A motor is not just for quarantine, it’s for life!

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Diffusion is a wonderful process that keeps us all alive. However, the cell cytoplasm is a crowded environment that severely impedes the movement of larger objects, such as vesicles. In addition, diffusion is definitely not going to move a vesicle from one location to another on a time scale that is actually useful. Given the physical limitations of a viscous cytoplasm, it is not surprising that cells have evolved elaborate mechanisms to ensure cellular cargoes are moved to the right locations at the appropriate time. Now, just imagine the sheer number of different cargoes that need to be moved in a cell; and there is of course the movement of cells themselves and muscle contraction. Considering the scale, this spectacular logistics problem is solved using a relatively small set of molecular motors – humans encode fewer than 100 of these exquisite machines (myosins, dyneins and kinesins). These motors keep us moving by converting the chemical energy of ATP into mechanical energy to generate force and movement. Moreover, these three different types of motor move or pull on only two tracks – actin and microtubules – that are also dynamic polymers that shrink and grow in response to the needs of the cell. Then there is the issue of the direction of movement. Fortunately, actin filaments and microtubules have polarity, and motors typically only go in one direction, so everything is always moved or pulled the right way. Given their importance, it will come as no surprise that loss or impairment of motor function results in a wide variety of conditions and diseases that are especially evident in the function of the nervous system.

The first myosin was isolated from skeletal muscle by the Hungarian biochemist Albert Szent-Györgyi in 1941-43. Today, we know that the human genome encodes some 40 myosins, which are grouped into 12 families based on sequence homologies outside their motor domains. All myosins motors bind actin filaments and move towards their plus- or fast-growing ends, with the exception of myosin VI. Dynein was first described as a motor protein driving the bending of cilia and flagella by Ian Gibbons in 1963. There are ∼15 human dynein motors, which form MDa-sized motor complexes with multiple associated subunits. Most dyneins function in cilia and flagella, and only two family members actually move cytoplasmic cargoes towards the minus end of microtubules. Kinesin was simultaneously described by several labs in 1985, but was given its name by Bruce Schnapp at the Marine Biological Laboratory in Woods Hole. There are 45 kinesins in humans that are grouped into 15 families. The majority of kinesins have an N-terminal motor domain that mediates plus-end-directed microtubule transport. A limited number of kinesin family members do not have this activity, but rather depolymerize microtubules or move cargoes to their minus ends.

We have come a long way since the first descriptions of molecular motors, so surely in this enlightened age of cell biology we have a pretty good understanding of how motors mediate cargo transport? After all, do we have the structures of many different motors, including the massive dynein motor complex, in various activation states. A wide variety of elegant in vitro reconstitution, biochemical and biophysical assays have also provided important fundamental motor parameters, including their speed, persistence and step size, as well as the forces they can generate. We can even image single motors inside cells to study their behaviour and have analysed their roles in a host of cellular processes using genetics, siRNA- and CRISPR-based approaches. This sounds like we are doing well; nevertheless, we still lack important insights into some of the most basic questions concerning motor function. For example, how many motors and which types are on your average endosome or virus zipping around a cell? Moreover, how many of them are actually active and how do their properties change when they work in a cooperative fashion – assuming they do? Do motors undergo turnover when moving cargoes and how much redundancy is there in the system? Also, if you stop and think about it, how does the cell ensure a motor such as kinesin-1, which can interact with a large number of very different cargoes, is only recruited to the right cargo when it needs to be moved in the first place? Basically, how do all these motors ensure the different components and systems of the cell are organized and transported correctly in space and time? We may know what motor domains look like, but we still know surprisingly little concerning the coordination, regulation and molecular basis of motor recruitment and activity on cargoes that can be as diverse as an mRNA molecule to a mitochondria. In addition, for most motors, I think it is fair to say, we also still lack details on the full repertoire of the cargoes they can move, let alone understanding of how their non-motor domains mediate their recruitment in the first place. Finally, while there are common themes in many cell types, the actual number of myosin,
kinesin and dynein motors varies considerably between different organisms. For example, flowering plants have expanded their repertoire of kinesins (61 in *Arabidopsis*), presumably at least in part because they lack dynein motors. We may know their sequence from genome projects but, in the vast majority of cases, the cellular function of these additional motors, which often contain uncharacterized domains, still remains to be established.

There is clearly still a lot of work that needs to be done and it is why we have decided that the seventh Journal of Cell Science special issue will focus on the cell biology of motors. This special issue will be guest edited by Anne Straube, who is based at the Centre for Mechanochemical Cell Biology at the University of Warwick, UK. Anne organizes the very successful ‘Motors in Quarantine’ webinar series (http://mechanochemistry.org/whatson/MiQ/) that was established during the COVID-19 pandemic. These talks have really helped bring the motor community together in what has been a very dark time for everyone, as well as enable early career researchers to present their work to the wider community. It is this spirit that we now want to build on with our special issue, and Anne is ideally placed to achieve this.

After receiving a Diploma in Biochemistry and Molecular Biology from the University of Hamburg, Germany, Anne joined the lab of Gero Steinberg at the Ludwig Maximilian University in Munich and later at the Max Planck Institute for Terrestrial Microbiology in Marburg. Her PhD project focused on cellular functions of dynein and microtubule organisation in the fungus *Ustilago maydis*. In a short postdoc period at Marburg she discovered the role of kinesin-1 in microtubule bundling and sliding. As a postdoctoral fellow of the Emmy Noether programme of the German Science Foundation (DFG), Anne then moved to the Wellcome Trust Centre for Cell Biology in Edinburgh, where she worked with Andreas Merdes on the microtubule cytoskeleton in differentiating muscle cells. In 2007, Anne started her own lab at the Marie Curie Research Institute (MCRI) in Oxted, Surrey. When the MCRI closed in 2010, she moved with her colleagues Rob Cross and Andrew McAinish to the University of Warwick to found the Centre for Mechanochemical Cell Biology. Anne won a Lister Institute Research Prize in 2013, a Wellcome Investigator Award in 2016 and became a Professor in 2020. Her research combines quantitative live-cell imaging approaches with *in vitro* reconstitution assays to study the mechanisms that generate specific microtubule arrays in polarised cells, the dynamic interactions of microtubule tips with intracellular structures and the cell cortex in the control of cell shape changes and the transport along microtubule arrays mediated by dynein and kinesins.

We will welcome submissions for our special issue on the Cell Biology of Motors until 15 July 2022. The special issue will also contain reviews and poster articles, commissioned by our in-house Reviews Editors. We look forward to working with Anne on this important topic. You can find out more at https://journals.biologists.com/jcs/pages/cell-biology-motors and contact us at jcs@biologists.com about any potential submissions.