

Major Resources Table

In order to allow validation and replication of experiments, all essential research materials listed in the Methods should be included in the Major Resources Table below. Authors are encouraged to use public repositories for protocols, data, code, and other materials and provide persistent identifiers and/or links to repositories when available. Authors may add or delete rows as needed.

Animals (in vivo or ex vivo studies)

| Species | Vendor or Source | Background Strain | Sex |
|---------|--------------------|-------------------|--------|
| Mouse | Jackson Laboratory | C57BL/6J | Male |
| Mouse | Jackson Laboratory | C57BL/6J | Female |

Cells

| Name | Species | Background Strain | Sex |
|---------------------|---------|-------------------|----------------|
| adult cardiomyocyte | mouse | C57BL/6J | Male or Female |

Plasmids

| Plasmid Name | Sequence |
|-----------------------------------|------------------------|
| pLV[shRNA]-EGFP-U6>mAdcy5 | AGAATCACTGTTTACGGATTA |
| pLV[shRNA]-EGFP-U6>mAdcy6 | CACCCTGATACTCGGGATTTA |
| pLV[shRNA]-EGFP-U6>mAbcc4 (MRP4) | GGTATACTTCAGACGGAATTA |
| pLV[shRNA]-EGFP-U6>mAbcc5 (MRP5) | GTGCATTC TCATCTCCAAATT |
| pLV[shRNA]-EGFP-U6>mEnpp1 | CCAGAGACATACTATTCAATT |
| pLV[shRNA]-EGFP-U6>mEnpp2 | CGACCCAAGATTCCTCAATAAT |
| pLV[shRNA]-EGFP-U6>mEnpp3 | CGGCAATGTATCAAGGTTTAA |
| pLV[shRNA]-EGFP-U6>mNt5e (CD73) | GCACTGGGAAATCATGAATTT |
| pLV[shRNA]-EGFP-U6>mAdora1 | CATGGAGTACAT GGTCTACTT |
| pLV[shRNA]-EGFP-U6>mEntpd1 (CD39) | CCAAGGACATTCAGGTTTCAA |
| pLV[shRNA]-EGFP-U6>mPANX1 | CCACCTTCGATGTTCTACATT |
| pLV[shRNA]-EGFP-U6>mP2RX7 | CCTGGACAATCTGAGGAAATT |
| pLV[shRNA]-EGFP-U6>Scramble | CCTAAGGTTAAGTCGCCCTCG |

QPCR primer

| Primer Name | Sequence |
|------------------------------|--------------------------|
| Mouse Adcy5, forward | ACCGCCAATGCCATAGACTT |
| Mouse Adcy5, reverse | TGCAGATACAGAGCCAGCAC |
| Mouse Adcy6, forward | CGGCTCATGGAGCAGATGAA |
| Mouse Adcy6, reverse | GGACCCATGTTCAACCCGAT |
| Mouse mAbcc4 (MRP4), forward | GTCAGAGGCCATCGTCAGCA |
| Mouse mAbcc4 (MRP4), reverse | CTTGTCAGAAAGCGGTGAAA |
| Mouse mAbcc5 (MRP5), forward | CGAAGGGTTGTGTGGATCTTTTG |
| Mouse mAbcc5 (MRP5), reverse | GGTTAGACTCTGTTGCCTGGGTG |
| Mouse ENPP1, forward | AGACGACTGCAAAACCCACA |
| Mouse ENPP1, reverse | GTGATTCAAACCTCTGCTGGACAC |
| Mouse ENPP2, forward | TGATAAGGTAGAGCCAAAGAACA |
| Mouse ENPP2, reverse | GCAGGTCGTCCATACAGGAG |
| Mouse ENPP3, forward | GCACTACAGAATACGCCTGG |
| Mouse ENPP3, reverse | GCAACCTCGCCTTCGCTA |
| Mouse Nt5e (CD73), forward | TCCTGCAAGTGGGTGGAATC |
| Mouse Nt5e (CD73), reverse | AGATGGGCACTCGACACTTG |

DOI [to be added]

| | |
|------------------------------|-----------------------|
| Mouse Adora1, forward | GTGATTTGGGCTGTGAAGGT |
| Mouse Adora1, reverse | AGTAGGTCTGTGGCCCAATG |
| Mouse PANX1, forward | ACTGTGGCTGCACAAGTTCT |
| Mouse PANX1, reverse | AGAGAAGCGCCAGAAGAGTG |
| Mouse P2X7R, forward | GGGGTGACGAAGTTAGGACA |
| Mouse P2X7R, reverse | ACTTGGCCTTCTGACTTGACA |
| Mouse Entpd1 (CD39), forward | ATCACCTTCGTGCCCAAAA |
| Mouse Entpd1 (CD39), reverse | CGCCACCACTTGAAACCTGA |
| Mouse GAPDH, forward | TCAAGAAGGTGGTGAAGCA |
| Mouse GAPDH, reverse | TGGGAGTTGCTGTTGAAGTC |

Reagents

| Name | Vendor or Source | Catalog # |
|--|--------------------------|-----------------|
| ¹⁰ PANX | ApexBio | A2700 |
| A804598 | Cayman Chemical Company | 20060 |
| Amthamine dihydrobromide | Tocris | 0668 |
| Apyrase | Sigma-Aldrich | A6535-200UN |
| ATP Determination Kit | Thermo Fisher Scientific | A22066 |
| Autocamtide-2-related inhibitory peptide myristoylated | Tocris | 5959 |
| Blebbistatin | Cayman Chemical Company | 13013 |
| Bovine Serum Albumin | Sigma-Aldrich | A9647 |
| cAMP | Cayman Chemical Company | 18820 |
| cAMP Colorimetric ELISA Kit | Cell Biolabs | STA-500 |
| Ceefourin1 | Tocris | 5867 |
| CGP20712 | Tocris | 1024 |
| collagenase type II | Worthington Biochemical | LS004176 |
| Creatine Kinase (CK) Activity Colorimetric Assay Kit | BioVision | K777-100 |
| CV1808 | Tocris | 1710 |
| Deaminase | Sigma-Aldrich | 10102105001 |
| Dextran 40 | Sigma-Aldrich | FD40 |
| DMEM | Corning | 15017CV |
| Duolink® In Situ Detection Reagents Red | Sigma-Aldrich | DUO92008-100RXN |
| Duolink® In Situ Mounting Medium with DAPI | Sigma-Aldrich | DUO82040-5ML |
| Duolink® In Situ PLA® Probe Anti-Mouse MINUS, Affinity purified Donkey anti-Mouse IgG | Sigma-Aldrich | DUO92004-100RXN |
| Duolink® In Situ PLA® Probe Anti-Rabbit PLUS, Affinity purified Donkey anti-Rabbit IgG | Sigma-Aldrich | DUO92002-100RXN |
| Duolink® In Situ Wash Buffers, Fluorescence | Sigma-Aldrich | DUO82049-4L |
| ENPP1 inhibitor c | Cayman Chemical Company | 29809 |
| EGTA | Sigma-Aldrich | 324626-25GM |
| Famotidine | Tocris | 7290 |
| Fetal Bovine Serum | Thermo Fisher Scientific | 10437028 |
| Fluo-4 AM | Ion Biosciences | 1041C |
| Gap 26 | Cayman Chemical Company | 36625 |
| Halt™ Phosphatase Inhibitor Cocktail | Thermo Fisher Scientific | 78420 |
| Human CGRP8-37 | Tocris | 1181 |
| Human α-CGRP | Tocris | 3012 |
| ICI118,551 | Tocris | 0821 |
| In Situ Cell Death Detection Kit, TMR red | Sigma-Aldrich | 12156792910 |
| Insulin-Transferrin-Selenium (ITS -G) (100X) | Thermo Fisher Scientific | 41400045 |
| Immobilon Western Chemiluminescent HRP Substrate | Millipore | WBKLS0100 |

DOI [to be added]

| | | |
|---|--------------------------|------------|
| iQ™ SYBR® Green Supermix | Bio-rad | 1708882 |
| iScript™ Reverse Transcription Supermix | Bio-rad | 1708841 |
| Isoprenaline hydrochloride | Sigma-Aldrich | I5627 |
| KN 92 | Tocris | 4130 |
| KN 93 | Tocris | 1278 |
| Laminin | VWR | 47743-734 |
| LDH Cytotoxicity Detection Kit | Takara Bio | MK401 |
| LY294002 | Tocris | 1130 |
| MEM | Thermo Fisher Scientific | 11095080 |
| MK-571 | Tocris | 2338 |
| MOUSE CARDIAC TROPONIN-I ELISA | Life diagnostics inc | CTNI1HSP |
| Novex DYNAL Dynabeads Protein | Thermo Fisher Scientific | G 10-003-D |
| Penicillin-Streptomycin (10,000 U/mL) | Thermo Fisher Scientific | 15140122 |
| Pierce™ Mem-PER™ Plus Membrane Protein Extraction Kit | Thermo Fisher Scientific | 89842 |
| PKI 14-22 | Tocris | 2546 |
| Pluronic F127 | Sigma-Aldrich | P2443 |
| POM1 | Tocris | 2689 |
| PolyJet In Vitro DNA Transfection Reagent | SignaGen Laboratories | SL100688 |
| Protease Inhibitor Cocktail | Sigma-Aldrich | P8340 |
| PSB12379 | Cayman Chemical Company | 28446 |
| PSB36 | Tocris | 2019 |
| Relaxin-2 | Sigma-Aldrich | SRP3147 |
| RIPA buffer | VWR | N653 |
| S32826 | Cayman Chemical Company | 13664 |
| scrambled ¹⁰ PANX | ApexBio | A2701 |
| TCS2510 | Tocris | 4069 |
| TrueBlot® Anti-Rabbit IgG Magnetic Beads | Rockland | 00-1800-20 |
| TRIZOL | Thermo Fisher Scientific | 15596026 |
| Trypan blue | ICN Biomedicals Inc | 194600 |
| Wheat Germ Agglutinin, Alexa Fluor™ 488 Conjugate | Thermo Fisher Scientific | W11261 |
| YO3-PRO3 | Thermo Fisher Scientific | Y3607 |
| Zinterol hydrochloride | Sigma-Aldrich | Z4402 |
| ZM241385 | Tocris | 1036 |

Antibodies

| Target antigen | Vendor or Source | Catalog # | Working concentration |
|--------------------------------|--------------------------|------------|----------------------------------|
| Rabbit anti-A2AR antibody | Alomone Labs | AAR-002 | PLA 1:100 |
| Mouse anti-A2AR antibody | Santa Cruz | sc-32261 | co-ip 1:200 |
| Rabbit anti-β1AR antibody | Alomone Labs | AAR-023 | PLA 1:100 |
| Rabbit anti-β1AR antibody | Proteintech | 28323-1-AP | co-ip 1:1000 |
| Mouse anti-cAMP antibody | Novus Biologicals | MAB2146 | <i>In vitro</i> study 0.25 µg/mL |
| Rabbit anti-CaMKIIδ antibody | ABclonal | A0656 | PLA 1:100 |
| Mouse anti-Calmodulin antibody | Thermo Fisher Scientific | MA3-917 | PLA 1:100 |
| Rabbit anti-CGRPR antibody | Novus Biologicals | NLS6731 | PLA 1:50 |
| Rabbit anti-CGRPR antibody | ABclonal | A11979 | co-ip 1:1000 |
| Mouse anti-GAPDH antibody | MilliporeSigma | MAB374 | western blot 1:5000 |
| Rabbit anti-H2R antibody | ABclonal | A14170 | PLA 1:100 co-ip 1:1000 |
| Rabbit anti-MRP4 antibody | AssayGenie | CAB2198 | |

DOI [to be added]

| | | | |
|---|--------------------------|------------|----------------------------------|
| Rat anti-MRP4 antibody | Novus Biologicals | NBP1 | co-ip 1:1000 |
| Mouse anti-MRP4 antibody | Santa Cruz | sc-376262 | PLA 1:50 |
| Rabbit anti-P2X7R antibody | Alomone Labs | APR-008 | western blot 1:1000 |
| Goat anti-P2X7R antibody | Abcam | ab93354 | co-ip 1:1000 |
| Mouse anti-pannexin-1 antibody | Novus Biologicals | MAB7097 | PLA 1:100 |
| Rabbit anti-pannexin-1 antibody | Proteintech | 12595-1-AP | western blot 1:1000 |
| Rabbit anti-Phospho-PKA substrate (RRXS*/T*) antibody | Cell Signaling | 96245 | PLA 1:100 western blot 1:1000 |
| Rabbit anti-RXFP1 antibody | Proteintech | 18419-1-AP | PLA 1:50 |
| Rabbit anti-RXFP1 antibody | ABclonal | A7127 | co-ip 1:1000 |
| Goat anti-Mouse IgG (H+L) cross adsorbed secondary antibody, DyLight 594 conjugated | Thermo fisher Scientific | 35510 | immunostaining 1:100 |
| Goat TrueBlot® : Anti-Goat IgG HRP | Rockland | 18-8814-31 | co-ip 1:5000 |
| Mouse TrueBlot® ULTRA: Anti-Mouse Ig HRP | Rockland | 18-8817-30 | co-ip 1:5000 |
| Mouse IgG HRP Linked Whole Ab | Millipore Sigma | GENA931 | western blot 1:5000 |
| Rabbit TrueBlot®: Anti-Rabbit IgG HRP | Rockland | 18-8816-31 | co-ip 1:5000 |
| Rabbit IgG HRP Linked Whole Ab | Millipore Sigma | GENA934 | western blot 1:5000 |
| Anti-rat IgG, HRP-linked Antibody | Cell Signaling | 7077s | co-ip 1:5000 |