

Supplemental Table 1: HCM variants

| Gene | Exon | Nucleotide Change | Protein variant | Count | Published |
|--------|------|-----------------------------------|------------------|-------|------------------|
| ACTC | 2 | c.301 G>A | p.Glu101Lys | 1 | Yes |
| ACTC | 4 | c.695 C>T | p.Ala232Val | 1 | Yes |
| MYBPC3 | 2 | c.26 -2 A>G | | 1 | Yes |
| MYBPC3 | 2 | c.177-187 del AGAGGGCACA | p.Glu60Argfs*49 | 7 | Yes |
| MYBPC3 | 2 | c.237 C>A | p.Tyr79Ter | 1 | Yes |
| MYBPC3 | 4 | c.481 C>A | p.Pro161Thr | 1 | Yes |
| MYBPC3 | 5 | c.506 G>A | p.Gly169Asp | 1 | Yes |
| MYBPC3 | 5 | c.557 C>T | p.Pro186Leu | 1 | Yes |
| MYBPC3 | 5 | c.646 G>A | p.Ala216Thr | 1 | Yes |
| MYBPC3 | 6 | c.655 G>C | p.Val219Leu | 2 | Yes |
| MYBPC3 | 6 | c.660 del T | p.Tyr220Tyrfs*78 | 1 | No |
| MYBPC3 | 6 | c.766 G>A | p.Val256Ile | 1 | Yes |
| MYBPC3 | 6 | c.772 G>A | p.Glu258Lys | 2 | Yes |
| MYBPC3 | 7 | c.821 +1 G>A | | 3 | Yes |
| MYBPC3 | 8 | c.833 del G | p.Gly277Glufs*22 | 1 | No |
| MYBPC3 | 12 | c.1091 -2 A>G | | 3 | Yes |
| MYBPC3 | 13 | c.1168 del C | p.His390Metfs*15 | 1 | Yes |
| MYBPC3 | 13 | c.1210 C>T | p.Gln404Ter | 1 | No |
| MYBPC3 | 15 | c.1235-1236 del TT | p.Phe412Terfs*1 | 3 | Yes |
| MYBPC3 | 15 | c.1308 C>A | p.Cys436Ter | 1 | Yes |
| MYBPC3 | 17 | c.1409-1410 del GG | p.Arg470Argfs*4 | 1 | Yes |
| MYBPC3 | 17 | c.1484 G>A | p.Arg495Gln | 7 | No |
| MYBPC3 | 17 | c.1483 C>T | p.Arg495Trp | 1 | Yes |
| MYBPC3 | 17 | c.1504 C>T | p.Arg502Trp | 9 | Yes ^a |
| MYBPC3 | 17 | c.1516 Del G | p.Asp506Thrfs*7 | 1 | Yes |
| MYBPC3 | 17 | c.1543-1545 del AAC | p.Asn515del | 1 | Yes |
| MYBPC3 | 17 | c.1591 G>C | p.Gly531Arg | 1 | No |
| MYBPC3 | 17 | c.1624 G>C | p.Glu542Gln | 8 | Yes ^a |
| MYBPC3 | 18 | c.1639-1640 del GT | p.Val547Valfs*20 | 1 | Yes |
| MYBPC3 | 18 | c.1700-1701 del AG | p.Glu567Glyfs*4 | 2 | Yes |
| MYBPC3 | 18 | c.1729-1730 del TG | p.Trp577Argfs*27 | 1 | Yes |
| MYBPC3 | 19 | c.1805 C>T | p.Thr602Ile | 1 | Yes |
| MYBPC3 | 19 | c.1811 A>T | p.Aps604Val | 1 | No |
| MYBPC3 | 19 | c.1823 C>T | p.Pro608Leu | 1 | Yes |
| MYBPC3 | 21 | c.1999-2000 del CT, 1999 ins G | p.Leu667Aspfs*15 | 1 | Yes |
| MYBPC3 | 22 | c.2096 del A | p.Pro699Profs*55 | 1 | Yes |
| MYBPC3 | 22 | c.2107 G>C | p.Glu703Gln | 1 | No |
| MYBPC3 | 23 | c.2149 -2 A>G | | 1 | Yes |
| MYBPC3 | 24 | c.2308 -2 A>G | | 1 | Yes |
| MYBPC3 | 24 | c.2347 G>T | p.Val783Leu | 1 | Yes |
| MYBPC3 | 24 | c.2373-2374 ins G | p.Trp792Valfs*41 | 15 | Yes |
| MYBPC3 | 24 | c.2374 T>C | p.Trp792Arg | 3 | Yes ^a |

| | | | | | |
|--------|----|------------------------------------|----------------------|----|-----|
| MYBPC3 | 24 | c.2382 Del G | p.Pro794Profs*26 | 1 | Yes |
| MYBPC3 | 25 | c.2431-2433 del AAG | p.Lys814del | 1 | Yes |
| MYBPC3 | 25 | c.2454 G>A | p.Trp818Ter | 1 | No |
| MYBPC3 | 25 | c.2455-2459 del ATGCG | p.Met819Alafs*12 | 1 | Yes |
| MYBPC3 | 25 | c.2459 G>A | p.Arg820Gln | 2 | Yes |
| MYBPC3 | 25 | c.2490-2491 ins T | p.His831Serfs*2 | 2 | Yes |
| MYBPC3 | 25 | c.2503 C>A | p.Arg835Ser | 1 | No |
| MYBPC3 | 25 | c.2527 G>T | p.Glu843Ter | 1 | Yes |
| MYBPC3 | 25 | c.2541 C>G | p.Tyr847Ter | 3 | Yes |
| MYBPC3 | 25 | c.2556 del C | p.Ile852Metfs*27 | 1 | Yes |
| MYBPC3 | 25 | c.2555-2556 ins T, subs G>T | p.Ile852Ilefs*32 | 2 | Yes |
| MYBPC3 | 25 | c.2558 del G | p.Gly853Alafs*26 | 1 | Yes |
| MYBPC3 | 26 | c.2670 G>A | p.Trp890Ter | 5 | No |
| MYBPC3 | 26 | c.2735 G>T | p.Gly912Val | 1 | No |
| MYBPC3 | 27 | c.2738 -2 A>G | | 1 | No |
| MYBPC3 | 27 | c.2748 G>A | p.Trp916Ter | 1 | Yes |
| MYBPC3 | 27 | c.2780-2781 ins CA | p.Thr927Thrfs*5 | 1 | Yes |
| MYBPC3 | 27 | c.2827 C>T | p.Arg943Ter | 3 | Yes |
| MYBPC3 | 27 | c.2864-2865 del CT | p.Pro955Argfs*95 | 10 | Yes |
| MYBPC3 | 27 | c.2873 C>T | p.Thr958Ile | 1 | Yes |
| MYBPC3 | 27 | c.2905 C>T | p.Gln969Ter | 1 | Yes |
| MYBPC3 | 27 | c.2905 +1 G>A | | 1 | Yes |
| MYBPC3 | 28 | c.2993 A>G | p.Gln998Arg | 1 | No |
| MYBPC3 | 29 | c.3064 C>T | p.Arg1022Cys | 1 | No |
| MYBPC3 | 29 | c.3065 G>C | p.Arg1022Pro | 1 | Yes |
| MYBPC3 | 29 | c.3083 C>G | p.Thr1028Ser | 1 | Yes |
| MYBPC3 | 29 | c.3124-3125 ins AA | p.Thr1042Lysfs*5 | 2 | Yes |
| MYBPC3 | 29 | c.3181 C>T | p.Gln1061Ter | 1 | Yes |
| MYBPC3 | 30 | c.3226-3227 ins T | p.Asp1076Valfs*6 | 2 | Yes |
| MYBPC3 | 30 | c.3233 G>A | p.Trp1078Ter | 1 | No |
| MYBPC3 | 30 | c.3288 del G | p.Glu1096Aspfs*93 | 2 | Yes |
| MYBPC3 | 30 | c.3330 + 2 T>G | | 17 | Yes |
| MYBPC3 | 31 | c.3372 C>A | p.Cys1124Ter | 1 | Yes |
| MYBPC3 | 31 | c.3337 T>A | p.Phe1113Ile | 2 | Yes |
| MYBPC3 | 31 | c.3407-3409 del ACT | p.Tyr1136Phefs*139 | 1 | No |
| MYBPC3 | 31 | c.3476-3479 dup TTAT | p.Ile1160Ilefs*10 | 1 | No |
| MYBPC3 | 32 | c.3512 del A | p.Asn1171Thrfs*18 | 1 | No |
| MYBPC3 | 32 | c.3548 T>G | p.Phe1183Cys | 1 | No |
| MYBPC3 | 32 | c.3565-3567 del AAC | p.Asn1189Argfs*86 | 1 | Yes |
| MYBPC3 | 32 | c.3572 C>T | p.Ser1191Leu | 1 | No |
| MYBPC3 | 32 | c.3611-3117 in GCTGCTT | p.Val1204Valfs*6 | 1 | Yes |
| MYBPC3 | 32 | c.3613 C>T | p.Arg1205Trp | 1 | Yes |
| MYBPC3 | 32 | c.3637 +1 G>A | | 1 | Yes |
| MYBPC3 | 33 | c.3697 C>T | p.Gln1233Ter | 9 | Yes |
| MYBPC3 | 33 | c.3716 A>G | p.Glu1239Gly | 1 | No |
| MYBPC3 | 33 | c.3739 G>A | p.Asp1247Asn | 1 | No |
| MYBPC3 | 33 | c.3742-3759 dup CGGGCCATCTATGTCTGC | p.Gly1248-Cys1253dup | 6 | Yes |

| | | | | | |
|--------|----|---------------------|-------------------|----|------------------|
| MYBPC3 | 33 | c.3746 G>T | p.Gly1249Val | 1 | Yes |
| MYBPC3 | 33 | c.3763 G>A | p.Ala1255Thr | 1 | Yes |
| MYBPC3 | 33 | c.3767-3769 del CCA | p.Thr1256Asnfs*19 | 1 | Yes |
| MYBPC3 | 33 | c.3771 C>A | p.Asn1257Lys | 2 | No |
| MYBPC3 | 33 | c.3775 C>T | p.Gln1259Ter | 1 | No |
| MYBPC3 | 33 | c.3791 G>A | p.Cys1264Tyr | 1 | Yes |
| MYBPC3 | 34 | c.3820 C>T | p.Asn1274Ter | 1 | No |
| MYBPC3 | 34 | c.3776 del | p.Ala1330Ter | 1 | No |
| MYBPC3 | 34 | c.3814 -1 G>A | | 1 | No |
| | | | | | |
| MYH7 | 3 | c.154 G>A | p.Val52Met | 1 | No |
| MYH7 | 4 | c.260 T>C | p.Ile87Thr | 1 | No |
| MYH7 | 4 | c.343 T>C | p.Tyr115His | 1 | Yes |
| MYH7 | 5 | c.428 G>A | p.Arg143Gln | 1 | Yes |
| MYH7 | 7 | c.595 G>A | p.Ala199Thr | 1 | No |
| MYH7 | 7 | c.619 A>C | p.Lys207Gln | 1 | Yes |
| MYH7 | 9 | c.789 A>G | p.Ile263Met | 1 | No |
| MYH7 | 11 | c.935 T>G | p.Phe312Cys | 1 | No |
| MYH7 | 12 | c.1046 T>C | p.Met349Thr | 2 | Yes |
| MYH7 | 12 | c.1063 G>A | p.Ala355Thr | 1 | Yes |
| MYH7 | 13 | c.1154 C>T | p.Ala385Val | 1 | No |
| MYH7 | 13 | c.1220 G>T | p.Gly407Val | 1 | No |
| MYH7 | 13 | c.1208 G>T | p.Arg403Leu | 1 | Yes |
| MYH7 | 13 | c.1208 G>A | p.Arg403Gln | 4 | Yes |
| MYH7 | 13 | c.1207 C>T | p.Arg403Trp | 1 | Yes |
| MYH7 | 13 | c.1210 G>A | p.Val404Met | 1 | No |
| MYH7 | 13 | c.1224 T>G | p.Asn408Lys | 1 | No |
| MYH7 | 13 | c.1231 G>A | p.Val411Ile | 1 | Yes |
| MYH7 | 14 | c.1283 C>T | p.Ala428Val | 1 | Yes |
| MYH7 | 14 | c.1319 T>C | p.Val440Ala | 1 | Yes |
| MYH7 | 14 | c.1318 G>A | p.Val440Met | 1 | No |
| MYH7 | 14 | c.1357 C>T | p.Arg453Cys | 1 | Yes |
| MYH7 | 15 | c.1491 G>T | p.Glu497Asp | 2 | Yes |
| MYH7 | 15 | c.1532 T>C | p.Ile511Thr | 1 | No |
| MYH7 | 15 | c.1544 T>G | p.Met515Arg | 1 | No |
| MYH7 | 15 | c.1570 A>C | p.Ile524Leu | 1 | No |
| MYH7 | 16 | c.1750 G>A | p.Gly584Ser | 2 | Yes |
| MYH7 | 16 | c.1816 G>A | p.Val606Met | 2 | Yes |
| MYH7 | 18 | c.1979 C>A | p.Thr660Asn | 1 | No |
| MYH7 | 18 | c.1987 C>T | p.Arg663Cys | 1 | Yes |
| MYH7 | 18 | c.1988 G>A | p.Arg663His | 14 | Yes ^a |
| MYH7 | 19 | c.2080 C>T | p.Arg694Cys | 2 | Yes |
| MYH7 | 19 | c.2146 G>A | p.Gly716Arg | 1 | Yes |
| MYH7 | 19 | c.2156 G>T | p.Arg719Leu | 1 | No |
| MYH7 | 19 | c.2156 G>A | p.Arg719Gln | 4 | Yes |
| MYH7 | 20 | c.2207 T>C | p.Ile736Thr | 1 | Yes |
| MYH7 | 20 | c.2206 A>G | p.Ile736Val | 1 | Yes |
| MYH7 | 20 | c.2221 G>C | p.Gly741Arg | 2 | Yes |

| | | | | | |
|------|----|---------------------|--------------|---|------------------|
| MYH7 | 20 | c.2221 G>T | p.Gly741Trp | 4 | Yes |
| MYH7 | 21 | c.2288 T>G | p.Val763Gly | 1 | Yes |
| MYH7 | 21 | c.2333 A>T | p.Asp778Val | 1 | Yes |
| MYH7 | 21 | c.2389 G>A | p.Ala797Thr | 2 | Yes ^a |
| MYH7 | 22 | c.2539-2541 Del AAG | p.Lys847del | 1 | No |
| MYH7 | 22 | c.2572 C>T | p.Arg858Cys | 1 | No |
| MYH7 | 22 | c.2594 A>T | p.Lys865Met | 1 | No |
| MYH7 | 22 | c.2606 G>A | p.Arg869His | 2 | No |
| MYH7 | 22 | c.2609 G>A | p.Arg870His | 1 | Yes |
| MYH7 | 23 | c.2681 A>G | p.GluE894Gly | 4 | No |
| MYH7 | 23 | c.2680 G>C | p.Glu894Gln | 1 | Yes |
| MYH7 | 23 | c.2700 T>A | p.Asp900Glu | 1 | No |
| MYH7 | 23 | c.2717 A>G | p.Asp906Gly | 4 | Yes |
| MYH7 | 23 | c.2722 C>G | p.Leu908Val | 8 | Yes |
| MYH7 | 23 | c.2791 G>A | p.Glu921Lys | 1 | No |
| MYH7 | 23 | c.2770 G>A | p.Glu924Lys | 3 | Yes |
| MYH7 | 23 | c.2791 G>A | p.Glu931Lys | 1 | No |
| MYH7 | 23 | c.2857 G>C | p.Asp953His | 1 | No |
| MYH7 | 25 | c.3133 C>T | p.Arg1045Cys | 1 | No |
| MYH7 | 25 | c.3152 C>T | p.Ala1051Val | 1 | No |
| MYH7 | 25 | c.3169 G>A | p.Gly1057Ser | 2 | No |
| MYH7 | 27 | c.3358 G>A | p.Glu1120Lys | 1 | No |
| MYH7 | 27 | c.3397 G>A | p.Glu1133Lys | 1 | No |
| MYH7 | 30 | c.4031 G>A | p.Arg1344Gln | 1 | No |
| MYH7 | 30 | c.4066 G>A | p.Glu1356Lys | 2 | No |
| MYH7 | 30 | c.4130 C>T | p.Thr1377Met | 4 | No |
| MYH7 | 32 | c.4377 G>T | p.Lys1459Asn | 2 | Yes ^a |
| MYH7 | 32 | c.4487 A>C | p.Glu1496Ala | 1 | No |
| MYH7 | 33 | c.4537 A>T | p.Thr1513Ser | 1 | No |
| MYH7 | 34 | c.4817 G>A | p.Arg1606His | 1 | No |
| MYH7 | 35 | c.5135 G>A | p.Agr1712Gln | 4 | Yes |
| MYH7 | 37 | c.5287 G>A | p.Ala1763Thr | 1 | No |
| MYH7 | 37 | c.5302 G>A | p.Glu1768Lys | 2 | No |
| MYH7 | 37 | c.5324 C>T | p.Thr1775Ile | 1 | No |
| MYH7 | 37 | c.5329 G>A | p.Ala1777Thr | 1 | Yes |
| MYH7 | 39 | c.5786 C>T | p.Thr1929Met | 1 | No |
| | | | | | |
| MYL2 | 2 | c.37 G>A | p.Ala13Thr | 1 | Yes |
| MYL2 | 2 | c.59 T>A | p.Met20Lys | 1 | No |
| MYL2 | 2 | c.64 G>A | p.Glu22Lys | 1 | Yes |
| MYL2 | 3 | c.103 A>G | p.Ile35Val | 1 | No |
| MYL2 | 4 | c.173 G>T | p.Arg58Leu | 2 | No |
| MYL2 | 4 | c.207 G>T | p.Met69Ile | 1 | No |
| MYL2 | 4 | c.239 C>A | p.Thr80Asn | 1 | No |
| MYL2 | 7 | c.488 A>C | p.Glu163A | 2 | No |
| MYL2 | 7 | c.496 G>C | p.Asp166His | 1 | No |
| | | | | | |
| MYL3 | 4 | c.461 G>A | p.Arg154His | 1 | Yes |

| | | | | | |
|--------------|----|-------------------|-------------|---|-----|
| <i>TNNC1</i> | 1 | c.23 C>T | p.Ala8Val | 1 | Yes |
| <i>TNNC1</i> | 4 | c.251 G>A | p.Cys84Tyr | 1 | Yes |
| <i>TNNC1</i> | 5 | c.402 G>T | p.Glu134Asp | 1 | Yes |
| <i>TNNC1</i> | 5 | c.435 C>A | p.Asp145Glu | 1 | Yes |
| <i>TNNI3</i> | 6 | c.318 G>C | p.Lys106Asn | 1 | No |
| <i>TNNI3</i> | 7 | c.407 G>A | p.Arg136Gln | 4 | No |
| <i>TNNI3</i> | 7 | c.422 G>A | p.Arg141Gln | 2 | Yes |
| <i>TNNI3</i> | 7 | c.485 G>A | p.Arg162Gln | 2 | Yes |
| <i>TNNI3</i> | 7 | c.493 G>T | p.Glu165Ter | 1 | No |
| <i>TNNI3</i> | 7 | c.497 C>T | p.Ser166Phe | 2 | Yes |
| <i>TNNI3</i> | 7 | c.526 G>A | p.Val176Met | 1 | No |
| <i>TNNI3</i> | 8 | c.557 G>A | p.Arg186Gln | 1 | No |
| | | | | | |
| <i>TNNT2</i> | 8 | c.236 T>C | p.Ile79Asn | 1 | Yes |
| <i>TNNT2</i> | 8 | c.257 A>C | p.Asp86Ala | 1 | Yes |
| <i>TNNT2</i> | 9 | c.274 C>T | p.Arg92Trp | 1 | Yes |
| <i>TNNT2</i> | 12 | c.571-573 del GAG | p.Gln191del | 1 | No |
| <i>TNNT2</i> | 16 | c.833 G>C | p.Arg278Pro | 1 | Yes |
| | | | | | |
| <i>TPM1</i> | 1 | c.82 G>A | p.Asp28Asn | 1 | No |
| <i>TPM1</i> | 2 | c.182 C>G | p.Ser61Cys | 1 | No |
| <i>TPM1</i> | 4 | c.345 -4 T>C | | 1 | No |
| <i>TPM1</i> | 5 | c.515 T>C | p.Ile172Thr | 1 | Yes |
| <i>TPM1</i> | 5 | c.554 T>G | p.Leu185Arg | 1 | Yes |
| <i>TPM1</i> | 6 | c.574 G>A | p.Glu192Lys | 1 | No |
| <i>TPM1</i> | 7 | c.644 C>T | p.Ser215Leu | 1 | No |
| <i>TPM1</i> | 9 | c.842 T>C | p.Met281Thr | 2 | Yes |

^aVariants seen in controls (frequency $\leq 0.01\%$) but significantly overrepresented in patients with HCM