Comparison of human cardiac gene expression profiles in paired samples of right atrium and left ventricle collected in vivo

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Asp J, Synnergren J, Jonsson M, Dellgren G, Jeppsson A. Comparison of human cardiac gene expression profiles in paired samples of right atrium and left ventricle collected in vivo. Physiol Genomics 44: 89–98, 2012. First published November 15, 2011; doi:10.1152/physiolgenomics.00137.2011.—Studies of expressed genes in the human heart provide insight into both physiological and pathophysiological mechanisms. This is of importance for extended understanding of cardiac function as well as development of new therapeutic drugs. Heart tissue for gene expression studies is generally hard to obtain, particularly from the ventricles. Since different parts of the heart have different functions, expression profiles should likely differ between these parts. The aim of the study was therefore to compare the global gene expression in cardiac tissue from the more accessible auricula of the right atrium to expression in tissue from the left ventricle. Tissue samples were collected from five men undergoing aortic valve replacement or coronary artery bypass grafting. Global gene expression analysis identified 542 genes as differentially expressed between the samples extracted from these two locations, corresponding to ~2% of the genes covered by the microarray; 416 genes were identified as abundantly expressed in right atrium, and 126 genes were abundantly expressed in left ventricle. Further analysis of the differentially expressed genes according to available annotations, information from curated pathways and known protein interactions, showed that genes with higher expression in the ventricle were mainly associated with contractile work of the heart. Transcription in biopsies from the auricula of the right atrium on the other hand indicated a wider area of functions, including immunity and defense. In conclusion, our results suggest that biopsies from the auricula of the right atrium may be suitable for various genetic studies, but not studies directly related to muscle work.

This is particularly evident in the heart where the atrium and ventricle have different functions and workload. From technical aspects it is markedly easier to collect biopsies from the auricula of the right atrium than from the other three chambers of the heart. The right atrium is easily accessed after sternotomy, and it is regularly manipulated when cardiopulmonary bypass is established. In the majority of open heart surgeries, a venous cannula is inserted through the auricula of the right atrium. During this procedure it is uncomplicated and safe to excise a small piece of the auricula tissue for further analyses. For studies of heart function, however, the less accessible left ventricle is of explicit interest since this compartment executes most of the contractile work.

Although studies on gene expression profiles from different parts of the heart have been performed, it is not fully elucidated to what extent the left ventricle is represented by the auricula of the right atrium at the transcriptional level. Gene expression profiling of left atrial and left ventricular myocardium has been performed to date in failing hearts in conjunction with heart transplantation (6). In addition, global gene expression studies comparing ventricle to atria has also been performed in nonfailing donor hearts that were not used for transplantation due to coronary calcification (13) or organizational difficulties (15). In a study by Kääb and coworkers (13) that included both failing hearts and donor hearts, a divergent gene expression between atrium and ventricle was demonstrated for ~5% of all the genes. However, failing hearts are perhaps not representative material for studies of mechanisms that are present in the nonfailing heart, and there is also a risk that the explanting procedure may influence the transcriptional patterns. Moreover, gene expression in the left ventricle of nonfailing donor hearts has been compared with the right atrium obtained during surgery, but in this study atrial and ventricular tissue was not obtained from the same heart (2). A comparative study of gene expression in atria and ventricle, performed on human paired samples collected in vivo, has to our knowledge not previously been performed.

In the present study we performed global transcriptional profiling of paired, myocardial samples from the auricula of the right atrium and the left ventricle that were collected in vivo during heart surgery. The aim of this study was to test the hypothesis that the more easily accessible auricula of the right atrium may be a representative tissue for various transcriptional studies of the heart. To accomplish this, differentially expressed genes between the right atrium and the left ventricle were identified and grouped according to their functional properties. Furthermore, a gene set enrichment analysis (GSEA) was

**GENE EXPRESSION ANALYSES** from tissue samples have significant importance for the understanding of physiological and pathophysiological mechanisms. Expression of genes may be influenced by a number of factors including tissue type, sample location, sampling technique, and postsampling handling of the tissue and isolated RNA (16). Thus, a strict reproducible sampling procedure is necessary to make any firm conclusions about gene expression in comparative studies. Furthermore, gene expression may vary also in different parts of an individual organ due to regional differences in functional properties, cell and tissue distribution, and strain.

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performed to identify pathways that respond differently in these two tissues.

MATERIALS AND METHODS

Patients

Five men with mean age 71 yr (range 59–79) who underwent aortic valve replacement \( (n = 3) \) or coronary artery bypass grafting \( (n = 2) \) were included after informed written consent. None of the patients have had a myocardial infarction, had known bleeding disorder, or were treated with anticoagulants or platelet inhibition other than aspirin before the study. The study was approved by the Regional Research Ethics Committee.

Tissue Sampling

Biopsies, \( 5 \times 5 \times 5 \) mm large, collected from the right atrium were cut with scissors just prior to venous cannulation. Needle biopsies using a 14G needle (Tru-Cut; Cardinal Health, Dublin, OH) were collected from the left ventricle immediately after cardiopulmonary bypass was initiated. The time interval between the right atrial and left ventricular sampling was \(< 2 \) min. The samples were immediately placed in RNAlater solution (QIAGEN, Hilden, Germany) according to the manufacturer’s instructions. The right atrium and left ventricle are further referred to as RA and LV, respectively.

RNA Extraction and Microarray Experiments

Total RNA was extracted according to the protocol for purification of total RNA using the RNeasy Lipid Tissue Mini Kit (QIAGEN). Briefly, disruption and homogenization of the biopsies were performed in QIAzol lysis reagent with a TissueLyser and purification on an RNeasy Mini spin column. Removal of residual genomic DNA from the samples was done with DNaseI. Quantification of nucleic acids was performed on NanoDrop ND-1000 (NanoDrop, Wilmington, DE). The quality of the RNA and cDNA, labeled by in vitro transcription, was verified using an Agilent Bioanalyzer (Agilent Technologies, Santa Clara, CA) with RNA integrity number values ranging from 6.8 to 8.9. Microarray experiments were performed on paired samples of RA and LV biopsies (Fig. 1A). To measure the mRNA expression, fragmented cDNA was hybridized at 45°C for 16 h to whole transcript Gene ST 1.0 arrays (Affymetrix, Santa Clara, CA). The microarrays were scanned on a GeneChip Scanner 3000 7G (Affymetrix), and expression signals were extracted and normalized by means of the Expression Console (Affymetrix) applying the Robust Multichip Average normalization method. The microarray data follow the MIAME standard.

Raw expression data are available at ArrayExpress (http://www.ebi.ac.uk/microarray-as/ae/), accession number E-MEXP-3396.

Data Analysis

Hierarchical clustering was performed on the global gene expression data to evaluate the expression variability between patients and to assess that RA and LV biopsies grouped separately and showed distinct gene expression profiles. To group transcripts that show similar expression profiles across the 542 genes that were identified as differentially expressed between RA and LV biopsies. Column-wise, these genes show a distinct expression pattern that clearly separates between RA and LV biopsies. Looking row-wise at the figure one sees a remarkably low variability within each group, meaning that the variability between different patients within each of the 2 groups RA and LV is low. The color red represents high gene expression, and blue represents low gene expression.

Identification and clustering of differentially expressed genes. Transcripts that were significantly either more or less abundantly expressed in biopsies of RA compared with LV were identified using the Significant Analysis of Microarray data (SAM) algorithm (29). SAM controls for false discovery rate (FDR), and transcripts with an FDR \(< 0.05 \) and with FC \( \geq 2 \) were defined here as differentially expressed. The gene lists were filtered to include only those genes with known official gene symbols. To group transcripts that show similar expression profiles across the different samples, a two-way hierarchical clustering was performed using Euclidian distance and complete linkage.
Analysis of functional annotation of differentially expressed genes.

A functional annotation analysis of differentially expressed genes was conducted. Gene Ontology (GO) annotations including biological process (BP), molecular function (MF), and cellular component (CC) (1) were investigated, and the genes were grouped according to their GO annotation. Moreover, a gene set (C2.CP.KEGG) consisting of 186 curated pathways present in the KEGG database (http://www.genome.jp/kegg) was investigated for enrichment in our data using the GSEA. This approach directly scores predefined pathways or gene sets based on differential expression and specifically aims to identify pathways with subtle but coordinated expression changes (26).

Protein interaction network analysis. To investigate possible interactions between the gene products from more abundantly expressed genes in RA and LV samples, the STRING search tool (25, 30) was used for creation of protein interaction networks (PIN) as previously described (27). To increase the validity of our results, this search was restricted to include only information extracted from biological experiments and confident interaction databases (30). The created networks were explored and compared based on topological characteristics, and gene products (proteins) with high connectivity [hubs, defined as proteins with ≥5 interactions to other proteins (9)] were identified.

Validation by Quantitative real-time PCR

Expression of genes coding for identified hub proteins was validated with quantitative real-time PCR (qPCR). All instruments, software, and reagents for the cDNA synthesis and qPCR analysis were purchased from Applied Biosystems (Applied Biosystems, Foster City, CA). In brief, cDNA was prepared from total RNA using High-Capacity cDNA Reverse Transcription Kit. The following TaqMan Gene Expression Assays were used: ALOX15 Hs00609608_m1, C3 Hs01100879_m1, FOS Hs00170630_m1, HLA-DRA Hs00219575_m1, PLA2G2A Hs00179898_m1, PLA2G4A Hs00233352_m1, PTGS1 Hs00377726_m1, PTGS2 Hs00153133_m1, STAT6 Hs00598625_m1, TPM2 Hs00268540_m1, CREBBP Hs00231733_m1 was used as a reference gene (12). Samples were analyzed in duplicates using the instrument 7900HT. The relative comparative method was used to analyze the qPCR data (Sequence Detector User Bulletin 2, Applied Biosystems). Gene expression data are presented in relative units. Statistical significance was determined using a paired, two-sided Student’s t-test. Logarithmic values of the gene expression data were used for statistical calculations. A value of P < 0.05 was considered statistically significant.

RESULTS

Transcriptional Similarities Between Atrial and Ventricle Samples

The number of similarly expressed transcripts in RA and LV was calculated for each patient separately. On average 27,400 (ranging from 26,963 to 28,085) transcripts demonstrate similar expression levels in both RA and LV in each of the five patients. In total 18,317 transcripts are defined as similarly expressed in RA and LV in each of the 5 patients. In total 67% of the genes previously reported to be higher expressed in the LV samples. Table 1 shows the genes that were identified in LV. In addition to such genes associated with cytoplasmic structure, genes linked to energy metabolism, e.g., UQCRQ and NDUF9, which are part of the mitochondrial respiratory chain, were noted to be significantly higher expressed in the LV samples. Table 1 shows the genes that displayed the highest average FC in each group.

To investigate how our result corresponds to previously published data, our dataset was compared with data from a study of atrium and ventricle extracted from failing and non-failing hearts, obtained in conjunction with transplantation (13). For this comparison, the GSEA algorithm was applied. Despite the underlying differences in biopsy sampling between these two studies, the results showed a high overlap between our data and the results presented by Kääb and coworkers (13). In total 67% of the genes previously reported to be higher expressed in atrial samples were also identified to have an elevated expression in our RA biopsies, while 69% of the genes that previously have been identified as more abundantly expressed in ventricular tissue were also significantly higher expressed in the LV than in the RA samples.

Fig. 2. Similarly expressed transcripts in atrium and ventricle. Bars show the number of similarly expressed transcripts in RA and LV in each of the 5 patients. The rightmost bar show the number of transcripts that are similarly expressed in all 5 patients investigated.

Identification of Differentially Expressed Genes Between Atrial and Vascular Samples

Using the SAM algorithm and a significance threshold of FDR ≤0.05 in combination with an FC threshold ≥2, we identified 542 genes as significantly differentially expressed between the samples extracted from RA and LV biopsies (Supplemental Table A1). This represents ~2% of the genes covered by the Gene ST 1.0 array. Although biopsies from five patients were analyzed, the global gene expression was remarkably concordant with a low variation between the patients (Fig. 1, B and C). To analyze the variability between biopsies, both within and between the two groups, Pearson correlation was calculated between all pairwise samples with an average value of 0.97 (ranging from 0.95 to 0.99), and with the highest correlation between samples within the same group.

In total 416 genes were higher expressed in RA samples compared with LV samples, and 126 genes showed higher expression in LV samples compared with RA samples. In both groups previously known genes were found, e.g., the myosin light chain MYL4 with a reported atrial expression pattern was found in RA, while known ventricular genes like ventricular isoforms of myosin light chain, MYL2 and MYL3, were identified in LV. In addition to such genes associated with cytoplasmic structure, genes linked to energy metabolism, e.g., UQCRQ and NDUF9, which are part of the mitochondrial respiratory chain, were noted to be significantly higher expressed in the LV samples. Table 1 shows the genes that displayed the highest average FC in each group.

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1 The online version of this article contains supplemental material.
genes with higher expression in RA, a smaller fraction of these were connected to the energy producing mitochondria. For including the contractile apparatus, while 10% of the genes of 16% of the genes were connected to the cytoskeleton proportion of the genes coded for cytoplasmic proteins. A total highly represented (25%). In the CC category, a strikingly high structural molecule activity, but catalytic activity was also the MF category, a large group of genes (17%) was linked to mechanisms), metabolism, or transport in the BP category. In among the genes with higher expression in LV more than half of 50% of the genes were recognized. The genes were annotated as related to structure (including contractile mechanisms) and biosynthesis, “development,” “degradation and cell death,” “signal transduction” (BP), “transporter activity,” “catalytic activity,” “gene expression,” or “protein binding” (MF).

**Pathway Analysis**

To identify gene pathways with different expression patterns in RA and LV, the GSEA algorithm was used to compare expression of gene sets consisting of curated pathways in the KEGG pathway database to expression patterns in our experimental set-up. Following to a suggestion in the documentation.
for the algorithm, we applied a significance threshold of FDR $< 0.25$ to identify differentially expressed pathways. Using this threshold, we identified 29 pathways as induced in the RA samples compared with the LV samples (Table 2). Among these pathways, nine were related to metabolism and biosynthesis and eight were involved in immunity and defense. Interestingly, the transforming growth factor (TGF)-β signaling pathway, which is regarded as one of the central cell signaling systems, was identified. Furthermore, 16 pathways were identified as significantly induced in the LV samples compared with the RA samples. Half of these were related to metabolism and biosynthesis, and four additional pathways were specifically related to energy metabolism. Interestingly, the PPAR signaling pathway, with a role in lipid metabolism and blood glucose uptake, was also identified as induced in the LV biopsies.

### Protein Interaction Network Analysis

To identify putative functional units that consist of proteins coded by the differentially expressed genes, direct and indirect interactions between these proteins were derived using the STRING search tool, which creates PIN based on previously reported interactions between proteins. Two PIN, based on induced genes in RA and LV, respectively (Fig. 4), were derived and investigated for the presence of hub proteins, defined as proteins with at least five interactions to other proteins. Altogether, nine hub proteins (ALOX15, C3, FOS, HLA-DRA, PLA2G2A, PLA2G4A, PTGS1, PTGS2, and STAT6) were identified among genes that were higher expressed in RA (Fig. 4A), and one hub protein (TPM2) was identified among genes with higher expression in the LV samples. Interestingly, TPM2 created a tight network, a functional module, with four additional proteins (TNNT1, TNNI3, MYL2, and MYL3), which are all involved in the contractile machinery (Fig. 4B). To validate the results, expression of the genes coding for the identified hub proteins was analyzed with qPCR in all individual samples included in the study. The results confirmed the microarray results for all genes (Fig. 5).

### DISCUSSION

Studies of gene expression in the human heart provide insight into both physiological and pathophysiological mechanisms. This is of importance for extended understanding of cardiac function as well as development of new therapeutic drugs. Biopsies from different locations of the human heart, however, are not easily available unless the heart is explanted in conjunction with transplantation. During cardiac surgery, biopsies from the auricula of the RA are more accessible than other locations and could be obtained in an uncomplicated and safe way. However, the heart is composed of distinct functional types of cardiomyocytes in addition to other types of cells, and this should likely affect the transcriptional pattern. Therefore, the representativity of cardiac tissue obtained from the auricula of the RA was compared from a global gene expression perspective to the LV, which performs most of the cardiac contractile work.
Our results suggest that there is generally a high transcriptional similarity between LV and RA samples with >18,000 transcripts similarly expressed in RA and LV in all patients, although for some groups of genes we observed pronounced differences. In comparison, 542 genes were identified as significantly differentially expressed between the compared locations. A similar number of genes have previously been reported as differentially expressed between atria and ventricle by Kääb et al. (13), who studied biopsies achieved in conjunction with transplantation. In contrast, our study was restricted to include biopsies collected in vivo during cardiac surgery from patients without histories of myocardial infarction. We observed a high consistency in gene expression between the different patients and interestingly, a GSEA comparison showed that almost 70% of the genes reported by Kääb and coworkers were also regulated in our data. This demonstrates an interesting overlap between these two studies regarding the distinct gene expression patterns present in atrial and ventricular regions of the human heart.

Among the differentially expressed genes in the present study, higher expression of several ion channel coding genes was identified in both RA (e.g., KCNA5, KCNJ3, KCNJ1, and KCNJ1) and LV (KCNAB2 and KCNJ2). This is in concordance with a previous study where the expression of ion channels was compared between RA and right ventricle (7). Moreover, a loss-of-function mutation of the atrial gene KCNA5 has been linked to atrial fibrillation (22). Regarding structural genes coding for contractile proteins, the myosin heavy and light chains MYH6 and MYL3 were found to be more highly expressed in RA, while MYH7 and MYL2 showed higher expression in LV, as previously described (18, 19).

To explore functional properties and identify groups of genes coding for proteins with similar function or with participation in common regulatory pathways, differentially expressed genes were grouped according to available GO annotations, information from curated pathways and known protein interactions. The genes showing a higher expression in the RA samples correspond to a wide area of functions including association with immunity and cellular defense. In contrast, a majority of the differentially expressed genes that show highest expression in LV samples were related to cytoplasmic structure and cellular contraction, in addition to metabolism and energy production. These results were concordant using both the GO annotations and information derived from the KEGG database and are reflective of the function of LV.

From the STRING interaction analysis only one hub protein was identified among genes that showed highest expression in LV, creating a tight network with contractile proteins (Fig. 4B). The identified hub protein coding gene TPM2, which codes for β-tropomyosin, has been reported to be mutated in cardiac cap myopathy, where it produces a shortened mutant protein that incorporates into the sarcomeric structure (5). When analyzing the genes more abundantly expressed in RA, we identified nine hub proteins. Eight of these have previously been associated to various forms of cardiovascular diseases, pointing out the likely key functions of such proteins. Allelic variants have been identified in three of the genes. In the lipoxygenase coding gene ALOX15, two single nucleotide polymorphisms have been reported to increase the risk of coronary artery disease (CAD) in a Chinese Han population (32). Moreover, genetic variations of the PTGS1 and PTGS2 genes, coding for a key enzyme in prostaglandin biosynthesis, have been associated with stroke and have also been mentioned as possible risk factors for cardiovascular disease (20). Other proteins have been reported to have increased expression in cardiovascular

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**Table 2. Pathways induced in RA and LV samples**

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<thead>
<tr>
<th>KEGG Accession</th>
<th>Pathway Name</th>
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<tr>
<td>HSA04514</td>
<td>cell adhesion molecules</td>
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<tr>
<td>HSA04940</td>
<td>Type I diabetes mellitus</td>
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<td>ribosome</td>
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<td>HSA04612</td>
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<td>HSA00760</td>
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**Pathways in RA**

- complement and coagulation cascades
- cell adhesion molecules
- Type I diabetes mellitus
- ribosome
- antigen processing and presentation
- Toll-like receptor signaling pathway
- arachidonic acid metabolism
- nicotinate and nicotine metabolism
- hematopoietic cell lineage
- alkaloid biosynthesis II
- N glycans biosynthesis
- snare interactions in vesicular transport
- natural killer cell mediated cytotoxicity
- cytokine cytokine receptor interaction
- biosynthesis of steroids
- FC epsilon RI signaling pathway
- linoleic acid metabolism
- TGF-β signaling pathway
- pathogenic *Escherichia coli* infection EHEC
- alpha linoic acid metabolism
- axon guidance
- pathogenic *Escherichia coli* infection EPEC
- Long-term depression
- T cell receptor signaling pathway
- B cell receptor signaling pathway
- regulation of actin cytoskeleton
- chondroitin sulfate biosynthesis
- ether lipid metabolism
- apoptosis

**Pathways in LV**

- oxidative phosphorylation
- citrate cycle
- pyruvate metabolism
- alanine and aspartate metabolism
- propanoate metabolism
- PPAR signaling pathway
- benzoate degradation via CoA ligation
- androgen and estrogen metabolism
- pentose and glucuronate interconversions
- fatty acid metabolism
- porphyrin and chlorophyll metabolism
- aminoacyl tRNA biosynthesis
- valine leucine and isoleucine degradation
- glycosylation and gluconeogenesis
- proteasome
- starch and sucrose metabolism

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Fig. 4. Protein interaction networks of differentially expressed genes. Protein interaction networks (PIN) showing known interactions between gene products of the differentially expressed genes. Nine genes are identified as hub proteins in the PIN derived from induced genes in RA (A), and 1 hub protein is present among the induced genes in LV (B).
diseases. Amplified expression of the signal transducer STAT6 was identified in ischemic heart disease (24), and expression of the transcription factor and proto-oncogene FOS has been noted in cardiac tissue from patients with atrial septal defect and tetralogy of Fallot (11). In patients with severe CAD, serum concentrations of the complement component C3 were elevated. C3 concentration was also able to predict major complications such as death by cardiac events and acute myocardial infarction (28). Moreover, increased circulating level of phospholipase A2, coded by PLA2GA2, has been reported as a significant risk factor for CAD (17). It has also been suggested to function as a strong predictor of recurrent events in patients with acute coronary syndromes such as myocardial infarction (21). The Pla2g4a gene, coding for a cytosolic form of phospholipase A2, has so far been shown to be necessary for normal growth, as well as playing an important role for pathological stress-induced hypertrophy of the mouse heart (10). HLA-DRA, on the other hand, has to our knowledge not previously been identified in the context of cardiovascular disease. This gene, as well as the others, will be interesting targets for further studies of the human heart.

Among abundantly expressed genes in RA samples that are annotated as “developmental,” BMP10 was observed. In mouse, Bmp10 has been shown to play an essential role both during cardiac development (3) and during postnatal hypertrophic growth (4). This gene belongs to the TGF-β family of growth factors. Results from the pathway analysis also identified the TGF-β signaling pathway as upregulated in the atrial samples. Interestingly, a recent study showed that TGF-β inhibits adipogenesis and induces myogenesis simultaneously in a dose-dependent manner in progenitor cells obtained from the left atrium of adult rats (14). TGF-β signaling has also shown to be involved in atrial fibrosis in patients with atrial fibrillation (8), which further strengthens the notion of an important role for TGF-β signaling in the atrium. The basic helix-loop-helix transcription factor HEY2, on the other hand, with a known role in cardiac development, was found to be more highly expressed in LV. Recent studies in the mouse have shown that Hey2 expression is required in the ventricle, to repress atrial-specific genes such as Slc, Myl4, Myl7, and Tbx5 (31). These atrial genes were identified as being more highly expressed in the RA samples in the present study.

Although differences in expression patterns between RA and LV were observed for specific genes related to development, cardiac stem or progenitor cell markers such as C-KIT or OCT4, previously reported to be expressed in cardiac biopsies from the same group of patients (12, 23), were, in this study, not identified as differentially expressed between the studied locations. This suggests that these cells are present in both locations.

Limitations

Although much effort has been invested to design a robust experimental set-up and produce valuable atrial and ventricular gene expression data that has been rigorously analyzed, there are limitations in this study that should be pointed out. Due to difficulties in accessing paired biopsies from atrial and ventricular tissue, the number of patients in this study is limited to five. However, the low variation observed between these samples allows for statistical significance in our findings.

This study has evaluated differences and similarities between atrial and ventricular tissues. Even though there are several methods to aid in finding differentially expressed genes between two groups, assessing similarity in gene expression pattern between two groups is more challenging, due to lack of appropriate statistical methods. Here we have defined an arbitrary threshold of FC < 1.5 as similarly expressed, although
the biological relevance of this limit needs to be further evaluated. For the identification of differentially expressed genes between these two groups we used a statistical method and analyzed the functionality of genes that differ significantly. Despite identified differences, it was observed that many functions of the induced genes in RA and LV actually overlap, indicating that even though different sets of genes are induced their functionality partly overlap. When interpreting results regarding similarity one should keep in mind that even though we have used a strict criterion for similarity, for some groups of genes, e.g., transcription factors, it is known that even small differences in expression may have large biological effects.

Conclusions
In conclusion, our data show that genes corresponding to a wide area of functions are more highly expressed in biopsies derived from the auricula of the RA. Several pathways related to metabolism and biosynthesis as well as immunity and defense were identified as differentially expressed in this location. Thus, these biopsies may be useful for a variety of molecular studies of the heart, even though more research assessing the similarity between biopsies from different cardiac regions is needed. An important conclusion from this work is that for studies related to the contractile work of the myocardium, the auricula of the RA is not a representative tissue. For such studies, biopsies from the LV should be used. Together, the results presented in this study provide important insight into the transcriptional patterns in atrial and ventricular tissues and are of critical importance for future studies on different regions of the heart.

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DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

REFERENCES


