Nucleotide Profiles in Normal Minipig Arterial Tissue

John M. Pap, Donald F. Hammer, Donald L. Fry, Robert E. Kelley, and Ruth A. Altschuld

The purpose of this study was to characterize the nucleotide profiles of a normal porcine elastic and muscular artery. Tissue samples (50 to 150 mg) were excised from the descending thoracic aorta and from the femoral artery of 14 normocholesterolemic, anesthetized minipigs. In three animals, transmural myocardial samples were also obtained. Nucleotide and nucleoside concentrations were analyzed by using a recently developed ion-pairing, reverse-phase, high-performance liquid chromatographic method. The arterial samples contained relatively low concentrations of adenosine triphosphate, approximately one-eighth that of the myocardial counterpart. Relative to the femoral artery, the aortic samples had significantly lower adenylate energy charges and higher levels of adenosine diphosphate, adenosine monophosphate, adenosine, and inosine. These baseline aortic levels did not change after in vitro exposure to 95% oxygen. The different energy states observed in the two arteries may reflect functional or metabolic differences in their medial smooth muscle cell populations. Alternatively, the lower energy state observed in the thicker walled aorta may be a manifestation of inadequate medial oxygen delivery that persists despite oxygen enrichment in vitro. We conclude that arterial energy states exhibit regional variation. This information will serve as a point of departure for the investigation of the role energy states may play in the atherosclerotic process. (Arteriosclerosis 10:745-750, September/October 1990)

Energy-requiring processes in the arterial wall, as in all tissues, require adequate levels of high-energy compounds, generally adenosine triphosphate (ATP). A significant proportion of the required high energy compounds is generated by the oxidative catabolism of various substrates. Since oxygen is required for such reactions, the ability to maintain adequate levels of high-energy compounds would appear to depend on oxygen delivery to the metabolizing arterial cells, of which the medial smooth muscle cells are quantitatively most important. Studies done in rabbits have suggested that oxygen delivery in many arteries is insufficient to maintain an aerobic environment in the mid-medial regions. It is plausible that such tissue hypoxia may be associated with alterations of high-energy phosphates and their metabolites. The purpose of this study was to characterize the nucleotide and nucleoside profiles of a normal porcine muscular artery (femoral artery) and elastic artery (descending thoracic aorta) to assess whether such profiles suggest the presence of medial hypoxia and to assess whether such profiles vary in these two types of arteries.

Methods

Experimental Animals

Fourteen 2- to 3-year-old normocholesterolemic minipigs (Sinclair Research Farm, Columbia, MO) with an average weight of 75 kg were used in this study. All procedures were approved by the Institutional Laboratory Animal Care and Use Committee at the Ohio State University. The animals were anesthetized with ketamine (40 mg/kg) plus acepromazine (0.04 ml/kg), and sodium pentobarbital (65 mg/ml) was infused intravenously as needed to maintain an adequate level of anesthesia. The animals were intubated and mechanically ventilated (Harvard Apparatus, Millis, MA) with supplemental oxygen. Arterial blood gases were monitored throughout the vessel harvest procedure so that the ventilator parameters could be adjusted to maintain adequate oxygenation. Multiple laboratory parameters were assessed at the beginning and end of the harvest procedure to assess anesthetic and procedural-related alterations of electrolyte milieu and acid/base status.

Vessel Harvest

With the animal fully anesthetized and well oxygenated, a cutdown was done in the region of the right or left inguinal region, and approximately 3 cm of femoral artery was exposed. A left lateral thoracotomy was done to expose the heart, great vessels, and the thoracic aorta to the level of the diaphragm. Tissue samples weighing approximately 50 to 150 mg were then excised from the femoral artery and from the descending thoracic aorta just distal to the origin of the left subclavian.
the vessel samples were removed within 10 minutes of one another, and the sequence of vessel removal was alternated from study to study. In some animals, a transmural myocardial sample was excised from the heart after both vessel segments were removed. The tissue samples were frozen by immersion in liquid nitrogen within 10 seconds of their removal, and they were stored in liquid nitrogen until processing.

**In Vitro Studies**

After the vessel samples to be analyzed were excised, the descending thoracic aorta from the ductus scar to the diaphragm was excised, was dissected free of adventitial tissue, and was used for in vitro protein transport studies (to be reported at a later date). The in vitro apparatus has been described, but it was modified in these recent studies to maintain a 37°C environment and to deliver humidified 95% oxygen/5% carbon dioxide. During the incubation period, both the luminal and abluminal vessel surfaces were exposed to sterile porcine serum. The morphologic appearance of the aortic tissue in this in vitro system was assessed by scanning and transmission electron microscopy. The stability of the nucleotide profiles after 3 hours in the in vitro state was assessed in five animals.

**Tissue Analyses**

Nucleotides and nucleosides were analyzed with a recently developed chromatographic method that has been described previously. In brief, the tissue samples were pulverized while still frozen, and the nucleotides were extracted with iced 0.6 N perchloric acid. The acid-solubilized nucleotides were quickly separated from the precipitate, and the supernatant was then neutralized and analyzed using a Hewlett-Packard Model 1090 high-performance liquid chromatography (HPLC) system with a reverse-phase method modified to include a pH gradient for nucleotide analysis as described previously.

**Statistical Analysis**

All of the data obtained are presented as means±SEM and were analyzed using the two-tailed Student's t test for paired samples. The p values were calculated, and significance was set at p<0.05.

**Table 1. Aortic Donor Pig Characteristics during Vessel Harvest**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>At harvest</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dl)</td>
<td>96±5</td>
<td>134±12</td>
<td>0.020</td>
</tr>
<tr>
<td>Lactate (mm/l)</td>
<td>2.9±0.4</td>
<td>3.7±0.5</td>
<td>0.000</td>
</tr>
<tr>
<td>pH</td>
<td>7.42±0.01</td>
<td>7.39±0.02</td>
<td>0.080</td>
</tr>
<tr>
<td>pCO₂ (mm Hg)</td>
<td>40±1</td>
<td>43±2</td>
<td>0.150</td>
</tr>
<tr>
<td>pO₂ (mm Hg)</td>
<td>149±4</td>
<td>103±4</td>
<td>0.001</td>
</tr>
<tr>
<td>HCO₃⁻ (meq/l)</td>
<td>27±1</td>
<td>28±1</td>
<td>0.160</td>
</tr>
</tbody>
</table>

**Pilot Studies**

**Effect of Temporal Delays between Vessel Removal and Immersion in Liquid Nitrogen**

To assess whether minor differences in the time interval from vessel excision to flash freezing might affect the nucleotide profiles, the following studies were done in two animals. An aortic sample was removed and immediately frozen to serve as a control. Other portions of this same sample were held in the air for 10, 30, or 90 seconds, before immersion in liquid nitrogen. The nucleotide profiles of these portions were performed as described previously.

**Effect of Variable Incubation Oxygen Tensions on Nucleotide Profiles**

To assess whether nucleotide profiles would vary with different oxygen tensions during incubation, the following studies were performed in two animals. A portion of the descending thoracic aorta was excised and divided into three equal samples. Each sample was placed in an incubation chamber containing serum that had been previously equilibrated with three different gas mixtures: 95% O₂/5% CO₂, 95% air/5% CO₂, and 95% N₂/5% CO₂. The aortic samples were incubated under their respective gases for 3 hours. At the end of this period, samples were removed from the incubation solutions, were frozen immediately in liquid nitrogen, and were subsequently processed for nucleotide analysis as described previously.

It should be noted that the incubation conditions in this pilot study differed from those present in the in vitro studies described above in the following important characteristics: the absence of physiologic strain and the absence of transmural pressure.

**Results**

**Donor Pig Characteristics during Vessel Harvest**

The metabolic characteristics of the minipigs during the vessel harvest procedure are shown in Table 1. A physiologic pH was maintained throughout the anesthesia and surgical procedure. A small, but significant, decrease in pO₂ associated with a small, but significant, increase in arterial lactate suggested a reduction in cardiac output associated temporally with the thoracotomy. The increase in glucose that occurred during the harvest procedure was consistent with a hyperadrenergic state. The heart was seen to be contracting vigorously at the times that vessel samples were taken for nucleotide analyses. Spasm of the femoral arteries was observed.
consistently during the course of dissection and excision of these vessels. It was also noted that the relaxed dimension of the excised aorta was approximately 60% that of the in vivo counterpart. Whether this dimensional change reflected active contraction of medial smooth muscle cells or simply recoil of elastic tissue is speculative.

### Nucleotide Profiles

In Table 2, the concentrations of ATP, ADP, and AMP are shown for the myocardial tissue samples (n=3) and for the paired vessel samples (n=14). The concentration of ATP in the arterial samples was roughly one-eighth that of the myocardial tissue. Whether this dimensional difference in nucleotide and nucleosome pool. The corresponding percentage for myocardial tissue was 4%.

In contrast, the relative concentration of guanosine triphosphate (GTP) was greater in the aorta and femoral artery than it was in the heart. In the arterial samples, GTP represented approximately 11% of the total measured nucleotide and nucleoside pool. The corresponding percentage for myocardial tissue was 4%. There were notable differences between the aortic and femoral arterial nucleotide profiles (Table 2). Relative to the femoral artery, the descending thoracic aorta had lower adenylic energy charges and a trend toward lower ATP levels. Moreover, the aorta had significantly greater concentrations of the less energetic compounds including AMP, adenosine, and inosine and trends for higher levels of ADP and inosine monophosphate (IMP).

### Protein/DNA Ratios

The mg protein/mg DNA ratios in the femoral artery and aorta were 133±26 and 124±14, respectively (13 determinations from three vessel pairs, p=0.3). This finding suggests that either tissue protein or DNA may be used as a normalizing factor with equal validity when comparing nucleotide concentrations in the two types of arteries. We chose the tissue protein as the normalizing factor for the data in Tables 2 through 5. Expression of the data as nmol/mg DNA (n=3) did not alter the relative magnitudes noted in Table 2.

### In Vitro Behavior of Excised Aorta

The pO2 and glucose level of the incubation serum during the in vitro incubation was 300±7 mm Hg and 145±6 mg/dl, respectively. In five animals, the nucleotide profiles for samples taken at the time of vessel harvest and immediately following the 3-hour incubation period did not change (Table 3). Scanning and transmission electron microscopy of a small aortic sample at baseline and after incubation was performed in two of five in vitro studies. These studies demonstrated that the cellular membrane, mitochondria, and nuclear constituents were not altered by in vitro incubation in our current in vitro system. Specifically, there was no evidence of endothelial disruption, vacuolization, mitochondrial cristolysis, or membrane disruption.

### Pilot Studies

**Effect of Temporal Delay before Freezing**

In Table 4, the effect of progressively increased intervals between excision of the aortic sample and flash freezing on nucleotide profiles is presented. A surprisingly rapid reduction of ATP associated with an increase in inosine is apparent with a delay of only 10 seconds before freezing. Many of the alterations in nucleotide profiles are progressive over the total interval studied.

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**Table 2. Summary of Nucleotide and Nucleoside Concentrations In Different Tissues**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Myocardium (n=3)</th>
<th>Aorta (n=14)</th>
<th>Femoral artery (n=14)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inosine</td>
<td>0.57±0.11</td>
<td>1.48±0.28†</td>
<td>0.40±0.04</td>
<td>0.001</td>
</tr>
<tr>
<td>Adenosine</td>
<td>0.13±0.06</td>
<td>0.36±0.05</td>
<td>0.05±0.01</td>
<td>0.000</td>
</tr>
<tr>
<td>IMP</td>
<td>0.29±0.08</td>
<td>0.31±0.03</td>
<td>0.21±0.03</td>
<td>0.070</td>
</tr>
<tr>
<td>AMP</td>
<td>0.99±0.02</td>
<td>1.32±0.14</td>
<td>0.64±0.09</td>
<td>0.003</td>
</tr>
<tr>
<td>ADP</td>
<td>9.41±0.26</td>
<td>3.70±0.26</td>
<td>3.05±0.39</td>
<td>0.052</td>
</tr>
<tr>
<td>GTP</td>
<td>1.78±0.06</td>
<td>1.18±0.07</td>
<td>1.31±0.16</td>
<td>0.444</td>
</tr>
<tr>
<td>ATP</td>
<td>39.05±0.93</td>
<td>4.55±0.31</td>
<td>0.00</td>
<td>0.070</td>
</tr>
<tr>
<td>Energy charge</td>
<td>0.67±0.02</td>
<td>0.68±0.02</td>
<td>0.78±0.01</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Values are nmol/mg protein. *p value reflects aorta vs. femoral artery, †Mean value excludes one outlying data point (>3 SDs from the mean).

**Table 3. Aortic Nucleotide Values and Energy Charges after a 3-hour In Vitro Exposure to 95% Oxygen**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline</th>
<th>T=3 hr</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inosine</td>
<td>1.30±0.53</td>
<td>0.98±0.20</td>
<td>0.150</td>
</tr>
<tr>
<td>Adenosine</td>
<td>0.38±0.25</td>
<td>0.36±0.13</td>
<td>0.845</td>
</tr>
<tr>
<td>IMP</td>
<td>0.30±0.18</td>
<td>0.16±0.08</td>
<td>0.225</td>
</tr>
<tr>
<td>AMP</td>
<td>1.31±0.74</td>
<td>1.28±0.85</td>
<td>0.963</td>
</tr>
<tr>
<td>ADP</td>
<td>3.09±0.64</td>
<td>4.13±0.93</td>
<td>0.091</td>
</tr>
<tr>
<td>GTP</td>
<td>1.12±0.15</td>
<td>1.30±0.54</td>
<td>0.474</td>
</tr>
<tr>
<td>ATP</td>
<td>4.67±1.59</td>
<td>5.56±0.89</td>
<td>0.318</td>
</tr>
<tr>
<td>Energy charge</td>
<td>0.68±0.03</td>
<td>0.70±0.03</td>
<td>0.412</td>
</tr>
</tbody>
</table>

Values are given as nmol/mg protein. n=5.

**Table 4. Summary of Nucleotide and Nucleoside Concentrations In Different Tissues**

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</tr>
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<td>1.18±0.07</td>
<td>1.31±0.16</td>
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</tr>
<tr>
<td>Energy charge</td>
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<td>0.000</td>
</tr>
</tbody>
</table>
variable oxygen tensions on nucleotide profiles are presented. It is apparent that the incubation conditions present in these pilot studies (absence of pressure, normal strain) yielded much lower ATP levels than those observed with the apparatus used in the other in vitro studies described in this paper. Nonetheless, the most prominent alterations of nucleotide profiles associated with reductions of oxygen tensions during incubation are reductions in ATP levels and energy charges. These changes were apparent as oxygen tensions were decreased from 603 to 159 mm Hg and increased further at very low oxygen tensions.

Effect of Variable Incubation Oxygen Tensions

In Table 5, the effects of aortic sample incubation at variable oxygen tensions on nucleotide profiles are presented. It is apparent that the incubation conditions present in these pilot studies (absence of pressure, normal strain) yielded much lower ATP levels than those observed with the apparatus used in the other in vitro studies described in this paper. Nonetheless, the most prominent alterations of nucleotide profiles associated with reductions of oxygen tensions during incubation are reductions in ATP levels and energy charges. These changes were apparent as oxygen tensions were decreased from 603 to 159 mm Hg and increased further at very low oxygen tensions.

Discussion

In this report, we have presented the first comprehensive description of the nucleotide profiles of normal vascular tissue. The HPLC method that we have used has been extensively validated against known standards, and it has been used previously for studies of freeze-clamped rat hearts and human endomyocardial biopsies. The analytical procedure was easily applied to vascular tissue without the need for methodologic modifications.

The measurement of nucleotides in any tissue is difficult because of the profound alterations that can be induced by methodologic variables during the procurement of samples. In this study, the time interval between excision of the sample and immersion in liquid nitrogen represents such a variable. Although this interval was kept to a minimum, the rapid changes we observed in the nucleotide profiles with relatively brief delays between excision and freezing (Table 4) reduce our confidence level that the measured nucleotide profiles are exact representations of the in vivo arterial energy states. Nonetheless, these data demonstrate important regional differences in arterial energy states that are unlikely to be related to methodologic variables. Moreover, we believe that the nucleotide profiles obtained in this study are the most accurate representations currently available of normal vascular tissue for the following reasons:

1) During the vessel harvest procedures, the pO2 and acid/base parameters of the arterial blood samples were maintained within physiologic ranges.

2) At the time of vessel harvest, the heart, which is one of the most metabolically active tissues in the body, was shown to have a nucleotide profile that compares closely with normal human12 and animal13 values (unpublished data). This suggests that the milieu to which the arterial tissue was exposed before excision was not affected adversely by our anesthetic technique.

3) The low ATP levels we detected in the aortas and femoral arteries are consistent with the limited data in the literature. For example, Takenaka and his colleagues14 have measured the ATP levels in isolated strips of canine coronary arteries and obtained an average ATP level of 1.2 nmol/mg protein. ATP levels (nmol/mg protein) in rabbit thoracic aorta have been reported to range from 1.6916 to 3.33 (based on mg protein=0.18 mg wet weight).1

4) Electron microscopic studies of the tissue at the time of harvest and after in vitro incubation demonstrated normal endothelial and smooth muscle cell morphology including intact cell membranes and mitochondria.

5) The spasm that occurred in the femoral arteries during excision is not likely to have produced alterations of their nucleotide profiles. Takenaka14 has noted that ATP remains stable in coronary arteries that are stimulated to contract as long as oxygen is present. Since the arterial oxygen tension at the time of harvest was within the physiologic range, it seems that ATP levels at least were not altered by the presence of spasm. Moreover, one might expect that, if present, spasm-associated nucleotide changes (i.e., depletion of ATP, increase in adenosine) would be of greater magnitude in the femoral artery than in the aorta. Such changes would tend to mask, rather than to augment, the differences we observed between the aorta and femoral arteries in this study.

The differences between the arterial and myocardial nucleotide profiles are not unexpected given the functional and morphologic differences that exist between these types of tissue. However, it is interesting to note that myocardial cells exhibit signs of reversible damage when ATP levels as low as those found in the aortas are induced by ischemia.15 Thus, vascular smooth muscle...
cells remain morphologically and functionally normal with ATP levels that are associated with myocardial cell death. This observation implies rather profound differences in the basal energy requirements of the two cell types. Low ATP levels also have been described for other tissues in which smooth muscle cells are the major cellular constituent. For example, Wuytack and Casteels\textsuperscript{18} found that the ATP, ADP, and AMP levels in guinea pig taenia coli were $6.7 \pm 0.6$, $2.2 \pm 0.3$, and $0.3 \pm 0.05$ nmol/mg protein, respectively (based on mg protein = $0.36$ mg fresh weight). The energy charge of this guinea pig tissue, however, was much higher than that noted for our arterial tissue (0.85 vs. 0.68 for aorta), and this implies important differences in their energy states. Nonetheless, it is likely that the low concentrations of ATP found in our arterial samples reflect a metabolic characteristic that is shared by smooth muscle cells in many types of tissue and that this characteristic is in marked contrast to that of the myocardial counterpart.

Another characteristic of arterial tissue that appears to represent a functional adaptation is the relative concentration of GTP. GTP is the high-energy compound that is used in preference to ATP for protein synthetic reactions on polyribosomes. Since the maintenance of arterial wall integrity requires the continual replacement of matrix proteins by smooth muscle cells, one might expect that a relatively large proportion of vascular smooth muscle nucleotide pools would be GTP.

Relative to the femoral artery, the lower aortic adenylate energy charge associated with higher concentrations of ADP, AMP, adenosine, and inosine suggest that the aorta exists at a lower energy state. The explanation for this observation remains speculative. The failure of aortic ATP level and energy charge to increase after the 3-hour, in vitro exposure to highly oxygenated serum suggests that the capability of aortic smooth muscle cells to increase energy stores may be limited. This would imply a basic metabolic difference relative to smooth muscle cells that exist in the femoral artery. Such a metabolic variable may represent a functional adaptation to the aortic environment. For example, given the extensive elastic components in the aortic media, aortic smooth muscle cells may never be required to develop active tension. In contrast, the medial smooth muscle cells of the femoral artery do develop active tension and shorten in response to a variety of neurohumoral and physical stimuli. It is plausible that the increased energy requirements imposed by this contractile activity are reflected by the relative increases in energy charge that are found in this artery. On the other hand, the lower aortic energy state may be a manifestation of lower aortic medial oxygen tensions. For example, in vivo microelectrode studies by Niinikoski and coworkers\textsuperscript{8} have demonstrated a medial pO$_2$ of $22 \pm 3$ mm Hg in the normal rabbit aortic arch. Jurrus and Weiss\textsuperscript{14} noted that medial oxygen tensions in normal and atherosclerotic rabbit aortas decreased from $55$ mm Hg to $0$ mm Hg as vessel thickness increased from $430$ to $720$ \textmu m. These studies suggest that the media is a formidable barrier to the diffusion of oxygen and that the impact of this barrier on medial oxygen tensions is directly related to vessel thickness. The rabbit arteries on which the above studies were performed were devoid of vasa vasorum, but it is possible that the sparse vasa vasorum in the thick-walled minipig aortas (average wall thickness $1400$ \textmu m) are not sufficient to increase medial oxygen tensions to levels found in the femoral artery (average wall thickness $240$ \textmu m). Since aerobic processes are felt to account for a significant proportion of high-energy phosphate production,\textsuperscript{1,2,3} such medial oxygen tension disparities in the two arteries might account for their different nucleotide profiles. If this hypothesis is correct, then the failure of the aorta to increase its energy level after in vitro incubation may simply reflect a persistent inability to deliver oxygen to the aortic media despite the presence of 95% oxygen. The pilot studies performed in two animals by use of crude incubation techniques provide preliminary support for such a hypothesis. The reductions in energy charge and ATP that occurred as incubation oxygen tensions decreased are consistent with the premise that reduced oxygen delivery to vascular smooth muscle cells is associated with a decline in their energy stores. Further studies with more sophisticated in vitro incubation systems will be required to explore further this possibility.

If the medial oxygen diffusion barrier cannot be overcome by oxygen enrichment in vitro and if the vasa vasorum are unable to augment oxygen delivery in vivo, then the media of some arterial vessels must function normally at very low oxygen tensions. This "physiologic" hypoxia could account for the consistent observation that the anerobic glycolytic pathway represents the major pathway of glucose metabolism and a major energy producer in arteries despite adequate luminal levels of pO$_2$.\textsuperscript{3} Since ATP production by the glycolytic pathway is only 6% that of Krebs cycle, the artery’s ability to maintain its energy state may be compromised by the apparent dependence on anerobic energy production. Moreover, dependence on the inefficient glycolytic pathway for energy production appears to vary in different vessels. For example, Zemplenyi\textsuperscript{17} has observed that glycolytic enzyme activities are greater in the aorta than in the coronary artery (a muscular artery that is morphologically similar to the femoral) and that Krebs cycle enzyme activities exhibit the opposite pattern of regional variation. Whether these patterns of enzyme activities reflect different medial oxygen tensions in the two types of arteries is speculative, but one would expect such patterns to yield a lower energy state and energy charge in the aorta than in its muscular artery counterpart. The aortic energy charge that we observed, $0.68 \pm 0.02$, was at a level predicted by Atkinson\textsuperscript{16,18} to augment the activity of "energy-repleting" reactions. Since glucose appears to be a major substrate for arterial energy production,\textsuperscript{3} augmentation of energy-repleting reactions in aortic tissue that has a low energy charge should require an increase in glucose consumption relative to muscular arteries, such as the femorals (and presumably the coronaries) that have higher energy charges. Such regional variation of glucose consumption has been reported by St. Clair and his colleagues.\textsuperscript{20} They observed that the glucose consumption of the aorta is almost twice that of the coronary artery. Thus, it appears that enzyme
activities, glucose consumption, medial oxygen tensions, and arterial energy states exhibit regional variations that occur in predictable patterns.

In conclusion, it appears that vascular smooth muscle cells operate at low energy states as manifested by their taw energy charges and, relative to cardiac muscle, extremely low levels of ATP. The two types of arteries analyzed in this study exhibited different nucleotide profiles. The pattern of the nucleotide profile differences suggests that the aorta exists at a much lower energy state than does the femoral artery. Whether these energy-state differences reflect functional adaptations or medial oxygen tension disparities is speculative, but these data will serve as a point of departure for the investigation of the role that energy states may play in the atherosclerotic process.

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References


Index Terms: nucleotides • arterial energy states • adenosine triphosphate
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