Kif15: The acrobatic motor protein that could pave the way for new cancer therapies

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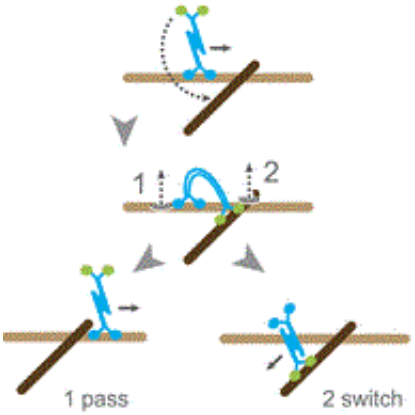

This image shows how Kif15 switches microtubules. Credit: McAinsh/University of Warwick

Researchers at Warwick Medical School have shown for the first time how a protein motor, Kif15, uses acrobatic flexibility to navigate within the mitotic spindle. Understanding how it works could prove vital for the development of targeted cancer therapies.

The new study, published in *eLife*, describes the behaviour of Kif15 for the first time and provides a breakthrough step towards understanding the role it plays in cell division.

Many frontline cancer drugs target microtubules, the molecular cables that are used to build the mitotic spindle - the protein machine that

drives equal separation of chromosomes during mitosis.

By breaking these microtubules, the uncontrolled multiplication of cancerous cells can be stopped. However, cells can become resistant to such drugs and as a result researchers are developing a new class of drug that targets the molecular motors – tiny protein machines that consume chemical fuel to walk along microtubules, move them around and organize them into the spindle.

One of these molecular motors, Kif11, is a key target for these drugs. Yet when Kif11 is inhibited, it is shown that cells are able to adapt and a second motor, Kif15, picks up some of the workload and enables the continuation of mitosis.

Previous research established that Kif11 is different to other kinesin protein motors, being referred to as a 'dumbbell' on account of having four limbs: allowing it to walk on microtubules and bind two microtubules together. During mitosis it slides these microtubules apart, a key process in cell division. The McAinsh lab at Warwick Medical School have now shown that Kif15 shares this four-limbed property, although it does not appear to be able to slide microtubules apart.

Dr McAinsh, said, "It's fascinating to see that Kif15 is also a dumbbell shape – but even more interesting are the differences between the two."

kifguide"Kif15 can actually switch between microtubules at intersecting points and therefore might be able to circumvent roadblocks or avoid traffic jams caused by other motors. It's the first motor protein we've seen using such a feature." (see video at bottom of release)

"We think that Kif15 switches between microtubules by using its additional two limbs: Where it encounters a track that it wants to move onto, it contorts and uses its two not yet attached limbs to grip the new

track. In the most basic sense it starts to walk on its hands in a manner not too dissimilar to a circus acrobat."

Along with the ability to easily navigate the spindle, it also moves along microtubules some seven and half times quicker than Kif11 – at 150nm/s (nanometres per second) rather than 20nm/s.

Now that the team have identified how Kif15 behaves, it is hoped that it will allow for further understanding of the role that it plays in supporting cell division.

Dr McAinsh explained, "A greater knowledge of this protein motor will open the door to developing targeted therapies that can work towards simultaneously restricting both Kif11 and Kif15."

Provided by University of Warwick

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