

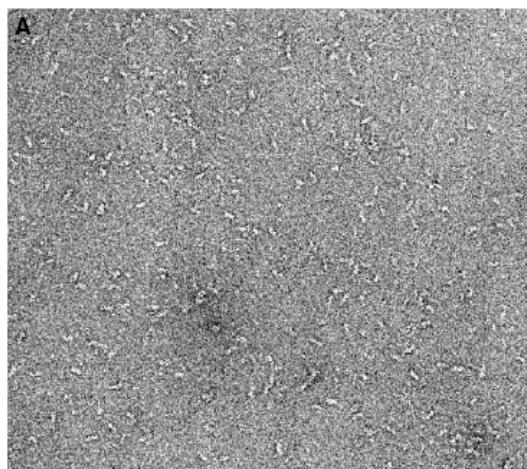
## Class VI myosins

Matthew Walker and John Trinick

We have continued to collaborate on class VI myosin with Dr John Kendrick-Jones (MRC Laboratory of Molecular Biology (Cambridge) and with Dr Claudia Veigel (National Institute for Medical Research, Mill Hill). Myosin VI is unusual in that it walks along actin filaments in the opposite direction to all other myosins so far studied. The mechanism of its reverse gear is therefore of great interest.

The tail of the myosin VI molecule was predicted to dimerise in a coiled-coil  $\alpha$ -helix, similar to muscle myosin II. Many papers analysing the kinetic and walking mechanism have been published describing preparations where dimerisation was enforced by inclusion of a GCN4 leucine zipper sequence. However, last year we published the surprising result that the full length molecule is monomeric, both *in vitro* and *in vivo*. Using optical tweezers, our colleagues at Mill Hill showed that the power stroke of myosin VI is much larger than predicted for a molecule with a lever arm containing only 2 light chains (18 vs 5 nm). This suggests that the angular throw of the lever may be substantially larger than seen in other myosins, or that part of the molecule tail may participate in the lever action.

During 2004, papers from other laboratories continued to appear exploring the properties of the obligate dimer. It may be that myosin VI will prove to be dimeric under some conditions *in vivo*, however, there is currently no direct evidence other than the sequence prediction that the molecule dimerises.



**Figure:** Field of negatively stained monomeric myosin VI molecules (each about 16 nm long).

### Publications

Lister, I., Schmitz, S., Walker, M., Trinick, J., Veigel, C. and Kendrick-Jones, J. (2004) Myosin VI is a non-processive monomer with a large working stroke. *EMBO J.*, **23**, 1729-1738.

Roberts, R., Lister, I., Schmitz, S., Walker, M., Veigel, C., Trinick, J., Buss, F. and Kendrick-Jones, J. (2004) Myosin VI: cellular functions and motor properties. *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences*, **359**, 1931-1944.

Lister, I., Roberts, R., Schmitz, S., Walker, M., Trinick, J., Veigel, C., Buss, F. and Kendrick-Jones, J. (2004) Myosin VI: a multifunctional motor. *Biochemical Society Transactions*, **3**, 685-688.

### Collaborators

Dr John Kendrick-Jones (MRC Laboratory of Molecular Biology (Cambridge) and with Dr Claudia Veigel (National Institute for Medical Research, Mill Hill)

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