|  |  |  |  |
| --- | --- | --- | --- |
|  | Gene | Disease | GDA score |
| 1 | KCNH2 | Cardiac Arrhythmia | 0.4 |
| 2 | HTR4 | Cardiac Arrhythmia | 0.3 |
| 3 | OPRK1 | Cardiac Arrhythmia | 0.3 |
| 4 | OPRL1 | Cardiac Arrhythmia | 0.3 |
| 5 | PTGS2 | Cardiac Arrhythmia | 0.3 |
| 6 | DRD2 | Tachyarrhythmia | 0.3 |
| 7 | HTR4 | Tachyarrhythmia | 0.3 |
| 8 | LMNA | Ventricular arrhythmia | 0.17 |
| 9 | LMNA | Atrial arrhythmia | 0.1 |
| 10 | LMNA | Cardiac Arrhythmia | 0.1 |
| 11 | GRIN2B | Hypsarrhythmia | 0.1 |
| 12 | LMNA | Primary atrial arrhythmia | 0.1 |
| 13 | LMNA | Supraventricular arrhythmia | 0.1 |
| 14 | KCNH2 | Ventricular arrhythmia | 0.04 |
| 15 | CHRM3 | Ventricular arrhythmia | 0.01 |
| 16 | CYP2D6 | Ventricular arrhythmia | 0.01 |

Table.1 predicted genes for arrhythmias caused by domperidone

|  |  |  |  |
| --- | --- | --- | --- |
|  | Gene | Disease | GDA score |
| 1 | LMNA | Sudden Cardiac Death | 0.4 |
| 2 | LMNA | Sudden Cardiac Arrest | 0.3 |
| 3 | LMNA | Sudden Cardiac Arrest | 0.3 |
| 4 | KCNH2 | Sudden Cardiac Death | 0.13 |
| 5 | KCNH2 | Cardiac Arrest | 0.12 |
| 6 | ATXN2 | Cardiac Arrest | 0.1 |
| 7 | NFKB1 | Cardiac Arrest | 0.02 |
| 8 | EGFR | Cardiac Arrest | 0.01 |
| 9 | LMNA | Cardiac Arrest | 0.01 |
| 10 | PTGS2 | Cardiac Arrest | 0.01 |
| 11 | CACNA1G | Cardiac Arrest | 0.01 |
| 12 | HDAC4 | Cardiac Arrest | 0.01 |
| 13 | GMNN | Cardiac Arrest | 0.01 |
| 14 | ADRA2B | Sudden Cardiac Death | 0.01 |

Table.2 predicted genes for cardiac arrest and death caused by domperidone

|  |  |  |  |
| --- | --- | --- | --- |
|  | Gene | Disease | GDA score |
| 1 | KCNH2 | Torsades de Pointes | 0.5 |
| 2 | ADRA2C | Torsades de Pointes | 0.01 |
| 3 | CYP2D6 | Torsades de Pointes | 0.01 |
| 4 | SLCO1B1 | Torsades de Pointes | 0.01 |

Table.3 predicted genes for Torsades de Pointes caused by domperidone

|  |  |  |  |
| --- | --- | --- | --- |
|  | Gene | Disease | GDA score |
| 1 | KCNH2 | Acquired long QT syndrome | 0.7 |
| 2 | KCNH2 | Congenital long QT syndrome | 0.7 |
| 3 | KCNH2 | Long QT Syndrome | 0.4 |
| 4 | KCNH2 | LONG QT SYNDROME 1/2, DIGENIC (disorder) | 0.3 |
| 5 | KCNH2 | Long Qt Syndrome 2 | 0.3 |
| 6 | ADRA1A | Long Qt Syndrome 2 | 0.3 |
| 7 | KCNH2 | LONG QT SYNDROME 2, ACQUIRED, SUSCEPTIBILITY TO | 0.3 |
| 8 | KCNH2 | LONG QT SYNDROME 2/3, DIGENIC | 0.2 |
| 9 | KCNH2 | LONG QT SYNDROME 2/5, DIGENIC (disorder) | 0.1 |
| 10 | KCNH2 | LONG QT SYNDROME 2/9, DIGENIC | 0.1 |
| 11 | KCNH2 | LONG QT SYNDROME 3 | 0.09 |
| 12 | KCNH2 | Long QT syndrome type 3 | 0.04 |
| 13 | KCNH2 | LONG QT SYNDROME, BRADYCARDIA-INDUCED | 0.01 |
| 14 | KCNH2 | Prolonged QT interval | 0.01 |

Table.4 predicted genes for long QT interval caused by domperidone

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Disease | SNP ID | consequence | alleles | SNP class | score |
|  | Arrhythmogenic Right Ventricular Dysplasia, Familial, 9 | rs1114167345 | missense variant | A/G | SNP | 0.7 |
|  | Arrhythmogenic Right Ventricular Dysplasia, Familial, 9 | rs727505038 | missense variant | G/C | SNP | 0.7 |
|  | Cardiac Arrhythmia | rs794728425 | frameshift variant | C/CGGGGCGATGGGAGCTGGCCG | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728426 | frameshift variant | GCGCG/GGCTTTT | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728428 | frameshift variant | TCGTCGGC/T | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728434 | frameshift variant | T/TGCAG | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728456 | frameshift variant | CG/C | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728457 | frameshift variant | GCTCTCCC/G | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728463 | frameshift variant | A/AGG | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728464 | frameshift variant | C/CGCCT | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728465 | frameshift variant | A/AG | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728467 | frameshift variant | G/GCCGCC,GCCGC | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728469 | frameshift variant | G/GCCCC,GCCC,GCC,GC | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728470 | frameshift variant | A/ACGTCGCCC,ACGTCGC | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728472 | frameshift variant | TG/T | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728476 | inframe insertion | C/CCTGCGCGAT | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728489 | frameshift variant | A/ACCAC | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728497 | frameshift variant | GC/G | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728499 | frameshift variant | AG/A | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728500 | frameshift variant | CG/C | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728506 | frameshift variant | GC/G | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728507 | frameshift variant | AC/A | in-del | 0.7 |
|  | Cardiac Arrhythmia | rs794728508 | frameshift variant | CA/C | in-del | 0.7 |
|  | Torsades de Pointes | rs1805123 | missense variant | T/A,C,G | SNP | 0.01 |
|  | Torsades de Pointes | rs189014161 | stop gained | G/A,C,T | SNP | 0.01 |
|  | Torsades de Pointes | rs201268831 | stop gained | C/A,T | SNP | 0.01 |
|  | Ventricular arrhythmia | rs56984562 | missense variant | C/A,G,T | SNP | 0.01 |

Table.5 predicted genetic variants for arrhythmias and Torsades de Pointes caused by domperidone

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Symbol | PDB/ SWISS-MODEL ID | Affinity Kcal/mol | Kd nM | Domperidone / DRD3 affinity nM |
|  | CACNA1G | O43497 (SM) | -5.7 | 64072 | 0.58 |
|  | CHRM3 | 4DAJ (PDB) | -9.7 | 73.11 |
|  | GRIN2B | 4PE5 (PDB) | -5.7 | 64072 |
|  | HDAC4 | 4CBY (PDB) | -8.6 | 471.22 |
|  | OPRL1 | 5DHG (PDB) | -8.5 | 558.2 |
|  | PTGS2 | 5F1A (PDB) | -10.1 | 37.13 |
|  | EGFR | 3BEL (PDB) | -7.7 | 2164.34 |

Table.6 predicted affinities for selected domperidone targets