Reports

Nature of Meromyosins

Following up the observation of Gergely (*1*) that a partial digestion of myosin with trypsin leaves its adenosine triphosphatase activity intact, Mihalyi (*2*) and Szent-Gyorgyi (*3*) isolated two large fragments of myosin from the digested mixture. The heavier of the two components carrying the adenosine triphosphatase activity was named H-meromyosin (H), the lighter component L-meromyosin (L) (*3*). Since these components are liberated in about equal weights and since H is about twice as heavy as L (L's molecular weight, 100,000) the myosin molecule must contain one H and two L components.

Since the meromyosins in their amino acid composition add up to myosin (*4*), they can be considered as the primary products of splitting, essentially unmodified by further digestion. In addition to trypsin other proteolytic enzymes such as chymotrypsin (*5*), subtilisin (*6*), and snake venom (*7*) have been found to split myosin, yielding products roughly similar to those produced by trypsin. Since these enzymes split ester bonds as well as peptide bonds, it is important to study the C-terminal groups of the split products to see whether those groups which appear correspond to the known specificity requirements of these enzymes.

Although the L-meromyosins produced by these enzymes appear very similar, they exhibit subtle differences. Gergely (*8*) found that L-meromyosin obtained with the digestion of chymotrypsin yielded 1 mole of phenylalanine as a C-terminal end group when studied with carboxypeptidase A (*8*). With the discovery of a new carboxypeptidase (*9*), specific for basic amino acids, it was possible to demonstrate the presence of a C-terminal lysine on the L-meromyosin produced by trypsin (*10*).

The appearance of these C-terminal groups is in agreement with the known specificity requirements of these proteolytic enzymes. The L-meromyosin produced by snake venom again is different since it has a C-terminal alanine (*7*). From these observations one must conclude that the meromyosins are the proteolytic split products of myosin and as such should not be considered as preexisting subunits of myosin. Nevertheless, since tracer studies show that the two fragments of myosin have different turnover rates (*11*), at least two subunits of some kind pre-existing in the muscle can be postulated.

For the arrangement of the meromyosins in the myosin molecule, Holtzer and Rice (*12*), from light-scattering evidence, proposed the arrangement LLH. In the interpretation of light-scattering data summation of shape considerations presents a difficult problem which can be solved only with simplifying assumptions.

The fact that both L- and H-meromyosin have "wounded" ends (*13*) supports the LHL arrangement. There are other chemical and biochemical facts that support this arrangement; here I want to point out one which appears quite decisive against the LLH arrangement.

The arrangement LHL is symmetrical and permits a molecular weight of the myosin monomer to be about 220,000, one-half of the current value of about 440,000.

The recent careful experiments of Ellenbogen and co-workers (*14*) show that the molecular weight of myosin from dog heart is about 223,000. Since myosin of twice this size, obviously a dimer, also has been obtained from heart muscle, an arrangement of the meromyosins in myosin (MW = ~ 440,000) must be such as to permit the halving of the molecule.

Evidence is mounting to show that myosin is more complex than the meromyosins would imply. Kominz in this laboratory isolated from myosin without the use of proteolytic enzymes a protein (about 12 percent myosin) rich in phenylalanine and very much different from the meromyosins (*15*). Alcohol denaturation was found to split L-meromyosin into a crystalline and noncrystalline component (*16*), showing the complexity of L-meromyosin.

To unravel the detailed composition of myosin is very important because it is becoming more and more apparent that without such knowledge the role of myosin in muscular contraction will not be understood.

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References

1. J. Gergely, *J. Biol Chem.* **200**, 543 (1953).
2. E. Mihalyi, *ibid.* **201**, 197 (1953); ——— and A. G. Szent-Györgyi, *ibid.* **201**, 189 (1953).
3. A. G. Szent-Györgyi, *Arch. Biochem. Biophys.* **42**, 305 (1953).
4. D. R. Kominz, A. Hough, P. Symonds, K. Laki, *ibid.* **50**, 148 (1954).
5. J. Gergely, M. A. Gouvea, D. Karibian, *J. Biol. Chem.* **212**, 165 (1955).
6. W. R. Middlebrook, *Abstr. 1958 Meeting Biophys. Soc.* (1958), p. 46.
7. D. R. Kominz, personal communication.
8. J. Gergely, H. Kohler, W. Ritschard, L. Varga, *Abstr. 1958 Meeting Biophys. Soc.* (1958), p. 46.
9. J. E. Folk, J. A. Gladner, K. Laki, *Federation Proc.* **16**, 181 (1957).
10. J. A. Gladner and J. E. Folk, *J. Biol. Chem.* **231**, 393 (1958).
11. S. F. Velick, *Biochim. et Biophys. Acta* **20**, 228 (1956).
12. A. Holtzer and S. A. Rice, *J. Am. Chem. Soc.* **79**, 4847 (1957).
13. K. Laki, *J. Cellular Comp. Physiol.* **49**, Suppl. 1, 249 (1957).
14. E. Ellenbogen, R. Iyengar, H. Stern, R. G. Olson, in preparation; personal communication.
15. D. R. Kominz, *Federation Proc.* **17**, 256 (1958).
16. C. Cohen and A. G. Szent-Györgyi, *J. Am. Chem. Soc.* **79**, 248 (1957).

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Soluble Deoxyribosidic Compounds in Relation to Duplication of Deoxyribonucleic Acid

One of the puzzling features of chromosome reproduction is the abruptness and relative rapidity with which the chromosomal substance is synthesized. Wherever the phenomenon has been adequately studied, whether in cells of plant, animal, or microorganism, the duplication of deoxyribonucleic acid (DNA) has consistently been found to occur during a comparatively brief interval in the life span of the cell. This behavior is in marked contrast to that of many other cell components which fluctuate in concentration or increase gradually in amount during cellular development.

The cause and course of DNA duplication is but little understood. Not even in phage-infected bacteria, where the

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper. (Since this requirement has only recently gone into effect, not all reports that are now being published as yet observe it.)

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* 125, 16 (1957)].