing, due to a genetic defect, for example, the machinery will fail—which, because of the [cilia](#)'s importance, is reflected in a long list of serious diseases."

More information: Mohamed A. A. Mohamed et al, Reconstitution reveals motor activation for intraflagellar transport, *Nature* (2018). [DOI: 10.1038/s41586-018-0105-3](https://doi.org/10.1038/s41586-018-0105-3)

Provided by Technical University Munich

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