Troponin T Isoform Expression in Humans
A Comparison Among Normal and Failing Adult Heart, Fetal Heart, and Adult and Fetal Skeletal Muscle

Page A.W. Anderson, Nadia N. Malouf, Annette E. Oakeley,
Edward D. Pagani, and Paul D. Allen

The expression of troponin (Tn) T, a thin-filament regulatory protein, was examined in left ventricular myocardium from normal and from failing adult human hearts. The differences in isoform expression between normal and failing myocardium led us to examine the ontogenic expression of TnT in human striated muscle. Left ventricular samples were obtained from patients with severe heart failure undergoing cardiac transplantation and normal adult organ donors. Fetal muscle was obtained from aborted fetuses after 14–15 weeks of gestation, and adult skeletal muscle was obtained from surgical biopsies. Western blots of normal and failing adult heart proteins demonstrated that two isoforms, TnT1 and TnT2, are expressed in different amounts, with TnT2 being significantly greater in failing hearts (p<0.004). Western blots of two-dimensional gels of these proteins resolved two predominant spots of both TnT1 and TnT2 and several minor TnT species. Alkaline phosphatase treatment converted the two major spots of each isoform into the single more basic spots. A comparison of the ATPase activities and the TnT percentage of total TnT in individual failing and normal adult hearts demonstrated an inverse and negative relation (r=0.7, p<0.02). In the fetal heart, four TnT isoforms were found, two of which had the same electrophoretic mobilities as the adult cardiac isoforms TnT1 and TnT2. Fetal skeletal muscle expressed two of the four fetal cardiac TnT isoforms, one of which comigrated with adult cardiac TnT1. These cardiac isoforms were expressed in low abundance in fetal skeletal muscle relative to seven fast skeletal muscle TnT isoforms. No cardiac isoforms were present in adult skeletal muscle. Because many etiologies caused heart failure in the transplant patients, we propose that the disease-associated increased expression of the TnT isoform TnT2 is an adaptation to the heart failure state and a partial recapitulation of the fetal expression of cardiac TnT isoforms. (Circulation Research 1991;69:1226–1233)

The clinical syndrome of heart failure has long been considered the consequence of abnormalities in myocardial function. Lower myofibrillar ATPase activity has been suggested, along with other abnormalities, as an important mechanism underlying the depressed mechanical function of the failing human heart.1–3 Recently, Pagani et al4 found that left ventricular myofibrillar ATPase activity in patients with end-stage heart failure is significantly lower than that in normal patients, whereas myosin ATPase activity of the failing left ventricle does not differ from that of the normal. Other human studies5–7 have shown that the β-isoform of the myosin heavy chain is the predominant isoform expressed in the normal human heart and is unchanged in the presence of hypertrophy and failure. The disease-induced decrease in human myofibrillar ATPase activity in the absence of a change in myosin isoform expression suggests that the change in myofibrillar ATPase activity may be the result of alterations in the isoform expression of contractile proteins that regulate the sensitivity of the myofilaments to calcium.

Thin-filament proteins that regulate the response of the myofilaments to calcium include the troponin (Tn) complex of TnT, TnI, and TnC.8 Isoforms of cardiac TnT have been found to undergo developmentally9–12 and regionally13 regulated expression (in species other than humans). The possibility that TnT isoforms differ in their regulatory function is supported by several biochemical and physiological studies; for example, the studies of Tobacman and Lee,14 Schachat et al,15 McAuliffe et al,16 and Nassar et al17
have suggested that myofibrillar ATPase activity and the contractile response to calcium are affected by TnT isoforms.

As a first step in understanding the role of TnT isoforms in the function of diseased human hearts, we investigated TnT expression in normal and failing hearts. We found that the proportions of the TnT isoforms, TnT$_1$ and TnT$_2$, are affected by disease, leading us to investigate whether the disease-associated increase in TnT$_2$ is a recapitulation of the ontogenic changes in TnT expression and an adaptive response to the disease state. Adult cardiac isoforms TnT$_1$ and TnT$_2$ were two of the four TnT isoforms found in the fetal heart. None of these isoforms were found in adult skeletal muscle, whereas small amounts of two cardiac isoforms, TnT$_1$ and a fetal cardiac TnT isoform, were found in fetal skeletal muscle. Finally, we related the myofibrillar ATPase activity to the percentage of total TnT composed of TnT$_1$ of individual heart failure patients and of organ donors and found a significant and inverse relation between ATPase activity and TnT$_2$ expression. We conclude that the disease-associated changes in TnT isoform expression are an adaptation to the heart failure state and a partial recapitulation of the fetal expression of TnT isoforms.

Material and Methods

Tissue Source

TnT isoform expression was examined in tissue from both failing and normal human left ventricular free wall, human fetal ventricle, and human fetal and adult skeletal muscle. Adult cardiac tissue was obtained either from patients with severe heart failure at the time of orthotopic cardiac transplantation ($n=10$) or at the time of organ harvest from patients whose hearts were unacceptable for transplantation for noncardiac reasons ($n=6$). Fetal tissues (after 14½ and 15 weeks of gestation) were obtained at the time of therapeutic abortion. Adult skeletal muscle samples were obtained from biopsies taken at the time of surgery for unrelated problems. All tissues were obtained using protocols approved by the Brigham and Women's Hospital institutional committee for the protection of human subjects.

Tissue Preparation

Left ventricular free wall was cut into small transmural pieces and frozen in liquid nitrogen within 5 minutes of excision of the heart. Fetal cardiac and skeletal muscle was treated in a similar fashion. The adult skeletal muscle biopsies were −1 g in size and were frozen in liquid nitrogen immediately after excision. Specimens were transported to Duke Medical Center and Sterling Research Group on dry ice and kept in liquid nitrogen until the specimens were prepared for electrophoresis and evaluation of myofibrillar ATPase activity. Adult rabbit cardiac and fast skeletal muscle were obtained as previously described.12

Materials

The reagents were the same as described previously.12 For the phosphorylation experiments, bacterial alkaline phosphatase was obtained from Gibco BRL. Monoclonal antibody 13-11 (MAb 13-11), raised against a rabbit cardiac TnT, was obtained from a hybridoma clone, as described previously.18 Briefly, Sendai virus–free Balb-C mice were immunized with rabbit cardiac TnT$_1$ purified by sodium dodecyl sulfate–polyacrylamide gel electrophoresis (SDS-PAGE).12 Mouse spleen cells were fused with P3×63Ag.8.6–5.3 mouse myeloma cells. The hybridomas were screened by enzyme-linked immunosorbertent assay and Western blots. The monoclonal antibody was purified on Fractogel CM$^+10$ and used at 50 μg/ml. A second monoclonal antibody (MAb JLT-12), raised against a fast skeletal muscle TnT isoform, was purchased from Amersham Corp., Arlington Heights, Ill.

Gel Electrophoresis and Western Blots

The failing and organ donor left ventricular myocardium was prepared for SDS-PAGE using the protocol of Anderson et al11 or of Bronson and Schachat20 and for two-dimensional electrophoresis using the method of O’Farrell.21 The fetal heart and skeletal muscle and adult skeletal muscle were prepared for SDS-PAGE and isoelectric focusing using the protocol of Bronson and Schachat.20 Some myocardium was placed directly in isoelectric focusing buffer and was not subjected to either protocol to examine whether these protocols affected the state of phosphorylation. To test for the effects of proteolysis on cardiac TnT isoform distribution, myocardium from normal and from failing left ventricles was left at room temperature in the absence of protease inhibitors, and samples were removed from the myocardium after 0.5, 1, 2, and 4 hours and were placed in sample buffer. SDS-PAGE was performed using the method of Laemmli,22 with the following modifications: 30% acrylamide and 1.1% bis-acrylamide stock solutions were used in either 8% or 7.5% running gels and a 3.3% stacking gel, as described previously.11,12 Protein concentration was determined with a Bradford reagent (Pierce Chemical Co., Rockford, Ill.), using bovine serum albumin as a standard. Comparable protein amounts were loaded in each gel lane. Silver staining of the gels was performed as described by Schachat et al.23 Western blots were performed as described previously,12 using MAb 13-11 or JLT-12 as a primary antibody and an alkaline phosphatase–labeled secondary antibody. Nitro blue tetrazolium and 5-bromo-4-chloro-3-indolyl-phosphate (Promega Corp., Madison, Wis.) were used as the color reagents. The Western blots were scanned using an LKB laser densitometric scanner (Pharmacia LKB, Piscataway, N.J.), and the area under the TnT densitometric waveform was integrated. The left ventricular content of TnT$_2$ (see “Results”) was described as a percentage of the total TnT integral.
Alkaline Phosphatase Treatment

Myofibrillar preparations obtained from normal and failing left ventricular myocardium were dephosphorylated following the method of Holroyde et al. These preparations were compared with myofibrillar preparations exposed to the reaction buffer in the absence of alkaline phosphatase.

Myofibrillar ATPase Activity

The ATPase activities were measured previously by Pagani et al in preparations from four of the hearts in the normal group and six of the hearts in the heart failure group. The maximal activities in those hearts, obtained using a pCa of 5, were compared.

Statistics

The percentages of total left ventricular TnT composed of TnT2 in the two groups of patients were compared by one-way analysis of variance and Kruskal-Wallis analysis. Linear regression analysis was used to test the relation between the percentage of TnT2 and the myofibrillar ATPase activity of individual hearts. A value of $p<0.05$ was considered significant.

Results

Heart Failure and Organ Donor Population

The control group ($n=6$) contained five men and one woman. Their ages ranged from 23 to 58 years (34±13 [mean±1 SD] years). The period of time that they were maintained on a life support system ranged from 12 to 72 hours. The severe heart failure group ($n=10$) contained nine males and one female with ages ranging from 16 to 54 years (38±16 years). The diseases that caused the clinical syndrome of heart failure were coronary artery disease (two patients), idiopathic dilated cardiomyopathy (six patients), idiopathic hypertrophic subaortic stenosis (one patient), and ventricular septal defect (one patient). The ages of the patients in the heart failure and in the normal group did not differ significantly.

Heart Failure and Organ Donor Left Ventricular Myocardium

One-dimensional SDS-PAGE of myofibrillar proteins from normal and failing myocardium demonstrated several proteins with electrophoretic mobilities that fell between those of actin and tropomyosin (Figure 1). In Western blots of normal heart myofibrillar proteins, MAb 13-11 identified one of these proteins as a cardiac TnT isoform (Figure 2). In Western blots of myofibrillar proteins from patients with severe heart failure, MAb 13-11 recognized its determinants in two polypeptides (Figure 2). One polypeptide had a mobility similar to that of the cardiac TnT isoform identified in the normal human heart; the second had a faster electrophoretic mobility. The two isoforms were termed TnT1 and TnT2, with TnT1 having the slowest mobility. Densitometric scans of Western blots of myofibrillar proteins from normal adult hearts did demonstrate a very small amount of a polypeptide with an electrophoretic mobility similar to that of TnT2 (Figure 3). The electrophoretic mobilities of these polypeptides were similar to those of the rabbit cardiac TnT isoforms (Figure 2).

Western blots of the normal and failing heart myofibrillar proteins were also probed with MAb JLT-12, which was raised against a rabbit fast skeletal muscle TnT and which recognizes its determinant in rabbit, rat, and chicken cardiac TnT. MAb JLT-12 recognized its determinant in the two polypeptides containing the epitope recognized by MAb 13-11 (Figure 2, right panel). MAb JLT-12 recognized its determinant in no other myofibrillar proteins from either failing or control adult hearts.

Two-dimensional gel electrophoresis was used to characterize more thoroughly the TnT isoforms recognized by MAb 13-11 and MAb JLT-12 in the normal and the failing heart. Isoelectric focusing gels separated TnT1 into two spots with identical electrophoretic mobilities (Figure 3). Two spots of TnT2 were also readily identified in failing myocardium (Figure 3). Myocardium placed directly into isoelectric focusing buffer demonstrated the same patterns...
of spots as myocardium that had been subjected to the protocol of Bronson and Schachat to obtain myofibrillar preparations.

Alkaline phosphatase treatment altered the relative density of the two major spots of TnT₁ and TnT₂. The more acidic spots of the two pairs of spots of TnT₁ and TnT₂ were markedly decreased in intensity, whereas the more basic spots were comparably increased (Figure 3). In both preparations, a minor isoform with an electrophoretic mobility similar to that of TnT₁ was unaffected by dephosphorylation (Figure 3).

**Figure 2.** Left panel: Western blot of one-dimensional 7.5% acrylamide gel loaded with myocardial preparations from normal human left ventricle (lane a), failing human left ventricle (lane b), and 2-day postnatal rabbit ventricle (lane c). Monoclonal antibody 13-11, which was used as the primary antibody, was raised against a rabbit cardiac troponin T isoform, troponin T₂. In lane c, the rabbit troponin T isoforms have been numbered (see Reference 11). Middle panel: Western blot of one-dimensional 7.5% acrylamide gel loaded with preparations from failing human left ventricle (lane a), fetal human ventricular myocardium (lane b), fetal human thigh muscle (lane c), adult human rectus abdominis (lane d), and rabbit fast skeletal muscle (lane e). The proteins were probed with monoclonal antibody 13-11. Right panel: Western blot of the same proteins loaded in the same sequence on the one-dimensional gel described in the middle panel. The same amounts of proteins were loaded on the corresponding lanes of the two gels. The proteins were probed with JLT-12, a monoclonal antibody raised against a rabbit fast skeletal muscle troponin T isoform.

**Figure 3.** The troponin T isoforms of a normal left ventricle (upper panels A–E) are contrasted with those of a failing left ventricle (lower panels A–E). 1, Troponin T₁, the slow isoform of troponin T; 2, troponin T₂, the fast isoform of troponin T. In panel A, troponin T₁ and troponin T₂ are labeled in Western blots of two lanes of an 8% acrylamide gel. In panel B, the densitometric scans of these Western blots are compared, and the troponin T isoforms are labeled. A very small amount of troponin T₂ is detected in the normal ventricle (top of panel B). In panel C, Western blots of two-dimensional gels of the myocardial preparations used in panels A and B are compared. In panel D, Western blots are illustrated of preparations of the proteins used in panels A and B that have been subjected to a dephosphorylation protocol. One of the minor isoforms of troponin T₁ is not affected by dephosphorylation, whereas the two major spots of troponin T₁ and troponin T₂ are collapsed into single spots. In panel E, Western blots of overloaded two-dimensional gels of the preparations used in panel C are compared. In panel E, minor isoforms of troponin T (e.g., see arrows) are detected that were not seen in the silver-stained gels. Monoclonal antibody 13-11 was used as the primary antibody.
Immunoblots of gels, overloaded with protein, suggested that TnT1 had undergone additional post-translational modifications in both normal and failing myocardium (Figure 3). In the normal heart, two small spots of TnT2 can be barely detected below TnT1, whereas in the failing heart, two or more spots of TnT2 are readily identified. The isoelectric points of some of these TnT2 spots are similar to the isoelectric points of some TnT1 spots. In these heavily loaded transfers, MAb 13-11 recognized its epitope in multiple minor TnT isoforms that had electrophoretic mobilities and isoelectric points that differed from those of TnT1 and TnT2 (Figure 3). These minor isoforms were not identified in the silver-stained gels. In the immunoblots of the heavily loaded gels, one minor isofrom (see arrows, Figure 3) is present in a relatively greater amount in the normal compared with failing left ventricle.

To assess how proteolysis may have contributed to the appearance or the relative amount of TnT2 in failing hearts, one-dimensional SDS-PAGE and Western blots were performed on samples obtained from normal and failing adult myocardium that had been left at room temperature in the absence of protease inhibitors for up to 4 hours (results not shown). Western blots of normal myocardium left at room temperature for this period of time did not demonstrate an increase in the very small amount of TnT2 that was found in frozen myocardium placed directly into sample buffer. However, other proteins with electrophoretic mobilities faster than TnT1 and TnT2 appeared in amounts that increased the longer the myocardium was left at room temperature. Western blots of myocardium from failing heart left at room temperature for up to 4 hours demonstrated no increase in the relative amount of TnT2 as compared with TnT1. Proteins with faster electrophoretic mobilities, similar to those observed in normal myocardium left at room temperature, appeared with increasing incubations at room temperature. These proteolytic products were not identified in myofibrillar preparations processed in the presence of protease inhibitors (after the protocol of Anderson et al11 or Bronson and Schachat20). These results support our conclusion that TnT2 is not a proteolytic fragment of TnT1.

Analysis of the densitometric scans of one-dimensional Western blots demonstrates that the preparations from the heart failure group had a significantly greater percentage of total TnT composed of TnT2 than did those from the normal adult hearts (12.0±4.9% versus 4.4±2.6% [mean±1 SD], p<0.004). Only one patient in the heart failure group, a 16-year-old patient with cardiomyopathy (the youngest in both groups), had a percentage of TnT2 that fell within the distribution of the normal group. A comparison of age to TnT2 percentage of total TnT did not demonstrate a significant correlation. A comparison of the endocardial TnT2 percentage to that of the epicardium, which was possible in some hearts because of the transmural orientation and shape of the preparation, demonstrated no difference in the transmural distribution of the TnT1 and TnT2 isoforms (results not shown).

Myofibrillar ATPase activities of six ventricles in the heart failure group were compared with those of four adult hearts in the control group. Pagani et al4 had measured these ATPase activities previously. A comparison of the myofibrillar ATPase activities of the patients and the organ donors, whose TnT isoform distribution was examined in this study, demonstrates that the ATPase activities of the normal hearts were significantly greater (p<0.018). The percentage of TnT2 also differed significantly between these two groups of hearts (p<0.001), with the failing hearts having a larger amount of TnT2.

When the myofibrillar ATPase activities of individual hearts were compared with their percentage of total TnT composed of TnT2, a significant and inverse relation was found between ATPase activity and the percentage of TnT2 (p<0.02, r=0.7) (Figure 4).

**Fetal Myocardium**

One-dimensional SDS-PAGE and Western blots of myofibrillar proteins prepared from fetal myocardium and probed with MAb 13-11 and MAb JTL-12 are illustrated in Figures 1 and 2. MAb 13-11 recognized its determinant in four cardiac proteins, one of which was a very minor species. The two proteins with the fastest electrophoretic mobilities were found to have the same electrophoretic mobilities as TnT1 and TnT2 of the adult heart; the two other fetal cardiac proteins were not identified in the adult heart. The relative amount of TnT2 to TnT1 was greater in the fetal heart than in the failing adult heart.

**Fetal and Adult Skeletal Muscle**

One-dimensional SDS-PAGE and Western blots of myofibrillar proteins prepared from fetal thigh muscle and adult skeletal muscle and probed with
MAb 13-11 and MAb JLT-12 are illustrated in Figures 1 and 2.

MAb 13-11 did not recognize its determinant in adult skeletal muscle (Figure 2). MAb 13-11 did recognize its determinant in two proteins in fetal skeletal muscle (Figure 2). These proteins had the same electrophoretic mobilities as two of the fetal cardiac isoforms, one having the electrophoretic mobility of TnT1.

MAb JLT-12 faintly recognized in fetal skeletal muscle the same two proteins that MAb 13-11 recognized (Figure 2). However, in contrast to MAb 13-11, MAb JLT-12 recognized in adult rectus abdominis four proteins and in fetal thigh muscle seven proteins that had electrophoretic mobilities similar to those of rabbit fast skeletal muscle TnT isoforms (Figure 2). Some of the human fetal and adult skeletal muscle TnT isoforms shared the same electrophoretic mobilities. Myofibrillar protein preparations from gluteus maximus were found not to have any proteins that contained the determinant of MAb JLT-12 (nor that of MAb 13-11), suggesting that only slow skeletal TnT was present in this muscle (results not shown).

Discussion

Two or more cardiac TnT isoforms9–13 have been described in several species and found to undergo maturationally and regionally regulated expression. The effects of disease and development on the expression of this thin-filament regulatory protein and its isoforms have not been examined previously in humans. The results of this study demonstrate that, in humans, disease and development alter myocardial TnT expression and that human myocardium has the potential to express multiple TnT isoforms.

These novel findings raise several issues: 1) Do these isoforms arise from several genes or one gene whose product has undergone transcriptional, translational, or posttranslational processing? 2) Does a functional relation exist between isoform expression and ATPase activity? 3) Are the disease-associated changes in TnT expression an underlying contributor to myofibrillar mechanical dysfunction and heart failure, or do they represent a response to the disease process?

We hypothesize that the molecular basis of the varied expression of cardiac TnT in normal and in failing human left ventricular myocardium is alternative splicing of a primary transcript from a single gene. Isolation and sequencing of genomic and cDNA will help resolve this issue. Alternative splicing has been found or suggested to be the basis of TnT isoform expression in chicken9 and rat20 heart and in rabbit,26 rat,27 and avian28 skeletal muscle. Most of this processing of the transcript involves the N-terminal region of the protein, resulting, for example, in the possible expression of 64 TnT isoforms in rat fast skeletal muscle. Indeed, the presence in avian fast skeletal muscle of multiple TnT isoforms has been supported by Western blot analysis.29,30

We propose that the major TnT isoforms expressed in the failing human left ventricle are the products of alternative RNA splicing rather than posttranslational modifications of a single protein or the result of proteolysis. Our finding isoforms of different electrophoretic mobilities but similar isoelectric points is consistent with the interpretation that the two major isoforms in the diseased heart are the products of different mRNA; posttranslational modifications of rabbit fast skeletal muscle TnT result in proteins with different isoelectric points but similar electrophoretic mobilities.26,31 This interpretation is supported by the dephosphorylation experiments. The two largest spots of TnT1 and those of TnT2 were converted into two single spots by the phosphatase treatment. Whether the family of TnT isoforms recognized by MAb 13-11 in the overloaded gels represents various products of alternative splicing and posttranslational modification will have to be resolved by mRNA analysis.

The discrete nature of the spots on the immunoblots and narrow range of molecular weights of the isoforms speaks against proteolysis as the basis of this diversity in the TnT isoforms. Our proteolysis experimental data further suggest that TnT2 is not a proteolytic product, given the absence of an increase in TnT2 in myocardium allowed to undergo proteolysis.

The possibility that the isoform TnT2, which is increased in expression in the failing human heart, may be encoded by skeletal muscle gene(s) should be considered. Studies by others have shown that skeletal muscle contractile protein genes are expressed transiently in the stressed adult heart32,33 and in the developing heart.32–34 MAb 13-11, which was raised against a rabbit cardiac TnT isoform, did not recognize this determinant in any of the myofibrillar proteins of adult human skeletal muscle. It did recognize in human fetal skeletal muscle two protein bands that had the same electrophoretic mobilities as two of the fetal cardiac TnT isoforms, one being the predominant isoform of the adult heart. The presence of these proteins in fetal skeletal muscle and their absence in adult skeletal muscle are consistent with the previous observations by Ordahl34 that cardiac TnT is expressed transiently in chicken embryonic skeletal muscle. MAb JLT-12, which was raised against a rabbit fast skeletal muscle TnT isoform, recognized in adult and fetal skeletal muscle multiple TnT isoforms that had electrophoretic mobilities similar to the TnT isoforms of rabbit fast skeletal muscle. MAb 13-11 or JLT-12 did not recognize proteins with these electrophoretic mobilities in the fetal heart, the adult normal heart, or the adult failing heart. These findings suggest that the determinant that MAb 13-11 recognizes is cardiac specific and that the expression of cardiac TnT isoforms is altered by development and heart failure.

Hypertrophy in the adult ventricle has been found to be associated with the expression of genes encoded in embryonic and fetal stages of development.32,35,36 Western blots indicate that TnT1 and
TnT isoforms are common isoforms in the fetal heart at 14–15 weeks of gestation. In comparing the isoforms of TnT found in the fetal heart with those of the normal adult heart, it is apparent that TnT1 is constitutively expressed and that the expression of the other three fetal TnT isoforms is downregulated with development. In contrast, an upregulation of TnT1 expression occurs with heart failure. These findings suggest that the increase in the relative amount of TnT1 in the failing human heart may be a recapitulation of ontogenic changes in TnT expression. Analyses of chicken and rat cardiac cDNA demonstrate that in these species a developmental decrease in TnT molecular size occurs as a result of alternative RNA splicing and the exclusion of an exon in the adult isoform. In the human, it would appear that decreased expression of a smaller and a larger isoform occurs with development.

TnT isoforms have been shown to affect myofibrillar ATPase activity in vitro, as is suggested by the correlation between these variables found in this study. Future experiments, using, for example, purified human cardiac TnT isoforms in reconstituted systems, will be required to test critically whether the fall in ATPase activity with heart failure is the result of a change in the proportion of the TnT isoforms. The possible advantage that the isoform TnT1 conveys to the function of the failing heart through a decrease in ATPase activity remains to be elucidated.

Since the etiologies of heart failure in the patients examined in this study were diverse, we suggest that the changes in human myocardial TnT isoform expression are an adaptive response to heart failure and a partial recapitulation of the fetal expression of TnT isoforms.

Acknowledgments

The authors thank Dr. Frederick Schoen, Division of Cardiac Pathology; Dr. Verdi Disesa and Dr. Lawrence Cohen, Division of Cardiothoracic Surgery; and Dr. Rosemarie Maddi, Dr. John Fox, and Mrs. Santawana Muckherjee, Department of Anesthesia, Brigham and Women’s Hospital; and the New England Organ Bank, Boston, Mass., for their help in procuring the tissue used in this study.

References


KEY WORDS • myofibrillar ATPase • heart failure • left ventricle • contractile proteins • monoclonal antibody • adult • fetus • skeletal muscle
Troponin T isoform expression in humans. A comparison among normal and failing adult heart, fetal heart, and adult and fetal skeletal muscle.

P A Anderson, N N Malouf, A E Oakeley, E D Pagani and P D Allen

Circ Res. 1991;69:1226-1233
doi: 10.1161/01.RES.69.5.1226

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1991 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/69/5/1226

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org//subscriptions/