Data Article

Inflammatory and mitochondrial gene expression data in GPER-deficient cardiomyocytes from male and female mice

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We previously showed that cardiomyocyte-specific G protein-coupled estrogen receptor (GPER) gene deletion leads to sex-specific adverse effects on cardiac structure and function; alterations which may be due to distinct differences in mitochondrial and inflammatory processes between sexes. Here, we provide the results of Gene Set Enrichment Analysis (GSEA) based on the DNA microarray data from GPER-knockout versus GPER-intact (intact) cardiomyocytes. This article contains complete data on the mitochondrial and inflammatory response-related gene expression changes that were significant in GPER knockout versus intact cardiomyocytes from adult male and female mice. The data are supplemental to our original research article “Cardiomyocyte-specific deletion of the G protein-coupled estrogen receptor (GPER) leads to left ventricular dysfunction and adverse remodeling: a sex-specific gene profiling” (Wang et al., 2016) [1]. Data have been deposited to the Gene Expression Omnibus (GEO) database repository with the dataset identifier GSE86843.

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Specifications Table

| Subject area | Biology |
|--------------|---------|
| More specific subject area | Heart disease, gene knockdown |
| Type of data | Tables |
| How data was acquired | Microarray data in cardiomyocytes generated using Affymetrix GeneAtlas 3′-IVT Express Kit |
| Data format | Analyzed |
| Experimental factors | Comparison of inflammatory and mitochondrial gene expression profiles of GPER-deficient versus intact cardiomyocytes from male and female mice |
| Experimental features | RNA isolation, global gene expression analysis, and bioinformatics analyses using Gene Set Enrichment Analysis (GSEA) software |
| Data source location | Wake Forest School of Medicine, Winston-Salem, NC, USA |
| Data accessibility | Dataset is within this article and available in the Gene Expression Omnibus with accession number GEO: GSE86843. |

Value of the data

- This dataset provides the complete list of altered genes related to mitochondria and inflammatory response in GPER-knockout versus intact cardiomyocytes from mice of both sexes.
- May facilitate further research that reveals the pathophysiology for sex-specific differences in heart disease.
- May serve as a benchmark for comparison with data obtained from estrogen receptor (ER) α and ERβ cardiomyocyte-specific knockout mice for further insight into the functional roles of the estrogen receptors in the maintenance of cardiac structure and function.
Table 1  
Core enrichment gene list of GSEA for mitochondrial genes in female mice.

| Gene symbol | Gene title | Rank in gene list | Rank metric score | Enrichment score |
|-------------|------------|-------------------|-------------------|------------------|
| 1 HMGCS2    | 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) | 37 | 0.274 | 0.0158 |
| 2 MAOB      | monoamine oxidase B | 39 | 0.272 | 0.0332 |
| 3 COX6B2    | cytochrome c oxidase subunit VIb polypeptide 2 (testis) | 48 | 0.261 | 0.0495 |
| 4 HSPA1B    | heat shock 70 kDa protein 1B | 63 | 0.244 | 0.0645 |
| 5 UCP3      | uncoupling protein 3 (mitochondrial, proton carrier) | 70 | 0.237 | 0.0794 |
| 6 ALAS2     | aminolevulinate, delta-, synthase 2 (sideroblastic/hypochromic anemia) | 206 | 0.175 | 0.0843 |
| 7 BCKDH8    | branched chain keto acid dehydrogenase E1, beta polypeptide (maple syrup urine disease) | 222 | 0.172 | 0.0946 |
| 8 DUT       | dUTP pyrophosphatase | 311 | 0.159 | 0.1007 |
| 9 HTRA2     | HtrA serine peptidase 2 | 313 | 0.158 | 0.1107 |
| 10 ME3      | malic enzyme 3, NADP(+)-dependent, mitochondrial | 431 | 0.145 | 0.1146 |
| 11 GSTZ1    | glutathione transferase zeta 1 (maleylacetocetate isomerase) | 575 | 0.143 | 0.1165 |
| 12 ACOT2    | acyl-CoA thioesterase 2 | 647 | 0.13 | 0.1215 |
| 13 PCCB     | propionyl Coenzyme A carboxylase, beta polypeptide | 660 | 0.13 | 0.1293 |
| 14 TIMMDC1  | Translocase of inner mitochondrial membrane domain-containing protein 1 | 795 | 0.124 | 0.1309 |
| 15 RAF1     | v-raf-1 murine leukemia viral oncogene homolog 1 | 851 | 0.121 | 0.1361 |
| 16 TMEM143  | transmembrane protein 143 | 880 | 0.12 | 0.1425 |
| 17 NME4     | non-metastatic cells 4, protein expressed in | 920 | 0.119 | 0.1483 |
| 18 ACAP6    | acid phosphatase 6, lysophosphatidic | 975 | 0.116 | 0.1532 |
| 19 FXN      | frataxin | 1014 | 0.114 | 0.1587 |
| 20 CRY1     | cryptochrome 1 (photolyase-like) | 1065 | 0.112 | 0.1636 |
| 21 HSD3B2   | hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2 | 1079 | 0.112 | 0.1701 |
| 22 ABCB8    | ATP-binding cassette, sub-family B (MDR/TAP), member 8 | 1234 | 0.107 | 0.1698 |
| 23 GCDH     | glutaryl-Coenzyme A dehydrogenase | 1258 | 0.107 | 0.1756 |
| 24 CASP7    | caspase 7, apoptosis-related cysteine peptidase | 1424 | 0.102 | 0.1744 |
| 25 MYL10    | myosin, light chain 10, regulatory | 1446 | 0.102 | 0.18 |
| 26 BCA2T    | branched chain aminotransferase 2, mitochondrial | 1546 | 0.099 | 0.1817 |
| 27 B2RAF1   | benzodiazapine receptor (peripheral) (associated protein 1 | 1591 | 0.098 | 0.186 |
| 28 MECR     | mitochondrial trans-2-enoyl-CoA reductase | 1638 | 0.097 | 0.19 |
| 29 MTIF3    | Mitochondrial Translational Initiation Factor 3 | 1773 | 0.094 | 0.198 |
| 30 BCL2L10  | BCL2-like 10 (apoptosis facilitator) | 1825 | 0.093 | 0.1934 |
| 31 ACADS    | acyl-Coenzyme A dehydrogenase, C-2 to C-3 short chain delta-isomerase 2 | 1827 | 0.093 | 0.1993 |
| 32 ECST1    | ECST homolog (Drosophila) | 1946 | 0.091 | 0.1996 |
| 33 MRPL23   | mitochondrial ribosomal protein L23 | 1970 | 0.09 | 0.2043 |
| 34 MRPS15   | mitochondrial ribosomal protein S15 | 2039 | 0.089 | 0.2068 |
| 35 MRPS28   | mitochondrial ribosomal protein S28 | 2158 | 0.087 | 0.2068 |
| 36 TBRG4    | transforming growth factor beta regulator 4 | 2223 | 0.085 | 0.2093 |
| 37 SLC25A22 | solute carrier family 25 (mitochondrial carrier: glutamate), member 22 | 2236 | 0.085 | 0.2142 |
| 38 MRPS11   | mitochondrial ribosomal protein S11 | 2257 | 0.085 | 0.2187 |
| 39 BCKDH1A  | branched chain keto acid dehydrogenase E1, alpha polypeptide | 2321 | 0.084 | 0.2211 |
| 40 TRIAP1   | TP53 regulated inhibitor of apoptosis 1 | 2336 | 0.084 | 0.2258 |
| 41 FDXR     | ferredoxin reductase | 2407 | 0.082 | 0.2278 |
| 42 RHOT2    | ras homolog gene family, member T2 | 2434 | 0.082 | 0.2319 |
| 43 MRPS24   | mitochondrial ribosomal protein S24 | 2473 | 0.081 | 0.2353 |
| 44 MRPS35   | mitochondrial ribosomal protein S35 | 2493 | 0.081 | 0.2396 |
| 45 MTCH1    | mitochondrial carrier homolog 1 (C. elegans) | 2494 | 0.081 | 0.2447 |
| 46 BCKDK    | branched chain ketoadic dehydrogenase kinase | 2503 | 0.081 | 0.2495 |
| 47 MRPS21   | mitochondrial ribosomal protein S21 | 2584 | 0.079 | 0.2509 |
| 48 SHMT2    | serine hydroxymethyltransferase 2 (mitochondrial) | 2609 | 0.079 | 0.2548 |
| 49 PKK2     | phosphoenolpyruvate carboxykinase 2 (mitochondrial) | 2761 | 0.077 | 0.2527 |
| 50 CPT1A    | carnitine palmitoyltransferase 1A (liver) | 2776 | 0.076 | 0.2569 |
| 51 DMGDH    | dimethylglycine dehydrogenase | 2946 | 0.074 | 0.2538 |
| 52 MSTO1    | misato homolog 1 (Drosophila) | 3029 | 0.073 | 0.2546 |
| 53 DGUOK    | deoxyguanosine kinase | 3045 | 0.073 | 0.2586 |
| 54 PET112   | glutamyl-TRNA(Gln) amidotransferase, subunit B | 3058 | 0.072 | 0.2626 |
| 55 AMACR    | alpha-methylacyl-CoA racemase | 3069 | 0.072 | 0.2668 |
| 56 MRPS22   | mitochondrial ribosomal protein S22 | 3103 | 0.072 | 0.2699 |
| Gene symbol | Gene title                                                                 | Rank in gene list | Rank metric score | Enrichment score |
|-------------|-----------------------------------------------------------------------------|-------------------|-------------------|------------------|
| ABCF2       | ATP-binding cassette, sub-family F (GCN20), member 2                         | 3118              | 0.072             | 0.2738           |
| EC2         | Enoyl-CoA Delta Isomerase 2                                                 | 3129              | 0.072             | 0.2779           |
| TXNRD2      | thioredoxin reductase 2                                                     | 3191              | 0.071             | 0.2796           |
| TEMEM186    | Transmembrane Protein 186                                                  | 3236              | 0.07               | 0.2821           |
| PINK1       | PTEN induced putative kinase 1                                              | 3351              | 0.069             | 0.2812           |
| ALDH4A1     | aldehyde dehydrogenase 4 family, member A1                                 | 3430              | 0.068             | 0.2819           |
| PITRM1      | pyruvate dehydrogenase kinase, isozyme 4                                   | 3548              | 0.067             | 0.2851           |
| MIPEP       | mitochondrial intermediate peptidase                                         | 3577              | 0.066             | 0.288            |
| MRPL40      | mitochondrial ribosomal protein 14                                           | 3589              | 0.066             | 0.2918           |
| TAMM41      | TAM41 Mitochondrial Translocator Assembly And Maintenance Homolog           | 3780              | 0.064             | 0.287            |
| MSTRB2      | methionine sulfoxide reductase B2                                           | 3929              | 0.063             | 0.2841           |
| SURF1       | surfeit 1                                                                   | 3949              | 0.062             | 0.2872           |
| ATGPS2      | ATP synthase, H+ transporting, mitochondrial F0 complex, subunit C2 (subunit 9) | 3962              | 0.062             | 0.2907           |
| SPG7        | spastic paraplegia 7, paraplegin (pure and complicated autosomal recessive) | 3988              | 0.062             | 0.2935           |
| BCS1L       | BCS1-like (yeast)                                                          | 4000              | 0.062             | 0.2969           |
| ALDH4A1     | aldehyde dehydrogenase 5 family, member A1 (succinate-semialdehyde dehydrogenase) | 4110              | 0.061             | 0.2957           |
| MARS2       | methionine-tRNA synthetase 2 (mitochondrial)                                | 4164              | 0.06               | 0.2971           |
| CLN3        | ceroid-lipofuscinosis, neuronal 3, juvenile (Batten, Spielemeyer-Vogt disease) | 4185              | 0.06               | 0.3              |
| FIS1        | fission 1 (mitochondrial outer membrane) homolog (S. cerevisiae)            | 4205              | 0.06               | 0.303            |
| POLG        | polymerase (DNA directed), gamma                                            | 4255              | 0.059             | 0.3045           |
| TUFM        | Tu translation elongation factor, mitochondrial                            | 4299              | 0.059             | 0.3062           |
| POLG2       | polymerase (DNA directed), gamma 2, accessory subunit                      | 4333              | 0.059             | 0.3085           |
| PMA1P       | phorbol-12-myristate-13-acetate-induced protein 1                            | 4394              | 0.058             | 0.3094           |
| COX11       | COX11 homolog, cytochrome c oxidase assembly protein (yeast)                | 4427              | 0.058             | 0.3116           |
| OGDH        | oxoglutarate (alpha-ketoglutarate) dehydrogenase (lipoamide)               | 4436              | 0.058             | 0.3149           |
| COX15       | COX15 homolog, cytochrome c oxidase assembly protein (yeast)                | 4447              | 0.058             | 0.3181           |
| MCAT        | malonyl CoA:ACP acyltransferase (mitochondrial)                            | 4527              | 0.057             | 0.3181           |
| DEC1R       | 2,4-dienoyl CoA reductase 1, mitochondrial                                  | 4638              | 0.056             | 0.3166           |
| C15P8       | caspase 8, apoptosis-related cysteine peptidase                             | 4729              | 0.055             | 0.3159           |
| TIMM17B     | translocase of inner mitochondrial membrane 17 homolog B (yeast)            | 4752              | 0.055             | 0.3184           |
| TIMM50      | translocase of inner mitochondrial membrane 50 homolog (S. cerevisiae)      | 4791              | 0.055             | 0.3201           |
| MRPS10      | mitochondrial ribosomal protein S10                                        | 4848              | 0.054             | 0.321            |
| AGPAT5      | 1-acylglycerol-3-phosphate O-acetyltransferase 5 (lysophosphatidic acid acyltransferase, epsilon) | 4921              | 0.053             | 0.3211           |
| GBAS        | gliblastoma amplified sequence                                              | 4930              | 0.053             | 0.3241           |
| HSD17B10    | Hydroxysteroid (17-Beta) Dehydrogenase 10                                  | 4977              | 0.053             | 0.3253           |
| OXA1L       | oxidase (cytochrome c) assembly 1-like                                      | 5075              | 0.052             | 0.3241           |
| ETFB        | electron-transfer-flavoprotein, beta polypeptide                            | 5085              | 0.052             | 0.327            |
| MRPL10      | mitochondrial ribosomal protein L10                                        | 5190              | 0.051             | 0.3254           |
| PHB2        | prohibitin 2                                                                | 5222              | 0.051             | 0.3272           |
| COQ4        | coenzyme Q4 homolog (S. cerevisiae)                                        | 5242              | 0.05               | 0.3295           |
| SDHC        | succinate dehydrogenase complex, subunit C, integral membrane protein, 15kDa | 5276              | 0.05               | 0.3312           |
| FDX1        | ferredoxin 1                                                                | 5338              | 0.049             | 0.3315           |
| THG1L       | tRNA-histidine guanylyltransferase 1-like (S. cerevisiae)                    | 5342              | 0.049             | 0.3345           |
| AIFM3       | Apoptosis Inducing Factor, Mitochondria Associated 3                        | 5344              | 0.049             | 0.3377           |
| SLC25A15    | solute carrier family 25 (mitochondrial carrier; ornithine transporter) member 15 | 5345              | 0.049             | 0.3408           |
| PTGES2      | prostaglandin E synthase 2                                                  | 5367              | 0.049             | 0.343            |
Table 2
Core enrichment gene list of GSEA for mitochondrial genes in male mice.

| Gene symbol | Gene title | Rank in gene list | Rank metric score | Enrichment score |
|-------------|------------|-------------------|-------------------|------------------|
| 1           | DBT        | dihydrolipoamide branched chain transacylase E2 | 199 | 0.195 | 0.009 |
| 2           | CRY1       | cryptochrome 1 (photolyase-like) | 255 | 0.181 | 0.023 |
| 3           | BCKDHB     | branched chain keto acid dehydrogenase E1, beta polypeptide (maple syrup urine disease) | 440 | 0.151 | 0.028 |
| 4           | MAOB       | monoamine oxidase B | 458 | 0.149 | 0.041 |
| 5           | HMGC2      | 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) | 631 | 0.132 | 0.045 |
| 6           | PDK4       | pyruvate dehydrogenase kinase, isozyme 4 | 1006 | 0.106 | 0.037 |
| 7           | ABCB7      | ATP-binding cassette, sub-family B (MDR/TAP), member 7 | 1092 | 0.102 | 0.042 |
| 8           | DUT        | diUTP pyrophosphatase | 1286 | 0.095 | 0.042 |
| 9           | METAP1D    | Methionyl Aminopeptidase Type 1D (Mitochondrial) | 1303 | 0.094 | 0.050 |
| 10          | GSTZ1      | glutathione transferase zeta 1 (maleylacetoacetate isomerase) | 1346 | 0.092 | 0.057 |
| 11          | UCP3       | uncoupling protein 3 (mitochondrial, proton carrier) | 1489 | 0.088 | 0.058 |
| 12          | NR3C1      | nuclear receptor subfamily 3, group C, member 1 (glucocorticoid receptor) | 1533 | 0.087 | 0.064 |
| 13          | MUT        | methylmalonyl Coenzyme A mutase | 1581 | 0.086 | 0.070 |
| 14          | OPA1       | optic atrophy 1 (dominant) | 1820 | 0.079 | 0.066 |
| 15          | NDUFS5     | NADH dehydrogenase (ubiquinone) Fe-S protein 5, 15kDa (NADH-coenzyme Q reductase) | 2107 | 0.073 | 0.059 |
| 16          | ASAH2      | N-acylsphingosine amidohydrolase (non-lysosomal ceramide) 2 | 2138 | 0.073 | 0.065 |
| 17          | ACOT2      | acyl-CoA thioesterase 2 | 2203 | 0.071 | 0.075 |
| 18          | MTIF2      | mitochondrial transcriptional initiation factor 2 | 2334 | 0.069 | 0.082 |
| 19          | MSRB3      | methionine sulfoxide reductase B3 | 2777 | 0.070 | 0.078 |
| 20          | RAF1       | v-raf-1 murine leukemia viral oncogene homolog 1 | 2334 | 0.069 | 0.082 |
| 21          | GLUD1      | glutamate dehydrogenase 1 | 2407 | 0.068 | 0.084 |
| 22          | ALDH5A1    | aldehyde dehydrogenase 5 family, member A1 (sucinate-semialdehyde dehydrogenase) | 2408 | 0.068 | 0.091 |
| 23          | NLRP5      | NLR Family, Pyrin Domain Containing 5 | 2469 | 0.066 | 0.094 |
| 24          | DLD        | dihydrolipoamide dehydrogenase | 2485 | 0.066 | 0.099 |
| 25          | PDK1       | pyruvate dehydrogenase kinase, isozyme 1 | 2529 | 0.065 | 0.103 |
| 26          | AASS       | aminoadipate-semialdehyde synthase | 2537 | 0.065 | 0.109 |
| 27          | LDHD       | lactate dehydrogenase D | 2610 | 0.063 | 0.111 |
| 28          | COX6B2     | cytochrome c oxidase subunit VIb polypeptide 2 (testis) | 2615 | 0.063 | 0.117 |
| 29          | ACAT1      | acyl-Coenzyme A acetyltransferase 1 (acetoacetyl Coenzyme A thiolase) | 2674 | 0.062 | 0.120 |
| 30          | CLPX       | ClpX caseinolytic peptidase X homolog (E. coli) | 2697 | 0.062 | 0.125 |
| 31          | L2HGHD     | L-2-hydroxyglutarate dehydrogenase | 2736 | 0.061 | 0.128 |
| 32          | AIFM1      | Apoptosis Inducing Factor, Mitochondria Associated 1 | 2820 | 0.060 | 0.130 |
| 33          | SUCLA2     | succinate-CoA ligase, ADP-forming, beta subunit | 2846 | 0.060 | 0.134 |
| 34          | HCCS       | holocysteine c synthase (cytochrome c heme-lyase) | 2931 | 0.058 | 0.136 |
| 35          | RHOT1      | ras homolog gene family, member T1 | 2974 | 0.058 | 0.139 |
| 36          | BCKDHA     | branched chain keto acid dehydrogenase E1, alpha polypeptide | 3019 | 0.057 | 0.142 |
| 37          | ACADSB     | acyl-Coenzyme A dehydrogenase, short/branched chain | 3061 | 0.056 | 0.146 |
| 38          | TRNT1      | tRNA nucleotidyl transferase, CCA-adding, 1 | 3237 | 0.053 | 0.142 |
| 39          | ABCE1      | ATP-binding cassette, sub-family E (OABP), member 1 | 3317 | 0.052 | 0.143 |
| 40          | TFB2M      | transcription factor B2, mitochondrial | 3417 | 0.051 | 0.143 |
| 41          | GBAS       | glioblastoma amplified sequence | 3429 | 0.050 | 0.148 |
| 42          | ETFA       | electron-transfer-flavoprotein, alpha polypeptide (glutaric aciduria II) | 3444 | 0.050 | 0.151 |
| 43          | HTRA2      | HtrA serine peptidase 2 | 3461 | 0.050 | 0.155 |
| 44          | HSPD1      | heat shock 60kDa protein 1 (chaperonin) | 3504 | 0.049 | 0.158 |
| 45          | POLG       | polymerase (DNA directed), gamma | 3642 | 0.048 | 0.156 |
| 46          | GCDH       | glutaryl-Coenzyme A dehydrogenase | 3649 | 0.048 | 0.160 |
| 47          | NIPSNA1    | nipsnap homolog 1 (C. elegans) | 3769 | 0.046 | 0.159 |
May stimulate further research on the clinical potential of targeting GPER in the treatment of heart disease and other age-related disorders, in which mitochondrial dysfunction and inflammation have central roles in the underlying pathophysiology.

1. Data

To examine the differences in the mitochondrial and inflammatory response gene expressions between GPER-knockout and intact cardiomyocytes, microarray data were loaded into GSEA 2.0.1 software using GSEA gene sets "MITOCHONDRION (including 314 genes)" and "HALLMARK_INFLAMMATORY_RESPONSE (including 193 genes)" [1,2]. The altered individual mitochondrial and inflammatory genes in GPER knockout versus intact cardiomyocytes from both sexes are presented in Tables 1–4.

2. Experimental design, materials and methods

2.1. Cardiomyocyte isolation from GPER KO and GPER-intact or wild-type mice

Mice at 18–20 weeks of age were injected i.p. with 200 μl heparin (Sagent Pharmaceutical Inc., Schaumburg, IL, 100 IU/mouse) 10 min prior to anesthesia with pentobarbital (Akorn Inc., Lake Forest, IL, 100 mg/kg body weight) by i.p. injection. Upon verification of deep anesthesia by the absence of response to tail/toe pinches, the heart was quickly removed and trimmed in an ice-cold, calcium-free perfusion buffer (126 mM NaCl, 4.4 mM KCl, 1 mM MgCl2, 4 mM NaHCO3, 10 mM HEPES, 11 mM glucose, 30 mM 2,3-butanedine monoxime [Sigma, St. Louis, MO], 5 mM taurine [Sigma], pH 7.35). The heart was then cannulated through the aorta on an Easycell System for Cardiomyocyte Isolation (Harvard Apparatus, Holliston, MA) and perfused at 37 °C with calcium-free perfusion buffer at a flow rate of 3 ml/min for 4–5 min until the effluent became clear. The heart was switched to digestion buffer (perfusion buffer plus 50 μM CaCl2 and 0.5 mg/ml collagenase II [Worthington Biochemical Corp., Freehold, NJ]), and perfused for 10–15 min at a flow rate of 4 ml/min until the heart was pale.
and flaccid. The heart was pulled from the cannula and the ventricles were transferred to a 60-mm sterile dish containing 5 ml of transfer buffer (perfusion buffer plus 0.1 mM CaCl2 and 2% bovine serum albumin [Sigma]) and cut into small pieces. The minced tissue was incubated in a 37 °C water bath for 10 min. The cell suspension was filtered through a 100-μm mesh cell strainer (BD Biosciences, San Jose, CA) to remove tissue debris and spun at 420 rpm at room temperature for 2 min. After removing the supernatant, cardiomyocytes were washed with 1 ml of PBS and centrifuged at 1500 rpm at 4°C for 3 min. The cells were suspended in 1 ml of QIAzol (Qiagen Inc, Valencia, CA), mixed, and homogenized before storing at −80°C.

2.2. DNA microarray assay

Total RNA was isolated from cardiomyocytes using the RNeasy Lipid Tissue Mini Kit (Qiagen Inc) and further purified using RNeasy MinElute Cleanup Kit (Qiagen Inc) followed by quality assessment on an Agilent 2100 bioanalyzer. Samples with RIN values > 8.0 and a 260/280 ratio between 1.8 and 2.1 were carried forward for cRNA synthesis and hybridization to GeneAtlas MG-430 PM Array Strips (Affymetrix, Santa Clara, CA) following the manufacturer’s recommended protocol [3]. Briefly, approximately 250 ng of purified total RNA was reverse transcribed and biotin labeled to produce biotinylated cRNA targets according to the standard Affymetrix GeneAtlas 3′-IVT Express labeling.
Following fragmentation, 6 μg of biotinylated cRNA was hybridized for 16 h at 45 °C on the Affymetrix GeneAtlas Mouse MG-430 PM Array Strip. Strips were washed and stained using the GeneAtlas Fluidics Station according to standard Affymetrix operating procedures (GeneAtlas™ System User's Guide, P/N 08-0306 Rev A January 2010). Strips were subsequently scanned using the GeneAtlas Imager system according to the standard Affymetrix protocol. Fluidics control, scan control, and data collection were performed using the GeneAtlas Instrument Control Software version 1.0.5.267. All microarray analyses were performed by the Wake Forest School of Medicine Microarray Shared Resource Core.

### 2.3. Gene set enrichment analysis (GSEA)

GSEA was performed to determine whether genes belonging to a biological pathway or a previously determined functional group were significantly overrepresented at the top or bottom of a table.

| Gene symbol | Gene title | Rank in gene list | Rank metric score | Enrichment score |
|-------------|------------|------------------|------------------|-----------------|
| TIMP1       | TIMP metalloproteinase inhibitor 1 | 3 | 0.804 | 0.061 |
| CD48        | CD48 molecule | 30 | 0.397 | 0.091 |
| CD14        | CD14 molecule | 59 | 0.322 | 0.114 |
| SCN1B       | sodium channel, voltage-gated, type I, beta | 76 | 0.303 | 0.136 |
| CYBB        | cytochrome b-245, beta polypeptide (chronic granulomatous disease) | 96 | 0.273 | 0.156 |
| CDKN1A      | cyclin-dependent kinase inhibitor 1A (p21, Cip1) | 159 | 0.227 | 0.171 |
| OSMR        | oncostatin M receptor | 163 | 0.223 | 0.188 |
| C3AR1       | complement component 3a receptor 1 | 215 | 0.200 | 0.201 |
| CCL7        | chemokine (C-C motif) ligand 7 | 246 | 0.188 | 0.214 |
| ICAM4       | intercellular adhesion molecule 4 (Landsteiner-Wiener blood group) | 269 | 0.182 | 0.227 |

Table 4
Core enrichment gene list of GSEA for inflammatory response genes in male mice.
ranked gene list compared to controls without a predefined cut-off value. This bioinformatic tool evaluates all significantly measured targets derived from a microarray experiment at the level of gene sets, which are defined based on prior biological knowledge. Thus, biologically relevant information is not missed by losing target genes due to an “arbitrarily” chosen cut-off value [4]. In this study, expression data of all 21,782 genes were compared against functional gene sets to determine whether any of these sets were enriched in GPER KO cardiomyocytes vs. intact cardiomyocytes.

Acknowledgments

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.dib.2016.11.057.

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