**Supporting Information**

Supplemental Figure A. Isolation of cardiomyocytes and fibroblasts from neonatal rat hearts.

Supplemental Figure B. Pik3ip1 does not interact with p110γ

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Supplemental Figure E. Fetal genes were increased in TAC operated mice.

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Supplemental Table A. The primer sets for qRT-PCR and RT-PCR

Supplemental Table B. Echocardiographic analysis in TAC operated and exercised mice.

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**Supplemental Figure A. Isolation of cardiomyocytes and fibroblasts from neonatal rat hearts.** (A, B) mRNA levels of *Vim* (A) and *Actn1* (B) were measured in cardiomyocytes (CMs) or fibroblasts (FBs) by qRT-PCR. (n = 3, \*\* p < 0.01 compared with fibroblasts, t test)

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**Supplemental Figure B. Pik3ip1 does not interact with p110γ.** The interaction between Pik3ip1 and p110γ was analyzed in adult mouse heart tissue (A) and NRCMs (B) using anti-p110γ or anti-Pik3ip1 antibodies.

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**Supplemental Figure C. Silencing of Pik3ip1 does not lead to pathological cardiac hypertrophy.** (A-C) qRT-PCR analysis of transcripts for *Nppa* (A), *Nppb* (B), and *Myh7* (C) in siNegative or siPik3ip1-transfected NRCMs. mRNA expression was normalized to 18S. (n = 3).

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**Supplemental Figure D. Pik3ip1 does not attenuates AngII-induced cardiomyocyte hypertrophy.** NRCMs were infected with the indicated adenovirus for 24 h and subsequently treated with or without 100 nM AngII. (A) Extracts from adenovirus-infected NRCMs treated for 30 min with or without IGF1 were verified by the indicated antibodies. (B) Adenovirus-infected NRCMs were incubated for 24 h with or without AngII, after which protein synthesis was assessed using a leucine incorporation assay (n = 4, \*\* p < 0.01 compared with AdControl-infected NRCMs).

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**Supplemental Figure E. Fetal genes were increased in TAC operated mice.** (A, B) qRT-PCR analysis of transcripts for *Nppa, Nppb, Myh7* in 2-weeks (A) and 4-weeks exercised mice (B) hearts. mRNA expression was normalized to 18S. (n = 3). (C, D) qRT-PCR analysis of transcripts for *Nppa, Nppb, Myh7,* in 1-week and 2-weeks TAC mice hearts. mRNA expression was normalized to 18S. (n = 3, \*\* p < 0.01 compared with Sham, t test).

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**Supplemental Figure F. Pik3ip1 was increased in 4-weeks exercised myocyte, not fibroblast.** (A, B) mRNA levels of Pik3ip1 were measured in 2-weeks TAC (A) and 4-weeks exercised mice (B) cardiomyocytes and fibroblasts using quantitative reverse transcription PCR (qRT-PCR). (n = 3, \* p < 0.05, t test).

**Supplemental Table A. The primer sets for qRT-PCR and RT-PCR** F and R represent forward and reverse, respectively.

|  |  |
| --- | --- |
| Name of primer | Sequence |
| Mouse 18s-F | TTCTGGCCAACGGTCTAGACAAC |
| Mouse 18s-R | CCAGTGGTCTTGGTGTGCTGA |
| Mouse Pik3ip1-F | CCATGGAGCTGGAAGAGAAG |
| Mouse Pik3ip1-R | AGCTCCAATAGCGAGGATGA |
| Mouse Nppa-F | TCGTCTTGGCCTTTTGGCT |
| Mouse Nppa-R | TCCAGGTGGTCTAGCAGGTTCT |
| Mouse Nppb-F | AGGGAGAACACGGCATCATT |
| Mouse Nppb-R | GACAGCACCTTCAGGAGAT |
| Mouse Myh7-F | CGCATCAAGGAGCTCACC |
| Mouse Myh7-R | CTGCAGCCGCAGTAGGTT |
| Rat 18s-F | AAGTTTCAGCACATCCTGCGAGTA |
| Rat 18s-R | TTGGTGAGGTCAATGTCTGCTTTC |
| Rat Pik3ip1-F | TGGCAAATAAGGGCTTCCACA |
| Rat Pik3ip1-R | CCTGGATGGCAAAGGCAGA |
| Rat Nppa-F | ACCTGCTAGACCACCTGGAGGAG |
| Rat Nppa-R | CCTTGGCTGTTATCTTCGGTACCG |
| Rat Nppb-F | GCTGCTTTGGGCACAAGATAG |
| Rat Nppb-R | GGTCTTCCTACAACAACTTCA |
| Rat Myh7-F | AAGTCCTCCCTCAAGCTCCTAAGT |
| Rat Myh7-R | TTGCTTTGCCTTTGCCC |
| Rat Actn1-F | CGACATCAGGAAGGACCTGT |
| Rat Actn1-R | ACATCTGCTGGAAGGTGGAC |
| Rat Vim-F | ATGAAAGTGTGGCTGCCAAGAA |
| Rat Vim-R | GTGACTGCACCTGTCTCCGGTA |

**Supplemental Table B. Echocardiographic analysis in TAC operated and exercised mice.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 1week | | 2weeks | | 2weeks | | 4weeks | |
|  | Sham | TAC | Sham | TAC | Sedentary | Swim | Sedentary | Swim |
| Number of animals | 5 | 5 | 5 | 6 | 5 | 6 | 5 | 5 |
| Heart weight/Body weight | 4.16 ± 0.04 | 5.62 ± 0.12 \* | 4.24 ± 0.04 | 5.78 ± 0.17 \* | 4.08 ± 0.13 | 4.20 ± 0.12 | 4.03 ± 0.05 | 4.77 ± 0.05 \* |
| IVS, mm | 0.50 ± 0.04 | 0.76 ± 0.05\* | 0.44 ± 0.03 | 0.72 ± 0.04\* | 0.52 ± 0.04 | 0.52 ± 0.04 | 0.52 ± 0.02 | 0.58 ± 0.04 |
| LVPWd | 0.58 ± 0.04 | 0.74 ± 0.05\* | 0.58 ± 0.06 | 0.71 ± 0.06\* | 0.54 ± 0.06 | 0.54 ± 0.05 | 0.52 ±0.05 | 0.68 ± 0.04\* |
| LVIDd | 0.40 ± 0.01 | 0.41 ±0.02 | 0.386 ± 0.03 | 0.42 ±0.02 | 0.40 ± 0.01 | 0.40 ± 0.01 | 0.39 ± 0.01 | 0.44 ± 0.01 |
| FS % | 41.8 ± 0.4 | 35.3 ± 1.6\* | 42.0 ± 1.4 | 33.1 ± 0.4\* | 36.5 ± 0.7 | 36.8 ± 0.6 | 37.3 ± 0.3 | 38.6 ± 1.1 |

|  |
| --- |
| TAC indicates aortic transverse banding; all parameters indicated are LV diastolic values. LVID, LV internal diameter; IVS, interventricular septum; LVPW, LV posterior wall; FS, Fractional shortening. Values are mean ± SEM \*P<0.05 vs Sham or Sedentary values |