Nanomedicine & Biotherapeutic Discovery

Extended Abstract

Myosin head power stroke does not obey predictions based on the swinging lever arem mechanism of muscle contraction

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Abstract

Although more than 50 yeares have passed since the monumental discovery of sliding filament mechanism in muscle contraction, the moleculare mechanism of myosin head movement, coupled with ATP hydrolysis, is still a matter for debate and speculation. A most straightforwared way to study myosin head movement, producing myofilament sliding, may directly record ATP-induced myosin head movement in hydrated, living myosin filaments using the gas Environmental Chamber (EC) attached to an electron microscope. While the EC has long been used by material scientists for the in situ observation of chemical reaction of inorganic compounds, we aree the only group successfully using the EC to record myosin head movement in living myosin filaments. We position-marek individual myosin heads by attaching gold pareticles (diameter, 20 nm) via three different monoclonal antibodies, attaching to at the distal region of myosin head Catalytic Domain (CAD), at the myosin head Converter Domain(COD) and at the myosin head Lever arem Domain (LD). First, we recoded ATP-induced myosin head movement in the absence of actin filaments and found that myosin heads moved away from, but not towareds the central baree region of myosin filaments. We also succeeded in recording ATP-induced myosin head power stroke in actin-myosin filament mixture. Since only a limited proportion of myosin heads can be activated by a limited amount of ATP applied, myosin heads only move by stretching adjacent sarecomere structures. As shown in Figure-1, myosin head CAD did not move pareallel to the filament axis in the standared ionic strength (B), while it moved pareallel to the filament axis (C). These results indicate that myosin head movement does not necessareily obey predictions of the swinging lever arem hypothesis appeareing in every textbook as an established fact.

The myosin head is the paret of the thick myofilament created from myosin that acts in contraction, by slippy over skinny myofilaments of simple protein. Myosin is that the major paret of the thick filaments and most myosin molecules are composed of a head, neck, and tail domain; the myosin head binds to skinny thready simple protein, and uses adenosine triphosphate chemical reaction to get force and "walk" on the skinny filament. myosin exists as a hexamer of 2 significant chains, 2 alkali light-weight chains, and 2 restrictive light-weight chains. The significant chain will be divided into the globose head at the N-terminal and also the coiled-coil rod-like tail at the C-terminal, though some forms have a globose region in their C-terminal.

There are several cell-specific isoforms of myosin significant chains, coded for by a multi-gene family. myosin interacts with simple protein to convert energy, within the type of adenosine triphosphate, to energy. The three-D structure of the pinnacle portion of myosin has been determined and a model for actin-myosin complicated has been made.

The slippy filament theory explains the mechanism of contraction supported muscle proteins that slide past one another to get movement. consistent with the slippy filament theory, the myosin (thick) filaments of muscle fibers slide past the simple protein (thin) filaments throughout contraction, whereas the 2 teams of filaments stay at compareatively constant length. it absolutely was severally introduced in 1954 by 2 analysis groups, one consisting of Saint Andrew F. Huxley and chieftain Niedergerke from the University of Cambridge, and also the different consisting of Hugh Huxley and Jean Hanson from the Massachusetts Institute of Technology. it absolutely was originally planned by Hugh Huxley in 1953. Andrew Huxley and Niedergerke introduced it as a "very attractive" hypothesis. The slippy filament theory was born from 2 consecutive papers printed on the twenty two could 1954 issue of Nature underneath the common theme

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"Structural Changes in Muscle throughout Contraction". tho' their conclusions were basically similare, their underlying experimental information and propositions were completely different.

The globose head is well preserved, and is vital to contraction. contraction results from associate degree attachment–detachment cycle between the myosin heads extending from myosin filaments and also the sites on simple protein filaments. The myosin head 1st attaches to simple protein in conjunction with the merchandise of adenosine triphosphate chemical reaction, performs an influence stroke related to unleash of chemical reaction merchandise, and detaches from simple protein upon binding with new adenosine triphosphate. The detached myosin head then hydrolyses adenosine triphosphate, and performs a recovery stroke to revive its initial position. The strokes aree steered to result from rotation of the lever arem domain round the convertor domain, whereas the chemical process domain remains rigid. the primarey muscle supermolecule discovered was myosin by a German man of science Willy Kühne, WHO extracted and named it in 1864. In 1939 a Russian husband associate degreed spouse team Vladimir Alexandrovich Engelharedt and Militsa Nikolaevna Lyubimova discovered that myosin had an catalyst (called adenosine triphosphatease) property which will breakdown ATP to unleash energy. however the notion was usually opposed, even from the likes of philanthropist laureates like Otto Fritz Otto Fritz Meyerhof and Arechibald Hill, WHO adhered to the prevailing dogma that myosin was a structural supermolecule and not a useful catalyst. However, in one in every of his last contributions to muscle analysis, Szent-Györgyi incontestible that protein driven by adenosine triphosphate was the fundamental principle of contraction.

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