

Class I myosins

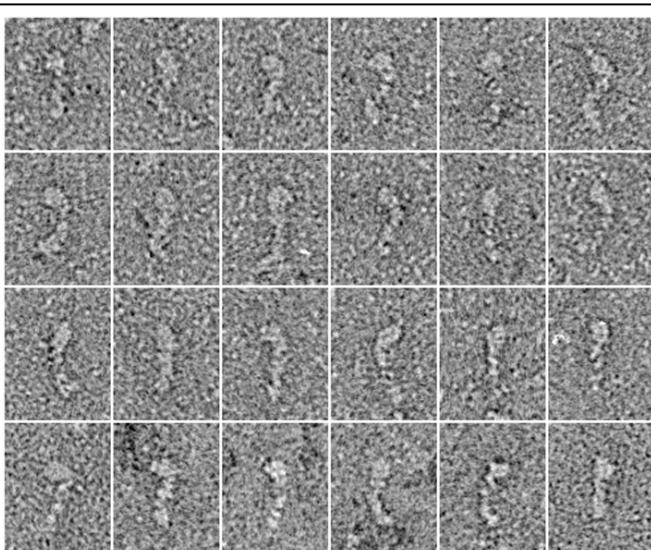
Matthew Walker and John Trinick

Myosins are identified on the basis of sequence similarities in their motor domain regions, which bind actin and have ATPase activity. Extending from the motor domain is a single α -helix, which binds light chains of the calmodulin class. This acts as a lever arm and produces motion by changing its angle relative to the motor domain. At the end of the lever arm the molecule tail binds cargo. The vast majority of work on myosin has focussed on the type found in muscle, which is called class II. Muscle myosin is a dimeric molecule, with two heads, each with a motor domain and a lever arm. The heads are dimerised through the tail, which is a coiled-coil α -helix and polymerises to form muscle thick filaments.

Recent years have seen the identification of 17 other, non-muscle myosin classes. Based on their sequences, these have similar motor domains, but vary widely in other respects. They may, or may not, dimerise and are also likely to vary in kinetic properties, regulatory mechanisms and cargo binding. Class I myosins are found across a large range of organisms, from amoeba to humans. They are thought to be involved in a range of cellular mechanisms where long persisting forces are needed; for example, in bracing and tensioning the cytoskeleton. The myosin I power stroke is thought to occur in two steps, coupled respectively to Pi and ADP release. ADP release may be strain-sensitive and this, together with a slow ATP-induced dissociation from actin, suggests that myosin I is uniquely suited for maintenance of tension. Studies in lower eukaryotes indicate the importance of myosin I in cell motility, establishment of polarity, and actin organization. A family of myosins I exists in higher cells involved, for instance, in hearing.

We have studied myosin I in collaboration with Drs Lynn Coluccio and Walter Stafford (Boston Biomedical Research Institute, Boston, Massachusetts). Our electron microscopy of purified myosin revealed a monomeric molecule. Consistent with our data, analytical ultracentrifugation gave a molecular mass of 213 kg/mol and dimensions of 28 x 4 nm.

Microscopy also suggests the presence of more than one actin binding site in each molecule.



Montage of myosin I molecules. The tadpole-shaped molecules are orientated with their motor domains (which bind actin and cleave ATP) at the top. The pictures appear to show flexibility between the motor domain and the lever arm which transmits force. Each molecule is ~22nm long.

Publication

Stafford, W. F., Walker, M.L., Trinick, J.A. and Coluccio, L.M. (2005) Mammalian class I myosin, Myo1b, is monomeric and cross-links actin filaments as determined by hydrodynamic studies and electron microscopy. *Biophysical Journal*, **88**, 384-391.

Collaborators

Drs Lynn Coluccio and Walter Stafford, Boston Biomedical Research Institute, Boston, Massachusetts.

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