Cell Motility and the Cytoskeleton 42:163–177 (1999)

unc-45 Gene of *Caenorhabditis elegans* Encodes a Muscle-Specific Tetratricopeptide Repeat-Containing Protein

Lee Venolia,[1] Wanyuan Ao,[2] Stuart Kim,[3] Caroline Kim,[1] and Dave Pilgrim[2]*

[1]*Department of Biology, Williams College, Williamstown, Massachusetts 01267-3147*
[2]*Department of Biological Sciences, University of Alberta, Edmonton, Alberta, Canada*
[3]*Department of Developmental Biology, Stanford University, School of Medicine, Stanford, California*

The *unc-45* gene of the nematode, *Caenorhabditis elegans,* is essential for muscle organization and embryonic development. Genetic evidence suggests the *unc-45* gene product controls muscle thick filament assembly. We report here on the determination of the gene's chromosomal location and the isolation and sequencing of its cDNA. The amino terminus of the predicted *unc-45* protein contains three tandem repeats that belong in the tetratricopeptide repeat family. Tetratricopeptide motifs have been shown to be involved in protein interactions, and some of the closest homologues have chaperone-like activity. The carboxy terminus of the protein has homology with the related fungal proteins, CRO1 and She4p, which have been postulated to play a role in assembly of or interactions with a cytoplasmic myosin. We have also determined the sequence of the homologous gene from *C. briggsae,* which demonstrates a high level of conservation. We show that the *unc-45* gene promoter can drive reporter gene expression, which is limited to muscle tissues (pharyngeal, body wall, vulval, and anal muscles), consistent with a role for the *unc-45* gene in muscle development or function. Cell Motil. Cytoskeleton 42:163–177, 1999.

Key words: embryo; thick filament; gene expression; GFP; TPR

INTRODUCTION

The structure of the contractile mechanism of muscle is widely conserved across metazoan evolution. This allows the use of model systems to investigate questions of muscle development, structure, and function. To date, organisms suitable for genetic analysis, such as the fruit fly *Drosophila melanogaster,* and the nematode *Caenorhabditis elegans,* have allowed the description of new muscle genes and the demonstration of new developmental mechanisms, which are likely to be conserved in vertebrates. All proteins so far identified in *C. elegans* striated muscle have orthologs in humans, so the description, in *C. elegans,* of a new muscle-affecting gene is likely to have ramifications in understanding human muscle. The *unc-45* gene of *C. elegans* has been shown to be essential for the development of functional muscles in the nematode. In particular, the *unc-45* gene product (UNC-45) is proposed to interact with muscle myosins to promote the assembly of thick filaments [Venolia and Waterston, 1990]. In this paper, we describe the molecular identity of the *unc-45* gene of *C. elegans.*

The myosins of *C. elegans* muscle are similar to those of vertebrates [Moerman and Fire, 1997; Harrington, 1979]. Thick filaments in *C. elegans* are composed of four myosin isoforms. Myosin heavy chain (MHC) A and

Contract grant sponsor: NIH; Contract grant sponsor: Natural Sciences and Engineering Research Council; Contract grant sponsor: Medical Research Council of Canada; Contract grant sponsor: Alberta Heritage Fund for Medical Research.

*Correspondence to: Dave Pilgrim, Dept. of Biological Sciences, University of Alberta, Edmonton, Alberta T6G 2E9 Canada.
E-mail: dave.pilgrim@ualberta.ca

Received 4 June 1998; accepted 25 November 1998