news and views

Rabbit–scallop transplants

COMPARING and contrasting animals of widely different form is a common pastime for muscle specialists, since in their field similarities generally outweigh differences and there is much common ground for detailed correlation. In general, muscle contraction takes place by some kind of sliding filament mechanism, that is, by relative movement of actin and myosin filaments, and regulation of the system is mediated by the level of calcium ions. Within this fundamental framework, however, there is considerable variation of detail in the Animal Kingdom—in the way, for example, the calcium control is exercised. In vertebrate skeletal muscle, changes of calcium level affect the muscle activity by modifying the troponin and tropomyosin components of the actin filaments, whereas in the muscles of molluscs and some primitive invertebrates myosin and not actin is controlled. In some invertebrates there is dual control, that is, both types of filament are involved in regulation. Evolutionary forces are clearly at work here, and the understanding of problems of animal specialisation and adaptation provides an interesting background to the more fundamental task of elucidating the molecular basis of muscle contraction.

Myosin is a protein with a long tail portion and two globular heads. From the heads may be dissociated polypeptides of relatively low molecular weight, the so-called light chains. In rabbit skeletal muscle myosin there are two classes of light chains, one class released by alkali and the other by DTNB (5,5′-dithiobis-(2-nitrobenzoic acid)). The alkali light chains have been shown to be involved in the enzymatic activity of the myosin, but the function of the DTNB light chain has long remained a mystery. Scallop muscle myosin, on the other hand, has light chains released by EDTA, and without these chains the splitting of ATP by the myosin–actin system is not susceptible to changes of calcium, that is, the myosin becomes 'desensitised'. Is it possible, therefore, that the DTNB light chain in the rabbit has a role analogous to that of the EDTA chain in the scallop? If it does play a part in calcium regulation, how significant is its function relative to the actin-linked control? Perhaps the existence of the DTNB light chain is vestigal, an evolutionary relic of the more primitive scallop type of myosin regulation that has been usurped by sophisticated actin control? To test these ideas, Kendrick-Jones (see page 631 of this issue of *Nature*) has carried out molecular transplants in which the DTNB light chain from rabbit is grafted onto desensitised scallop myosin. Sure enough, the sensitivity is retrieved. This is a most remarkable result, and a triumph for advanced protein techniques which, together with the investigator's skill, can bridge a gap that was many millions of years in the making.

The DTNB light chain restores the calcium sensitivity more fully to the intact scallop myofibrils that have been treated with EDTA than to preparation of pure scallop myosin similarly treated. There is no evidence that the DTNB reacts directly with any protein other than the myosin, however, and it is possible therefore that actin in the myofibrils may have an indirect effect by stabilising the myosin in some way. Experiments with radioactivity labelled DTNB light chains show that one mole is bound per myosin molecule. Since the myosin molecule normally releases one mole of EDTA light chain, and this must be removed before the DTNB chain will attach, the binding sites for the two polypeptides are likely to be essentially the same. The binding of the DTNB light chain is tight and specific, and the other rabbit light chains—the ones released by alkali—cannot be made to bind to scallop myosin or to affect its calcium sensitivity.

Since rabbit turns on scallop, what can the latter do in return? Kendrick-Jones has not omitted this intriguing alternative, but, disappointingly, the full reciprocal relationship is not established. Although radioactive labelling shows that the scallop EDTA light chain will bind to rabbit myosin that has been treated with DTNB, the myosin does not then become calcium sensitive. Still, the fact that the two chain types are interchangeable is interesting enough, and the interest is intensified by the knowledge that their chemical structures have no obvious similarities.

There is little direct evidence for myosin playing a part in the regulation of vertebrate skeletal muscle activity by calcium. X-ray diffraction of stretched living muscle has indicated that the positions of the myosin cross-bridges alter when the calcium level is changed. When, however, the myosin is extracted from the muscle, its ability to split ATP in the presence of pure actin is unaffected by the calcium level, though it does bind small amounts of calcium. The fault may lie here in the extraction and purification procedure.

Some living organisms have myosin-linked regulation, some actin-linked, and some have both. The transition and gradation between these regulatory mechanisms, their evolutionary significance and what particular physiological advantages are conferred by the possession of one or other or both remain fascinating questions. It could be argued, however, that the scope at least of the problem has been encompassed by Kendrick-Jones's successful matching of the light chains separated by aeons, and union of two animals sufficiently dissimilar to startle even Edward Lear.

E. J. O'BRIEN

Aspects of the asthenosphere

IT may be a cliché to say that the Earth's asthenosphere exerts a profound influence on the crust and lithosphere above, but it is neither less true nor less important a statement for that. Irrespective of whether convection currents are limited to it or go deeper, the asthenosphere clearly plays a crucial part in the horizontal motion of continents and ocean floors; it is the source of at least some of the material which finds its way from the mantle to the Earth's surface, and is closely related in composition to that part of the mantle which provides the rest; and it is the ultimate means by which a crust with a changed load may achieve isostatic equilibrium. In other words, it governs the behaviour of the upper layers of the Earth to such a degree that the determination of its physical and chemical properties can be safely said to be one of the genuinely fundamental problems in the Earth sciences.

And for obvious reasons it is a problem both difficult