

***Supplementary Material:***

**Novel two-step classifier for Torsdes de  
Pointes risk stratification from direct features**

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## 1 SUPPLEMENTARY DATA

### 2 1.1 Datasets

3 **Dataset 1: Mirams et al. 2011** (Mirams et al., 2011). The study analyzed 31 drugs for torsadogenic  
4 risk.  $IC_{50}$  values for drug-induced blocks of  $I_{Kr}$ ,  $I_{Na,fast}$  and  $I_{CaV}$  were considered. The TdP risk of the  
5 compound was defined based on the risk classification proposed in Redfern et al. (Redfern et al., 2003) with  
6 modifications in the risk category based on the updated literature. For binarized TdP definition, drugs in  
7 R1, R2 and R3 categories were considered TdP+ and the ones in R4 and R5 categories as TdP-. Integrated  
8 effect of multi-channel block were simulated using *in-silico* models of cardiac cells. The classifier was  
9 built on  $APD_{90}$  as the feature of interest.

	$IC_{50, I_{Kr}}$	$IC_{50, I_{CaV}}$	$IC_{50, I_{Na}}$	$EFTPC$	$Target$
Ajmaline	1040.0	71000	8200.0	1500.00	1.0
Amiodarone	30.0	270	4800.0	0.50	1.0
Amitriptyline	3280.0	11600	20000.0	41.00	0.0
Bepriidil	33.0	211	3700.0	33.00	1.0
Chlorpromazine	1470.0	-	4300.0	38.00	1.0
Cibenzoline	22600.0	30000	7800.0	976.00	0.0
Cisapride	6.5	-	14700.0	4.90	1.0
Desipramine	1390.0	1709	1520.0	108.00	0.0
Diltiazem	17300.0	450	9000.0	122.00	0.0
Diphenhydramine	5200.0	228000	41000.0	34.00	0.0
Dofetilide	5.0	60000	300000.0	2.00	1.0
Fluvoxamine	3100.0	4900	39400.0	377.00	0.0
Haloperidol	27.0	1700	7000.0	3.60	1.0
Imipramine	3400.0	8300	3600.0	106.00	0.0
Mexiletine	50000.0	100000	43000.0	4129.00	0.0
Mibefradil	1800.0	156	980.0	12.00	0.0
Nifedipine	275000.0	60	37000.0	7.70	0.0
Nitrendipine	10000.0	0.35	36000.0	3.02	0.0
Phenytoin	100000.0	103000	49000.0	4500.00	0.0
Pimozide	20.0	162	54.0	1.00	1.0
Prenylamine	65.0	1240	2520.0	17.00	1.0
Propafenone	440.0	1800	1190.0	241.00	0.0
Propranolol	2828.0	18000	2100.0	26.00	0.0
Quetiapine	5800.0	10400	16900.0	33.00	0.0
Quinidine	300.0	15600	16600.0	3237.00	1.0
Risperidone	150.0	73000	102000.0	1.81	0.0
Sertindole	14.0	8900	2300.0	1.59	1.0
Tedisamil	2500.0	-	20000.0	85.00	1.0
Terfenadine	8.9	375	971.0	9.00	1.0
Thioridazine	33.0	1300	1830.0	979.00	1.0
Verapamil	143.0	100	41500.0	81.00	0.0

**Table S1.**  $IC_{50}$ , Hill coefficients, EFTPC values and risk categorization for the (Mirams et al., 2011) dataset. 0: TdP- 1: TdP+

10 **Dataset 2: Kramer et al. 2013** (Kramer et al., 2013). *In-vitro* ion channel screening of drug-induced  
11 effects on  $I_{Kr}$ ,  $I_{Na,fast}$  and  $I_{CaV}$  was carried out for 55 compounds using automated patch clamp systems.  
12 Logistic regression classifiers were built on negative log transformed EFTPC indexes (i.e., ratio of  $IC_{50}$  for  
13 channel block to the EFTPC). Drugs in R1, R2, R3, CM1, CM2 and CM3 groups or drugs with package  
14 inserts containing a warning for TdP were defined as TdP+.

	$IC_{50, I_{Kr}}$	$IC_{50, I_{CaV}}$	$IC_{50, I_{Na}}$	$h_{I_{Kr}}$	$h_{I_{CaV}}$	$h_{I_{Na}}$	EFTPC	Target
Amiodarone	860.0	1900.0	15900.0	1.09	0.69	0.97	0.8	1.0
Astemizole	4.0	1100.0	3000.0	0.78	1.66	1.95	0.3	1.0
Bepidil	160.0	1000.0	2300.0	0.88	1.28	1.26	35.0	1.0
Ceftriaxone	445700.0	153800.0	555900.0	1.00	1.00	1.00	23170.0	0.0
Chlorpromazine	1500.0	3400.0	3000.0	1.40	1.73	1.14	38.0	1.0
Cilostazol	13800.0	91200.0	93700.0	0.91	1.00	1.00	128.0	1.0
Cisapride	20.0	11800.0	337000.0	1.04	1.00	1.00	3.0	1.0
Clozapine	2300.0	3600.0	15100.0	0.97	1.00	1.14	71.0	1.0
Dosatinib	24500.0	81100.0	76300.0	1.16	1.00	1.43	41.0	0.0
Diazepam	53200.0	30500.0	306400.0	1.07	0.89	1.00	29.0	0.0
Diltiazem	13200.0	760.0	22400.0	1.16	1.14	1.29	122.0	0.0
Disopyramide	14400.0	1036700.0	168400.0	0.91	1.00	1.09	742.0	1.0
Dofetilide	30.0	26700.0	162100.0	1.20	1.00	1.00	2.0	1.0
Donepezil	700.0	34300.0	38500.0	0.98	0.83	1.00	3.0	0.0
Droperidol	60.0	7600.0	22700.0	1.10	1.16	1.24	16.0	1.0
Duloxetine	3800.0	2800.0	5100.0	1.39	1.41	1.66	16.0	0.0
Flecainide	1500.0	27100.0	6200.0	0.88	0.97	1.14	753.0	1.0
Halofantrine	380.0	1900.0	331200.0	1.31	0.99	1.00	172.0	1.0
Haloperidol	40.0	1300.0	4300.0	1.18	1.38	1.58	4.0	1.0
Ibutilide	18.0	62500.0	42500.0	1.53	1.16	1.03	140.0	1.0
Lamivudine	2054000.0	54200.0	1571400.0	1.00	0.89	1.00	19540.0	0.0
Linezolid	1147200.0	105400.0	2644500.0	1.00	0.94	1.00	59110.0	0.0
Loratadine	6100.0	11400.0	28900.0	1.44	1.38	1.64	0.4	0.0
Methadone	3500.0	37400.0	31800.0	1.00	1.67	1.37	507.0	1.0
Metronidazole	1340200.0	177900.0	2073200.0	1.00	0.66	1.00	187000.0	0.0
Mibefradil	1700.0	510.0	5600.0	1.38	1.44	1.53	12.0	0.0
Mitoxantrone	539400.0	22500.0	93500.0	1.00	0.64	1.05	225.0	0.0
Moxifloxacin	86200.0	173000.0	1112000.0	0.94	1.00	1.00	10960.0	1.0
Nifedipine	44000.0	12.0	88500.0	0.80	1.02	0.71	8.0	0.0
Nilotinib	1000.0	17500.0	13300.0	0.96	1.00	2.11	172.0	1.0
Nitrendipine	24600.0	25.0	21600.0	0.82	0.78	1.25	3.0	0.0
Paliperidone	780.0	193900.0	109000.0	1.01	1.00	1.33	69.0	1.0
Paroxetine	1900.0	3900.0	9800.0	1.26	1.39	1.34	14.0	1.0
Pentobarbital	1433900.0	299000.0	2686000.0	1.00	1.38	1.00	5171.0	0.0
Phenytoin	147000.0	21900.0	72400.0	1.00	0.99	1.06	4360.0	0.0
Pimozide	40.0	240.0	1100.0	1.16	1.49	1.05	0.5	1.0
Piperacillin	3405100.0	1226000.0	2433800.0	1.00	1.00	1.00	1378000.0	0.0
Procainamide	272400.0	389500.0	746600.0	1.00	0.83	1.00	54180.0	1.0
Quinidine	720.0	6400.0	14600.0	1.06	0.68	1.22	3237.0	1.0
Raltegravir	782800.0	246700.0	842200.0	1.00	1.00	1.00	7000.0	0.0
Ribavirin	967000.0	622500.0	2997500.0	1.00	1.00	1.00	27880.0	0.0
Risperidone	260.0	34200.0	43400.0	0.99	0.79	0.98	2.0	1.0
Saquinavir	16900.0	1900.0	12100.0	1.72	1.15	2.34	130.0	0.0
Sertindole	33.0	6300.0	6900.0	1.25	1.29	1.19	2.0	1.0
Sitagliptin	174700.0	147100.0	1220800.0	1.00	1.00	1.00	442.0	0.0
Solifenacin	280.0	4300.0	1500.0	0.90	1.47	1.32	3.0	1.0
Sotalol	111400.0	193300.0	7013900.0	0.73	1.00	1.00	14690.0	1.0
Sparfloxacin	22100.0	88800.0	2555000.0	0.93	1.00	1.00	1766.0	1.0
Sunitinib	1200.0	33400.0	16500.0	1.00	1.09	1.22	13.0	1.0
Telbivudine	422700.0	713900.0	1095200.0	1.00	1.00	1.00	19720.0	0.0
Terfenadine	50.0	930.0	2000.0	1.25	1.80	1.81	9.0	1.0
Terodiline	650.0	4800.0	7400.0	1.02	1.01	1.23	145.0	1.0
Thioridazine	500.0	3500.0	1400.0	0.98	1.35	1.11	980.0	1.0
Verapamil	250.0	200.0	32500.0	0.89	0.80	1.33	88.0	0.0
Voriconazole	490900.0	414200.0	1550500.0	1.00	1.00	1.00	7563.0	1.0

**Table S2.**  $IC_{50}$ , Hill coefficients, EFTPC values and risk categorization for the (Kramer et al., 2013) dataset. Binary risk categorization - 0: TdP- 1: TdP+

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15 **Dataset 3: Okada et al. 2015** (Okada et al., 2015). *In-vitro* ion channel assay was carried out on the  
16 Chinese hamster ovary cells to examine the modulation of six ion channel currents ( $I_{Kr}$ ,  $I_{Na,fast}$ ,  $I_{CaV}$ ,  
17  $I_{to}$ ,  $I_{Ks}$ , and  $I_{K1}$ ) under the influence of 12 drugs. Late sodium current block was examined for Ranolazine  
18 only. The TdP risk of the drugs was defined based on the categories in Redfern et al. (Redfern et al., 2003)  
19 with compounds in R1, R2 and R3 categories as TdP+. For the drugs not listed in Redfern et al., other  
20 literature was utilized to determine the drugs TdP risk. A 3-D heart model coupled with a torso model was  
21 utilized to simulate the drug-induced effects at drug concentrations ranging from EFTPC to 200x EFTPC.  
22 Drugs were classified as torsadogenic if arrhythmias were observed in the computational model below  
23 200x EFTPC drug concentrations.

	$IC_{50,I_{K_r}}$	$IC_{50,I_{C_{\alpha V}}}$	$IC_{50,I_{N_{\alpha,peak}}}$	$IC_{50,I_{K_s}}$	$IC_{50,I_{K_1}}$	$IC_{50,I_{I_{\alpha}}}$	$IC_{50,I_{N_{\alpha,late}}}$	$h_{I_{K_r}}$	$h_{I_{C_{\alpha V}}}$	$h_{I_{N_{\alpha,peak}}}$	$h_{I_{K_s}}$	$h_{I_{K_1}}$	$h_{I_{I_{\alpha}}}$	$h_{I_{N_{\alpha,late}}}$	EFTPC	Target
Amiodarone	755.70	4832	975.4	-	-	-	-	0.817	0.850	0.746	1.000	1.0	1.000	1.0	0.775	0.0
Astemizole	28.12	987.8	1862	-	-	-	-	1.745	2.531	1.532	1.000	1.0	1.000	1.0	0.288	1.0
Bepridil	130.20	1455	646.5	6031.2	-	4521	-	1.461	2.317	1.155	1.779	1.0	1.853	1.0	34.630	1.0
Cisapride	14.72	4278	2072	-	-	-	-	1.326	1.378	0.894	1.000	1.0	1.000	1.0	2.579	1.0
Dofetilide	38.28	184100	124500	-	-	-	-	1.983	0.897	0.329	1.000	1.0	1.000	1.0	1.600	1.0
E4031	26.27	713700	737300	-	-	-	-	1.996	0.454	0.334	1.000	1.0	1.000	1.0	5.668	1.0
Moxifloxacin	135800.00	469700	2.721e+06	2.011e+06	-	2.624e+06	-	0.910	1.549	2.173	1.173	1.0	0.687	1.0	10950.000	0.0
Quinidine	637.70	7731	24790	73330	-	1906	-	1.012	0.823	1.300	1.336	1.0	1.198	1.0	3235.000	1.0
Ranolazine	3930.00	118300	41115	-	-	433510	26260	0.710	0.894	0.904	1.000	1.0	1.309	1.5	2310.000	0.0
Sotalol	356400.00	-	-	-	-	-	-	1.023	1.000	1.000	1.000	1.0	1.000	1.0	14680.000	1.0
Terfenadine	98.52	861.5	479.8	-	-	-	-	1.176	2.091	0.516	1.000	1.0	1.000	1.0	9.000	1.0
Verapamil	201.30	333.1	4272	29880	-	3523	-	1.040	1.148	0.850	0.933	1.0	0.992	1.0	87.970	0.0

**Table S3.**  $IC_{50}$ , Hill coefficients, EFTPC values and risk categorization for the (Okada et al., 2015) dataset. Target column represents the binary risk categorization assigned in Okada et al., 0: TdP- 1: TdP+

24 **Dataset 4: Lancaster and Sobie. 2016** (Lancaster and Sobie, 2016). The dataset consist of 86 compounds  
25 (data from Dataset 1 and 2 combined) with  $IC_{50}$  values for  $I_{Kr}$ ,  $I_{Na,fast}$  and  $I_{CaV}$ . Drugs in the group  
26 CM1 in AZCERT and the category CH1 in (Champeroux et al., 2005) were defined as torsadogenic (TdP+).  
27 Drugs in the AZCERT CM2 and CM3 groups were defined as torsadogenic (TdP+) only if a warning  
28 of TdP appeared in the package insert. The effects of drug-induced multi-channel block were simulated  
29 using computational models of the cardiac cells. Classifiers built on  $APD_{50}$  and  $Diastolic - Ca^{2+}$  levels  
30 provided the highest classification accuracy scores.



	$IC_{50, I_{Kr}}$	$IC_{50, I_{CaV}}$	$IC_{50, I_{Na}}$	$h_{I_{Kr}}$	$h_{I_{CaV}}$	$h_{I_{Na}}$	EFTPC	Target
Ajmaline	1040.0	71000	8200.0	1.00	1.00	1.00	1500.00	1.0
Amiodarone1	860.0	1900	15900.0	1.09	0.69	0.97	0.80	1.0
Amiodarone2	30.0	270	4800.0	1.00	1.00	1.00	0.50	1.0
Amitriptyline	3280.0	11600	20000.0	1.00	1.00	1.00	41.00	0.0
Astemizole	4.0	1100	3000.0	0.78	1.66	1.95	0.30	1.0
Bepriidil1	160.0	1000	2300.0	0.88	1.28	1.26	35.00	1.0
Bepriidil2	33.0	211	3700.0	1.00	1.00	1.00	33.00	1.0
Ceftriaxone	445700.0	153800	555900.0	1.00	1.00	1.00	23170.00	0.0
Chlorpromazine1	1500.0	3400	3000.0	1.40	1.73	1.14	38.00	1.0
Chlorpromazine2	1470.0	-	4300.0	1.00	1.00	1.00	38.00	1.0
Cibenzoline	22600.0	30000	7800.0	1.00	1.00	1.00	976.00	0.0
Cilostazol	13800.0	91200	93700.0	0.91	1.00	1.00	128.00	1.0
Cisapride1	20.0	11800	337000.0	1.04	1.00	1.00	3.00	1.0
Cisapride2	6500.0	-	14700.0	1.00	1.00	1.00	4.90	1.0
Clozapine	2300.0	3600	15100.0	0.97	1.00	1.14	71.00	1.0
Dosatinib	24500.0	81100	76300.0	1.16	1.00	1.43	41.00	0.0
Desipramine	1390.0	1709	1520.0	1.00	1.00	1.00	108.00	0.0
Diazepam	53200.0	30500	306400.0	1.07	0.89	1.00	29.00	0.0
Diltiazem1	13200.0	760	22400.0	1.16	1.14	1.29	122.00	0.0
Diltiazem2	17300.0	450	9000.0	1.00	1.00	1.00	122.00	0.0
Diphenhydramine	5200.0	228000	41000.0	1.00	1.00	1.00	34.00	0.0
Disopyramide	14400.0	1.0367e+06	168400.0	0.91	1.00	1.09	742.00	1.0
Dofetilide1	30.0	26700	162100.0	1.20	1.00	1.00	2.00	1.0
Dofetilide2	5.0	60000	300000.0	1.00	1.00	1.00	2.00	1.0
Donepezil	700.0	34300	38500.0	0.98	0.83	1.00	3.00	0.0
Droperidol	60.0	7600	22700.0	1.10	1.16	1.24	16.00	1.0
Duloxetine	3800.0	2800	5100.0	1.39	1.41	1.66	16.00	0.0
Flecainide	1500.0	27100	6200.0	0.88	0.97	1.14	753.00	1.0
Fluvoxamine	3100.0	4900	39400.0	1.00	1.00	1.00	377.00	0.0
Halofantrine	380.0	1900	331200.0	1.31	0.99	1.00	172.00	1.0
Haloperidol1	40.0	1300	4300.0	1.18	1.38	1.58	4.00	1.0
Haloperidol2	27.0	1700	7000.0	1.00	1.00	1.00	3.60	1.0
Ibutilide	18.0	62500	42500.0	1.53	1.16	1.03	140.00	1.0
Imipramine	3400.0	8300	3600.0	1.00	1.00	1.00	106.00	1.0
Lamivudine	2054000.0	54200	1571400.0	1.00	0.89	1.00	19540.00	0.0
Linezolid	1147200.0	105400	2644500.0	1.00	0.94	1.00	59110.00	0.0
Loratadine	6100.0	11400	28900.0	1.44	1.38	1.64	0.40	0.0
Methadone	3500.0	37400	31800.0	1.00	1.67	1.37	507.00	1.0
Metronidazole	1340200.0	177900	2073200.0	1.00	0.66	1.00	187000.00	0.0
Mexiletine	50000.0	100000	43000.0	1.00	1.00	1.00	4129.00	0.0
Mibefradil1	1700.0	510	5600.0	1.38	1.44	1.53	12.00	0.0
Mibefradil2	1800.0	156	980.0	1.00	1.00	1.00	12.00	0.0
Mitoxantrone	539400.0	22500	93500.0	1.00	0.64	1.05	225.00	0.0
Moxifloxacin	86200.0	173000	1112000.0	0.94	1.00	1.00	10960.00	1.0
Nifedipine1	44000.0	12	88500.0	0.80	1.02	0.71	8.00	0.0
Nifedipine2	275000.0	60	37000.0	1.00	1.00	1.00	7.70	0.0
Nilotinib	1000.0	17500	13300.0	0.96	1.00	2.11	172.00	1.0
Nitrendipine1	24600.0	25	21600.0	0.82	0.78	1.25	3.00	0.0
Nitrendipine2	10000.0	0.35	36000.0	1.00	1.00	1.00	3.02	0.0
Paliperidone	780.0	193900	109000.0	1.01	1.00	1.33	69.00	1.0
Paroxetine	1900.0	3900	9800.0	1.26	1.39	1.34	14.00	1.0
Pentobarbital	1433900.0	299000	2686000.0	1.00	1.38	1.00	5171.00	0.0
Phenytoin1	147000.0	21900	72400.0	1.00	0.99	1.06	4360.00	0.0
Phenytoin2	100000.0	103000	49000.0	1.00	1.00	1.00	4500.00	0.0
Pimozide1	40.0	240	1100.0	1.16	1.49	1.05	0.50	1.0
Pimozide2	20.0	162	54.0	1.00	1.00	1.00	1.00	1.0
Piperacillin	3405100.0	1.226e+06	2433800.0	1.00	1.00	1.00	1378000.00	0.0
Prenylamine	65.0	1240	2520.0	1.00	1.00	1.00	17.00	1.0
Procainamide	272400.0	389500	746600.0	1.00	0.83	1.00	54180.00	1.0
Propafenone	440.0	1800	1190.0	1.00	1.00	1.00	241.00	1.0
Propranolol	2828.0	18000	2100.0	1.00	1.00	1.00	26.00	0.0
Quetiapine	5800.0	10400	16900.0	1.00	1.00	1.00	33.00	0.0
Quinidine1	720.0	6400	14600.0	1.06	0.68	1.22	3237.00	1.0
Quinidine2	300.0	15600	16600.0	1.00	1.00	1.00	924.00	1.0
Raltegravir	782800.0	246700	842200.0	1.00	1.00	1.00	7000.00	0.0
Ribavirin	967000.0	622500	2997500.0	1.00	1.00	1.00	27880.00	0.0
Risperidone1	260.0	34200	43400.0	0.99	0.79	0.98	2.00	1.0
Risperidone2	150.0	73000	102000.0	1.00	1.00	1.00	1.81	1.0
Saquinavir	16900.0	1900	12100.0	1.72	1.15	2.34	130.00	0.0
Sertindole1	33.0	6300	6900.0	1.25	1.29	1.19	2.00	1.0
Sertindole2	14.0	8900	2300.0	1.00	1.00	1.00	1.59	1.0
Sitagliptin	174700.0	147100	1220800.0	1.00	1.00	1.00	442.00	0.0
Solifenacin	280.0	4300	1500.0	0.90	1.47	1.32	3.00	1.0
Sotalol	111400.0	193300	7013900.0	0.73	1.00	1.00	14690.00	1.0
Sparfloxacin	22100.0	88800	2555000.0	0.93	1.00	1.00	1766.00	1.0
Sunitinib	1200.0	33400	16500.0	1.00	1.09	1.22	13.00	1.0
Tedisamil	2500.0	-	20000.0	1.00	1.00	1.00	85.00	1.0
Telbivudine	422700.0	713900	1095200.0	1.00	1.00	1.00	19720.00	0.0
Terfenadine1	50.0	930	2000.0	1.25	1.80	1.81	9.00	1.0
Terfenadine2	8.9	375	971.0	1.00	1.00	1.00	9.00	1.0
Terodiline	33.0	6300	6900.0	1.02	1.01	1.23	2.00	1.0
Thioridazine1	500.0	3500	1400.0	0.98	1.35	1.11	980.00	1.0
Thioridazine2	33.0	1300	1830.0	1.00	1.00	1.00	208.00	1.0
Verapamil1	250.0	200	32500.0	0.89	0.80	1.33	88.00	0.0
Verapamil2	143.0	100	41500.0	1.00	1.00	1.00	81.00	0.0
Voriconazole	490900.0	414200	1550500.0	1.00	1.00	1.00	7563.00	1.0

**Table S4.**  $IC_{50}$ , Hill coefficients, EFTPC values and risk categorization for the (Lancaster and Sobie, 2016) dataset. Target column represents the binary risk categorization assigned in Lancaster and Sobie., 0: TdP- 1: TdP+

31 **Dataset 5: Crumb et al. 2016** (Crumb et al., 2016). 30 compounds were analyzed using *in-vitro* ion  
32 channel screening for their potencies to block seven ion-channel currents ( $I_{Kr}$ ,  $I_{Na,fast}$ ,  $I_{NaL}$ ,  $I_{CaV}$ ,  $I_{to}$ ,  
33  $I_{Ks}$ , and  $I_{K1}$ ) using manual patch clamps. Effects of the block of different ion channel currents for these  
34 12 (out of 30) drugs were compared, and important roles of  $I_{NaL}$  and  $I_{CaV}$ , in addition to  $I_{Kr}$ , in TdP risk  
35 prediction were suggested. However, no statistical analysis was performed.

	$IC_{50,JKr}$	$IC_{50,ICaV}$	$IC_{50,JKs,peak}$	$IC_{50,JKs}$	$IC_{50,JK1}$	$IC_{50,JKo}$	$IC_{50,JKs,late}$	$h_{JKr}$	$h_{ICaV}$	$h_{JKs,peak}$	$h_{JKs}$	$h_{JK1}$	$h_{JKo}$	$h_{JKs,L}$	EFTPC	Target
Amiodarone	941	1281	4577	5666	-	3758	9423	0.6	0.6	0.7	1.0	1.0	0.4	0.4	0.7	1.0
Amiripryline	3660	1291	5760	2737	-	2543	4433	1.0	1.0	1.3	0.5	1.0	0.4	0.5	36.4	0.0
Azithromycin	70796	-	-	470131	-	88764	189128	0.5	1.0	1.0	1.4	1.0	0.5	1.9	1937.0	1.0
Bepriidil	149	2808	2929	28628.3	-	8594	1814	0.9	0.6	1.2	0.7	1.0	3.5	1.4	31.5	1.0
Chloroquine	6889	-	80000	-	10595	-	70000	0.6	1.0	1.0	1.0	0.8	1.0	1.0	249.5	1.0
Chlorpromazine	1118	8192	4536	-	9270	-	4560	0.9	0.8	2.0	1.0	0.7	0.4	0.9	34.5	1.0
Cibenzoline	2097	-	21752	-	-	-	46581	0.9	1.0	1.2	1.0	1.0	1.0	0.6	673.0	0.0
Cisapride	12	9.25808e+06	1e+10	8.11929e+07	29498	219112	-	1.3	0.4	1.0	0.3	0.5	0.2	1.0	2.6	1.0
Diltiazem	6569	112	110859	-	-	2.8e+09	21862.5	0.8	0.7	0.7	1.0	1.0	0.2	0.7	127.5	0.0
Dofetilide	1	260.3	-	-	394.3	18.8	753160	0.6	1.0	0.9	1.0	0.8	0.8	1.0	2.1	1.0
Flecainide	692	25599	6677	-	-	9266	18870	0.8	1.4	1.9	1.0	1.0	0.7	0.6	752.9	1.0
Lidocaine	-	-	-	-	-	-	10790	1.0	1.0	1.0	1.0	1.0	1.0	1.3	2560.0	0.0
Lopinavir	5170	15601	-	-	-	-	-	1.2	1.0	1.0	1.0	1.0	1.0	1.0	703.7	1.0
Mexiletine	80000	40000	-	-	-	-	-	1.0	1.0	1.0	1.0	1.0	1.0	1.4	2503.2	0.0
Mibefradil	307	652	5866	-	-	-	3628	0.9	1.1	1.0	1.0	1.0	1.0	1.2	10.6	0.0
Moxifloxacin	93041	-	-	-	-	-	382337	0.6	1.0	1.0	1.0	1.0	1.0	1.1	3562.5	1.0
Nilotinib	91	-	-	-	-	-	4706	0.8	1.0	1.0	1.0	1.0	1.0	1.0	60.4	1.0
Ondansetron	1492	22551	57666.4	-	-	1.02338e+06	19181	1.0	0.8	1.0	0.7	1.0	1.0	1.0	358.5	1.0
Propafenone	481	1550	3886	-	-	-	4036	0.8	0.9	1.0	1.0	1.0	1.0	0.9	131.0	1.0
Quinidine	343	51592.3	12329	4899	3.95899e+07	3487	9417	1.0	1.0	1.5	1.4	0.4	1.3	1.0	842.9	1.0
Quinine	5170	27178	24151	37453	-	79254	11053	1.0	1.0	1.1	1.1	1.0	1.0	0.4	3956.7	1.0
Ranolazine	6490	-	-	3.6155e+07	-	-	7884	0.8	1.0	1.0	0.5	1.0	1.0	0.9	1948.2	0.0
Ritonavir	5157	8228	17000	-	-	-	7175	1.0	1.3	1.0	1.0	1.0	1.0	0.7	436.9	1.0
Rufinamide	-	264448	-	-	-	-	-	1.0	0.9	1.0	1.0	1.0	1.0	1.0	83126.9	0.0
Saquinavir	3477	3161	15568	-	-	-	7088	1.0	1.4	1.2	1.0	1.0	1.0	1.2	417.2	1.0
Sertindole	11	-	-	-	-	-	-	0.8	1.0	1.0	1.0	1.0	1.0	1.0	1.6	1.0
Sotalol	86369	7.06153e+06	1.14e+09	4.22186e+06	3.05026e+06	4.31435e+07	-	0.9	0.9	0.5	1.2	1.2	0.7	1.0	14686.4	1.0
Terfenadine	19	700	4803	399754	-	239961	20056	0.6	0.7	1.0	0.5	1.0	0.3	0.6	9.0	1.0
Toremifene	3500	-	-	-	-	-	4000	1.0	1.0	1.0	1.0	1.0	1.0	1.0	26.3	1.0
Verapamil	499	202	-	-	3.49e+08	13429.2	7028	1.1	1.1	1.0	1.0	0.3	0.8	1.0	45.0	0.0

**Table S5.**  $IC_{50}$ , Hill coefficients, EFTPC values, and risk categorization for the (Crumb et al., 2016) dataset. Binary risk categorization based on table (Table S11), 0: TdP- 1: TdP+

36 **Dataset 6: Ando et al. 2017** (Ando et al., 2017). Drug-induced effects of 57 compounds were evaluated  
37 through recording of extracellular field potentials in human induced pluripotent stem cell-derived  
38 cardiomyocytes (hiPSC-CMs). A two-dimensional risk map with risk potential according to the degree of  
39 FP duration prolongation and early afterdepolarization occurrence in one dimension and risk margin based  
40 on the ratio of the free concentration of the drug in medium and EFPTC in another dimension provided the  
41 high classification accuracies.  $IC_{50}$  values for drug-induced blocks of  $I_{Kr}$ ,  $I_{Na,fast}$  and  $I_{CaL}$  were also  
42 provided. Drugs were classified into three categories (high, intermediate, and low risk); and 36 drugs that  
43 were assigned to low and high risk were validated against the CredibleMeds categorization. Drugs in CM1  
44 category were considered TdP+ for validation, and the remainder were considered TdP-.

	$IC_{50, I_{Kr}}$	$IC_{50, I_{CaV}}$	$IC_{50, I_{Na}}$	EFTPC	Target
Ajmaline	1040.0	71000	8200	25.00	0.0
Amiodarone	860.0	1900	15900	150.00	1.0
Bepiridil	160.0	1000	2300	35.00	1.0
Sotalol	111400.0	193300	7.0139e+06	13000.00	1.0
Diltiazem	13200.0	760	22400	180.00	0.0
Disopyramide	14400.0	1.0367e+06	168400	750.00	1.0
Dofetilide	30.0	26700	162100	2.00	1.0
Dronedarone	59.0	400	700	1.80	1.0
E4031	14.0	-	-	8.40	1.0
Flecainide	1500.0	27100	6200	1200.00	1.0
Ibutilide	18.0	62500	42500	150.00	1.0
Metoprolol	145000.0	-	40000	450.00	0.0
Mexiletine	62200.0	125000	38000	5400.00	0.0
Mibefradil	1700.0	510	5600	63.00	0.0
Nifedipine	44000.0	12	88500	10.00	0.0
Nitrendipine	24600.0	25	21600	3.00	0.0
Prenylamine	65.0	1200	2500	3.50	1.0
Procainamide	272400.0	389500	746600	52000.00	1.0
Quinidine	720.0	6400	14600	3200.00	1.0
Ranolazine	11500.0	296000	294000	2300.00	3.0
Sematilide	25000.0	-	-	4400.00	1.0
Verapamil	250.0	200	32500	92.00	0.0
Astemizole	4.0	1100	3000	0.51	1.0
Chlorpheniramine	13000.0	-	-	12.00	0.0
Diphenhydramine	5200.0	228000	41000	57.00	3.0
Levocetirizine	100000.0	-	-	63.00	0.0
Loratadine	6100.0	11400	28900	0.60	0.0
Terfenadine	50.0	930	2000	9.50	1.0
Famotidine	10000.0	-	-	330.00	2.0
Cisapride	20.0	11800	337000	2.60	1.0
Dolasetron	5950.0	-	38000	360.00	2.0
Domperidone	160.0	-	5600	27.00	1.0
Ondansetron	1500.0	22600	20000	77.00	1.0
Terodiline	650.0	4800	7400	240.00	1.0
Tolterodine	17.0	143	1000	0.14	2.0
Aspirin	100000000.0	-	-	7700.00	0.0
Cilostazol	13800.0	91200	93700	140.00	1.0
Amitriptyline	5800.0	11600	1600	41.00	3.0
Chlorpromazine	1500.0	3400	3000	38.00	1.0
Clozapine	2300.0	3600	15100	320.00	2.0
Droperidol	60.0	7600	22700	21.00	1.0
Haloperidol	40.0	1300	4300	3.60	1.0
Paliperidone	780.0	193900	109000	30.00	2.0
Pimozide	40.0	240	1100	0.43	1.0
Risperidone	260.0	34200	43400	15.00	2.0
Sertindole	33.0	6300	6900	1.60	2.0
Thioridazine	500.0	3500	1400	45.00	1.0
Ziprasidone	240.0	-	170000	7.30	3.0
Clarithromycin	32900.0	-	-	3300.00	1.0
Erythromycin	38900.0	-	-	12000.00	1.0
Gatifloxacin	130000.0	-	-	9000.00	1.0
Moxifloxacin	86200.0	173000	1.112e+06	5600.00	1.0
Sparfloxacin	22100.0	88800	2.555e+06	1900.00	1.0
Quinine	42200.0	14000	17800	4300.00	3.0
Nilotinib	1000.0	17500	13300	170.00	2.0
Tamoxifen	777.0	-	-	18.00	2.0
Vandetanib	400.0	-	-	110.00	1.0

**Table S6.**  $IC_{50}$ , Hill coefficients, EFTPC values, drug trapping parameter and risk categorization for the (Ando et al., 2017) dataset. Target column represents the risk categorization according to crediblemeds, 0: Drugs not present in the CredibleMeds database. 1: Drugs with known risk (CM1) 2: Drugs with possible risk (CM2) 3: Drugs with conditional risk (CM3). Binarized definition assigned in Ando. et al., TdP+: 1 TdP-: 0,2,3

45 **Dataset 7: Li et al. 2017.** A subset consisting of 12 of the 30 drugs in Dataset 5, categorized into  
46 low (CP3), intermediate (CP2) and high risk (CP1) categories (Fermini et al., 2016; Colatsky et al.,  
47 2016), were analyzed using the OHR model that was modified to include dynamics drug-hERG channel  
48 interactions.  $IC_{50}$  for the hERG channels were measured while the  $IC_{50}$  for other channels were taken from  
49 the (Crumb et al., 2016). The summation of the ratio of the area under the curve of calcium and late sodium  
50 current traces obtained at steady state action potential simulation in the presence to the absence of the  
51 drugs (i.e.,  $\frac{AUCI_{NaL,drug}}{AUCI_{NaL,control}} + \frac{AUCI_{CaV,drug}}{AUCI_{CaV,control}}$ ). In this study, we developed our classifier using the identical  
52 ternary categories as in (Li et al., 2017) as well as binary TdP definitions. For binary TdP definition, we  
53 merged high and intermediate risk drugs (CP1 and CP2 categories) to represent drugs that are torsadogenic  
54 (TdP+). Drugs with low TdP risk (CP3 category) were considered to be non-torsadogenic (TdP-).

	$IC_{50,I_{K-}}$	$IC_{50,I_{CaV}}$	$IC_{50,I_{Na,peak}}$	$IC_{50,I_{Ks}}$	$IC_{50,I_{K1}}$	$IC_{50,I_{to}}$	$IC_{50,I_{Na,late}}$	$h_{I_{K-}}$	$h_{I_{CaV}}$	$h_{I_{Na,peak}}$	$h_{I_{Ks}}$	$h_{I_{K1}}$	$h_{I_{to}}$	$h_{I_{Na,late}}$	EFTPC	Target	Vtrap
Bepridil	50.0	2808	2929.3	28628.3	-	8594	1814	0.9	0.6	1.2	0.7	1.0	3.5	1.4	33.0	2.0	-54.93
Chlorpromazine	929.2	8192	4535	-	9269.9	1.76167e+07	4560	0.8	0.8	2.0	1.0	0.7	0.4	0.9	38.0	1.0	-14.00
Cisapride	10.0	9.25808e+06	1e+10	8.11929e+07	29498	219112	-	0.7	0.4	1.0	0.3	0.5	0.2	1.0	2.6	1.0	-199.00
Diltiazem	13150.0	112	110859	-	-	2.8e+09	21868.5	0.9	0.7	0.7	1.0	1.0	0.2	0.7	122.0	0.0	-90.00
Dofetilide	4.9	260.3	380.5	-	394.3	18.8	753160	0.9	1.2	0.9	1.0	0.8	0.8	0.3	2.0	2.0	-1.00
Mexiletine	28880.0	38243.6	-	-	-	-	8956.8	0.9	1.0	1.0	1.0	1.0	1.0	1.4	4129.0	0.0	-86.00
Ondansetron	1320.0	22551	57666.4	569807	-	1.02338e+06	19181	0.9	0.8	1.0	0.7	1.0	1.0	1.0	139.0	1.0	-82.00
Quinidine	992.0	51592.3	12329	4899	3.95899e+07	3487.4	9417	0.8	0.6	1.5	1.4	0.4	1.3	1.3	3237.0	2.0	-64.70
Ranolazine	8270.0	-	68774	3.6155e+07	-	-	7884	0.9	1.0	1.4	0.5	1.0	1.0	0.9	1948.2	0.0	-94.00
Sotalol	110600.0	7.06153e+06	1.14e+09	4.22186e+06	3.05026e+06	4.31435e+07	-	0.8	0.9	0.5	1.2	1.2	0.7	1.0	14690.0	2.0	-55.00
Terfenadine	23.0	700	4803.2	399754	-	239961	20056	0.6	0.7	1.0	0.5	1.0	0.3	0.6	4.0	1.0	-77.00
Verapamil	288.0	201	-	-	3.49e+08	13429.2	7028	1.0	1.1	1.0	1.0	0.3	0.8	1.0	81.0	0.0	-100.00

**Table S7.**  $IC_{50}$ , Hill coefficients, EFTPC values, drug trapping parameters and risk categorization for the (Li et al., 2017) dataset. Target column represents the tertiary risk categorization assigned in Li et al., 0: Low Risk(CP3) 1: Intermediate Risk(CP2) 2: High Risk (CP1). Binary risk categorization used for this study, TdP+: 1 and 2, TdP-: 0.

55 **Dataset 8: Merged Dataset.** In this study we also combine Datasets 1, 2, 3, 5, 6, and 7 to form a single  
56 merged dataset. Drug-induced block of different channels at drug's EFTPC and at drug concentrations  
57 equal to hERG  $IC_{60}$  for the merged dataset is reported in the Table S8 and the Table S9. The merged  
58 dataset comprises of 197 drugs of which 95 were unique. Several drugs were common across more than  
59 one datasets. The *in-vitro* block values of the channels and maximum EFTPCs were different for different  
60 datasets; we analyzed the common drugs across the datasets as distinct compounds to build/test the  
61 classifiers. For the merged dataset, we carried out simulation for two different conditions. First, considering  
62 the block of hERG and *CaV* channels. Second, considering the block of all the available channels for the  
63 particular drug. Taking into account the block of other ion-channels in addition to hERG and *CaV* for TdP  
64 risk classification did not result in significant improvement in the classification accuracies.



	<i>EFTPC</i>	<i>Source</i>	$I_{CaV}$	$I_{K1}$	$I_{Kr}$	$I_{Ks}$	$I_{NaL}$	$I_{Na}$	<i>Ratio</i>	<i>target</i>	$I_{to}$	<i>vtrap</i>	<i>CMt1</i>	$t2$	$t3$	
Ajmaline	1500.00	Mirams et al.	2.07	-	59.06	-	-	15.46	0.69	1	-	-	0	0	0	0
Ajmaline	25.00	Ando et al.	0.04	-	2.35	-	-	0.30	41.60	1	-	-	0	0	0	0
Amiodarone	150.00	Ando et al.	7.32	-	14.85	-	-	0.93	5.73	1	-	-	1	1	1	1
Amiodarone	0.77	Okada et al.	0.06	0	0.36	0	0	0.48	975.47	1	0	-	1	1	1	1
Amiodarone	0.80	Kramer et al.	0.47	-	0.05	-	-	0.01	1075.00	1	-	-	1	1	1	1
Amiodarone	0.70	Crumb et al.	1.09	0	1.31	0.01	2.18	0.21	1344.29	1	3.12	-	1	1	1	1
Amiodarone	0.50	Mirams et al.	0.18	-	1.64	-	-	0.01	60.00	1	-	-	1	1	1	1
Amitriptyline	36.40	Crumb et al.	2.74	0	0.98	10.34	8.31	0.14	100.55	0	15.46	-	3	0	0	1
Amitriptyline	41.00	Mirams et al.	0.35	-	1.23	-	-	0.20	80.00	0	-	-	3	0	0	1
Amitriptyline	41.00	Ando et al.	0.35	-	0.70	-	-	2.50	141.46	0	-	-	3	0	0	1
Aspirin	7700.00	Ando et al.	0.00	-	0.01	-	-	0.00	12987.01	0	-	-	0	0	0	0
Astemizole	0.30	Kramer et al.	0.00	-	11.71	-	-	0.00	13.33	1	-	-	1	1	1	1
Astemizole	0.29	Okada et al.	0.00	0	0.03	0	0	0.00	97.71	1	0	-	1	1	1	1
Astemizole	0.51	Ando et al.	0.05	-	11.31	-	-	0.02	7.84	1	-	-	1	1	1	1
Azithromycin	1937.00	Crumb et al.	0.00	0	14.19	0.05	0.02	0.00	36.55	1	12.87	-	1	1	1	1
Bepridil	31.50	Crumb et al.	6.33	0	19.80	0.84	0.34	0.43	4.73	1	0	-	1	1	1	1
Bepridil	33.00	Mirams et al.	13.52	-	50.00	-	-	0.88	1.00	1	-	-	1	1	1	1
Bepridil	35.00	Ando et al.	3.38	-	17.95	-	-	1.50	4.57	1	-	-	1	1	1	1
Bepridil	35.00	Kramer et al.	1.35	-	20.79	-	-	0.51	4.57	1	-	-	1	1	1	1
Bepridil	33.00	Li et al.	6.50	0	40.76	0.87	0.36	0.46	1.52	1	0	-54.93	1	1	1	1
Bepridil	34.63	Okada et al.	0.02	0	12.62	0.01	0	3.29	3.76	1	0.01	-	1	1	1	1
Ceftriaxone	23170.00	Kramer et al.	13.09	-	4.94	-	-	4.00	19.24	0	-	-	0	0	0	0
Chloroquine	249.50	Crumb et al.	0.00	4.75	12.02	0	0.36	0.31	27.61	1	0	-	1	1	1	1
Chlorpheniramine	12.00	Ando et al.	0.00	-	0.09	-	-	0.00	1083.33	1	-	-	0	0	0	0
Chlorpromazine	38.00	Ando et al.	1.11	-	2.47	-	-	1.25	39.47	1	-	-	1	1	1	1
Chlorpromazine	38.00	Mirams et al.	0.00	-	2.52	-	-	0.88	38.68	1	-	-	1	1	1	1
Chlorpromazine	38.00	Kramer et al.	0.04	-	0.58	-	-	0.68	39.47	1	-	-	1	1	1	1
Chlorpromazine	34.50	Crumb et al.	1.24	1.95	4.19	0	1.22	0.01	32.41	1	0.52	-	1	1	1	1
Chlorpromazine	38.00	Li et al.	1.34	2.09	7.19	0	1.33	0.01	24.45	1	0.54	-14	1	1	1	1
Cibenzoline	673.00	Crumb et al.	0.00	0	26.45	0	7.29	1.52	3.12	0	0	-	0	0	0	0
Cibenzoline	976.00	Mirams et al.	3.15	-	4.14	-	-	11.12	23.16	0	-	-	0	0	0	0
Cilostazol	140.00	Ando et al.	0.15	-	1.00	-	-	0.15	98.57	1	-	-	1	1	1	1
Cilostazol	128.00	Kramer et al.	0.14	-	1.39	-	-	0.14	107.81	1	-	-	1	1	1	1
Cisapride	2.60	Crumb et al.	0.24	0.93	12.04	0.56	0	0.00	4.62	1	9.38	-	1	1	1	1
Cisapride	2.60	Ando et al.	0.02	-	11.50	-	-	0.00	7.69	1	-	-	1	1	1	1
Cisapride	2.60	Li et al.	0.24	0.93	28.03	0.56	0	0.00	3.85	1	9.38	-199	1	1	1	1
Cisapride	2.58	Okada et al.	0.00	0	9.03	0	0	0.25	5.71	1	0	-	1	1	1	1
Cisapride	4.90	Mirams et al.	0.00	-	42.98	-	-	0.03	1.33	1	-	-	1	1	1	1
Cisapride	3.00	Kramer et al.	0.03	-	12.21	-	-	0.00	6.67	1	-	-	1	1	1	1
Clarithromycin	3300.00	Ando et al.	0.00	-	9.12	-	-	0.00	9.97	1	-	-	1	1	1	1
Clozapine	71.00	Kramer et al.	1.93	-	3.31	-	-	0.22	32.39	1	-	-	2	1	0	0
Clozapine	320.00	Ando et al.	8.16	-	12.21	-	-	2.08	7.19	1	-	-	2	1	0	0
Desipramine	108.00	Mirams et al.	5.94	-	7.21	-	-	6.63	12.87	0	-	-	2	1	0	0
Diazepam	29.00	Kramer et al.	0.20	-	0.03	-	-	0.01	1834.48	0	-	-	0	0	0	0
Diltiazem	122.00	Mirams et al.	21.33	-	0.70	-	-	1.34	141.80	0	-	-	0	0	0	0
Diltiazem	122.00	Li et al.	51.50	0	1.46	0	2.58	0.84	107.79	0	3.26	-90	0	0	0	0
Diltiazem	127.50	Crumb et al.	52.27	0	4.09	0	2.66	0.87	51.52	0	3.29	-	0	0	0	0
Diltiazem	180.00	Ando et al.	19.15	-	1.35	-	-	0.80	73.33	0	-	-	0	0	0	0
Diltiazem	122.00	Kramer et al.	11.05	-	0.43	-	-	0.12	108.20	0	-	-	0	0	0	0
Diphenhydramine	57.00	Ando et al.	0.02	-	1.08	-	-	0.14	91.23	0	-	-	3	0	0	1
Diphenhydramine	34.00	Mirams et al.	0.01	-	0.65	-	-	0.08	152.94	0	-	-	3	0	0	1
Disopyramide	750.00	Ando et al.	0.07	-	4.95	-	-	0.44	19.20	1	-	-	1	1	1	1
Disopyramide	742.00	Kramer et al.	0.07	-	6.30	-	-	0.27	19.41	1	-	-	1	1	1	1

Dofetilide	1.60	Okada et al.	0.00	0	0.18	0	0	2.40	23.92	1	0	-	1	1	1	1
Dofetilide	2.00	Ando et al.	0.01	-	6.25	-	-	0.00	15.00	1	-	-	1	1	1	1
Dofetilide	2.10	Crumb et al.	0.80	1.49	60.95	0	0	0.00	0.48	1	14.76	-	1	1	1	1
Dofetilide	2.00	Li et al.	0.29	1.44	30.86	0	2.08	0.88	2.45	1	14.28	-1	1	1	1	1
Dofetilide	2.00	Mirams et al.	0.00	-	28.57	-	-	0.00	2.50	1	-	-	1	1	1	1
Dofetilide	2.00	Kramer et al.	0.01	-	3.73	-	-	0.00	15.00	1	-	-	1	1	1	1
Dolasetron	360.00	Ando et al.	0.00	-	5.71	-	-	0.94	16.53	1	-	-	2	1	0	0
Domperidone	27.00	Ando et al.	0.00	-	14.44	-	-	0.48	5.93	1	-	-	1	1	1	1
Donepezil	3.00	Kramer et al.	0.04	-	0.48	-	-	0.01	233.33	1	-	-	1	1	1	1
Dosatinib	41.00	Kramer et al.	0.05	-	0.06	-	-	0.00	597.56	0	-	-	2	1	0	0
Dronedarone	1.80	Ando et al.	0.45	-	2.96	-	-	0.26	32.78	1	-	-	1	1	1	1
Droperidol	16.00	Kramer et al.	0.08	-	18.94	-	-	0.01	3.75	1	-	-	1	1	1	1
Droperidol	21.00	Ando et al.	0.28	-	25.93	-	-	0.09	2.86	1	-	-	1	1	1	1
Duloxetine	16.00	Kramer et al.	0.07	-	0.05	-	-	0.01	237.50	0	-	-	0	0	0	0
E4031	5.67	Okada et al.	0.48	0	4.47	0	0	1.93	4.63	1	0	-	0	0	0	0
E4031	8.40	Ando et al.	0.00	-	37.50	-	-	0.00	1.67	1	-	-	0	0	0	0
Erythromycin	12000.00	Ando et al.	0.00	-	23.58	-	-	0.00	3.24	1	-	-	1	1	1	1
Famotidine	330.00	Ando et al.	0.00	-	3.19	-	-	0.00	30.30	0	-	-	2	1	0	0
Flecainide	753.00	Kramer et al.	3.00	-	35.29	-	-	8.29	1.99	1	-	-	1	1	1	1
Flecainide	1200.00	Ando et al.	4.24	-	44.44	-	-	16.22	1.25	1	-	-	1	1	1	1
Flecainide	752.90	Crumb et al.	0.71	0	51.69	0	12.64	1.56	0.92	1	14.72	-	1	1	1	1
Fluvoxamine	377.00	Mirams et al.	7.14	-	10.84	-	-	0.95	8.22	0	-	-	3	0	0	1
Gatifloxacin	9000.00	Ando et al.	0.00	-	6.47	-	-	0.00	14.44	1	-	-	1	1	1	1
Halofantrine	172.00	Kramer et al.	8.49	-	26.15	-	-	0.05	2.21	1	-	-	1	1	1	1
Haloperidol	4.00	Kramer et al.	0.03	-	6.20	-	-	0.00	10.00	1	-	-	1	1	1	1
Haloperidol	3.60	Mirams et al.	0.21	-	11.76	-	-	0.05	7.50	1	-	-	1	1	1	1
Haloperidol	3.60	Ando et al.	0.28	-	8.26	-	-	0.08	11.11	1	-	-	1	1	1	1
Ibutilide	150.00	Ando et al.	0.24	-	89.29	-	-	0.35	0.12	1	-	-	1	1	1	1
Ibutilide	140.00	Kramer et al.	0.08	-	95.85	-	-	0.28	0.13	1	-	-	1	1	1	1
Imipramine	106.00	Mirams et al.	1.26	-	3.02	-	-	2.86	32.08	0	-	-	2	1	0	0
Lamivudine	19540.00	Kramer et al.	28.74	-	0.94	-	-	1.23	105.12	0	-	-	0	0	0	0
Levocetirizine	63.00	Ando et al.	0.00	-	0.06	-	-	0.00	1587.30	0	-	-	0	0	0	0
Lidocaine	2560.00	Crumb et al.	0.00	0	0.00	0	13.35	0.00	39062500.00	0	0	-	0	0	0	0
Linezolid	59110.00	Kramer et al.	36.73	-	4.90	-	-	2.19	19.41	0	-	-	0	0	0	0
Lopinavir	703.70	Crumb et al.	4.32	0	8.37	0	0	0.00	7.35	1	0	-	0	0	0	0
Loratadine	0.60	Ando et al.	0.01	-	0.01	-	-	0.00	10166.67	0	-	-	0	0	0	0
Loratadine	0.40	Kramer et al.	0.00	-	0.00	-	-	0.00	15250.00	0	-	-	0	0	0	0
Methadone	507.00	Kramer et al.	0.08	-	12.65	-	-	0.34	6.90	1	-	-	1	1	1	1
Metoprolol	450.00	Ando et al.	0.00	-	0.31	-	-	1.11	322.22	0	-	-	0	0	0	0
Metronidazole	187000.00	Kramer et al.	50.82	-	12.24	-	-	8.27	7.17	0	-	-	0	0	0	0
Mexiletine	2503.20	Crumb et al.	5.89	0	3.03	0	14.37	0.00	31.96	0	0	-	0	0	0	0
Mexiletine	5400.00	Ando et al.	4.14	-	7.99	-	-	12.44	11.52	0	-	-	0	0	0	0
Mexiletine	4129.00	Mirams et al.	3.97	-	7.63	-	-	8.76	12.11	0	-	-	0	0	0	0
Mexiletine	4129.00	Li et al.	9.74	0	14.80	0	25.27	0.00	6.99	0	0	-86	0	0	0	0
Mibefradil	63.00	Ando et al.	10.99	-	3.57	-	-	1.11	26.98	0	-	-	0	0	0	0
Mibefradil	12.00	Mirams et al.	7.14	-	0.66	-	-	1.21	150.00	0	-	-	0	0	0	0
Mibefradil	10.60	Crumb et al.	1.07	0	4.61	0	0.09	0.18	28.96	0	0	-	0	0	0	0
Mibefradil	12.00	Kramer et al.	0.45	-	0.11	-	-	0.01	141.67	0	-	-	0	0	0	0
Mitoxantrone	225.00	Kramer et al.	4.99	-	0.04	-	-	0.18	2397.33	0	-	-	0	0	0	0
Moxifloxacin	10950.00	Okada et al.	0.30	0	9.19	0.22	0	0.00	12.40	1	2.26	-	1	1	1	1
Moxifloxacin	3562.50	Crumb et al.	0.00	0	12.37	6.61	0.58	0.00	26.12	1	0	-	1	1	1	1
Moxifloxacin	10960.00	Kramer et al.	5.96	-	12.58	-	-	0.98	7.86	1	-	-	1	1	1	1
Moxifloxacin	5600.00	Ando et al.	3.14	-	6.10	-	-	0.50	15.39	1	-	-	1	1	1	1
Nifedipine	8.00	Kramer et al.	39.81	-	0.10	-	-	0.13	5500.00	0	-	-	0	0	0	0

Nifedipine	7.70	Mirams et al.	11.37	-	0.00	-	-	0.02	35714.29	0	-	-	0	0	0	0
Nifedipine	10.00	Ando et al.	45.45	-	0.02	-	-	0.01	4400.00	0	-	-	0	0	0	0
Nilotinib	60.40	Crumb et al.	0.00	0	41.88	0	1.27	0.00	1.51	1	0	-	2	1	0	0
Nilotinib	172.00	Kramer et al.	0.97	-	15.58	-	-	0.01	5.81	1	-	-	2	1	0	0
Nilotinib	170.00	Ando et al.	0.96	-	14.53	-	-	1.26	5.88	1	-	-	2	1	0	0
Nitrendipine	3.02	Mirams et al.	89.61	-	0.03	-	-	0.01	3311.26	0	-	-	0	0	0	0
Nitrendipine	3.00	Ando et al.	10.71	-	0.01	-	-	0.01	8200.00	0	-	-	0	0	0	0
Nitrendipine	3.00	Kramer et al.	16.06	-	0.06	-	-	0.00	8200.00	0	-	-	0	0	0	0
Ondansetron	358.50	Crumb et al.	3.51	0	19.37	0.57	1.83	0.62	4.16	1	0.04	-	1	1	1	1
Ondansetron	77.00	Ando et al.	0.34	-	4.88	-	-	0.38	19.48	1	-	-	1	1	1	1
Ondansetron	139.00	Li et al.	1.68	0	11.65	0.3	0.72	0.24	9.50	1	0.01	-82	1	1	1	1
Paliperidone	69.00	Kramer et al.	0.04	-	7.95	-	-	0.01	11.30	1	-	-	2	1	0	0
Paliperidone	30.00	Ando et al.	0.02	-	3.70	-	-	0.03	26.00	1	-	-	2	1	0	0
Paroxetine	14.00	Kramer et al.	0.04	-	0.21	-	-	0.02	135.71	0	-	-	3	0	0	1
Pentobarbital	5171.00	Kramer et al.	0.37	-	0.36	-	-	0.19	277.30	0	-	-	0	0	0	0
Phenytoin	4360.00	Kramer et al.	16.83	-	2.88	-	-	4.84	33.72	0	-	-	0	0	0	0
Phenytoin	4500.00	Mirams et al.	4.19	-	4.31	-	-	8.41	22.22	0	-	-	0	0	0	0
Pimozide	0.50	Kramer et al.	0.01	-	0.62	-	-	0.03	80.00	1	-	-	1	1	1	1
Pimozide	0.43	Ando et al.	0.18	-	1.06	-	-	0.04	93.02	1	-	-	1	1	1	1
Pimozide	1.00	Mirams et al.	0.61	-	4.76	-	-	1.82	20.00	1	-	-	1	1	1	1
Piperacillin	1378000.00	Kramer et al.	52.92	-	28.81	-	-	36.15	2.47	0	-	-	3	0	0	1
Prenylamine	3.50	Ando et al.	0.29	-	5.11	-	-	0.14	18.57	1	-	-	0	0	0	0
Prenylamine	17.00	Mirams et al.	1.35	-	20.73	-	-	0.67	3.82	1	-	-	0	0	0	0
Procainamide	52000.00	Ando et al.	11.78	-	16.03	-	-	6.51	5.24	1	-	-	1	1	1	1
Procainamide	54180.00	Kramer et al.	16.28	-	16.59	-	-	6.77	5.03	1	-	-	1	1	1	1
Propafenone	241.00	Mirams et al.	11.81	-	35.39	-	-	16.84	1.83	1	-	-	0	0	0	0
Propafenone	131.00	Crumb et al.	9.76	0	26.10	0	4.37	3.26	3.67	1	0	-	0	0	0	0
Propranolol	26.00	Mirams et al.	0.14	-	0.91	-	-	1.22	108.77	0	-	-	0	0	0	0
Quetiapine	33.00	Mirams et al.	0.32	-	0.57	-	-	0.19	175.76	0	-	-	3	0	0	1
Quinidine	3200.00	Ando et al.	33.33	-	81.63	-	-	17.98	0.22	1	-	-	1	1	1	1
Quinidine	3237.00	Li et al.	15.96	2.27	72.03	35.89	19.97	11.86	0.31	1	47.58	-64.7	1	1	1	1
Quinidine	842.90	Crumb et al.	1.61	1.33	71.08	7.84	8.22	1.76	0.41	1	13.64	-	1	1	1	1
Quinidine	3237.00	Kramer et al.	38.62	-	83.11	-	-	13.73	0.22	1	-	-	1	1	1	1
Quinidine	3235.00	Okada et al.	32.80	0	83.80	1.52	0	6.62	0.20	1	65.33	-	1	1	1	1
Quinidine	3237.00	Mirams et al.	17.18	-	91.52	-	-	16.32	0.09	1	-	-	1	1	1	1
Quinine	4300.00	Ando et al.	23.50	-	9.25	-	-	19.46	9.81	1	-	-	3	0	0	1
Quinine	3956.70	Crumb et al.	12.71	0	43.35	7.78	39.87	12.03	1.31	1	4.76	-	3	0	0	1
Raltegravir	7000.00	Kramer et al.	2.76	-	0.89	-	-	0.82	111.83	0	-	-	0	0	0	0
Ranolazine	2310.00	Okada et al.	2.87	0	40.68	0	2.54	6.90	1.70	0	0.11	-	3	0	0	1
Ranolazine	1948.20	Li et al.	0.00	0	21.40	0.73	22.13	0.68	4.24	0	0	-94	3	0	0	1
Ranolazine	2300.00	Ando et al.	0.77	-	16.67	-	-	0.78	5.00	0	-	-	3	0	0	1
Ranolazine	1948.20	Crumb et al.	0.00	0	27.63	0.73	22.13	0.00	3.33	0	0	-	3	0	0	1
Ribavirin	27880.00	Kramer et al.	4.29	-	2.80	-	-	0.92	34.68	0	-	-	0	0	0	0
Risperidone	2.00	Kramer et al.	0.05	-	0.80	-	-	0.01	130.00	1	-	-	2	1	0	0
Risperidone	1.81	Mirams et al.	0.00	-	1.19	-	-	0.00	82.87	1	-	-	2	1	0	0
Risperidone	15.00	Ando et al.	0.04	-	5.45	-	-	0.03	17.33	1	-	-	2	1	0	0
Ritonavir	436.90	Crumb et al.	2.15	0	7.81	0	12.36	2.51	11.80	1	0	-	3	0	0	1
Rufinamide	83126.90	Crumb et al.	26.09	0	0.00	0	0	0.00	1202980.02	0	0	-	0	0	0	0
Saquinavir	130.00	Kramer et al.	4.38	-	0.02	-	-	0.00	130.00	1	-	-	2	1	0	0
Saquinavir	417.20	Crumb et al.	5.55	0	10.71	0	3.23	1.28	8.33	1	0	-	2	1	0	0
Sematilide	4400.00	Ando et al.	0.00	-	14.97	-	-	0.00	5.68	1	-	-	0	0	0	0
Sertindole	1.59	Mirams et al.	0.02	-	10.20	-	-	0.07	8.81	1	-	-	2	1	0	0
Sertindole	1.60	Ando et al.	0.03	-	4.62	-	-	0.02	20.62	1	-	-	2	1	0	0
Sertindole	2.00	Kramer et al.	0.00	-	2.92	-	-	0.01	16.50	1	-	-	2	1	0	0

Sertindole	1.60	Crumb et al.	0.00	0	17.62	0	0	0.00	6.88	1	0	-	2	1	0	0
Sitagliptin	442.00	Kramer et al.	0.30	-	0.25	-	-	0.04	395.25	0	-	-	0	0	0	0
Solifenacin	3.00	Kramer et al.	0.00	-	1.66	-	-	0.03	93.33	1	-	-	3	0	0	1
Sotalol	14680.00	Okada et al.	0.00	0	3.69	0	0	0.00	24.28	1	0	-	1	1	1	1
Sotalol	13000.00	Ando et al.	6.30	-	10.45	-	-	0.18	8.57	1	-	-	1	1	1	1
Sotalol	14686.40	Crumb et al.	0.38	0.17	16.87	0.11	0	0.36	5.88	1	0.37	-	1	1	1	1
Sotalol	14690.00	Kramer et al.	7.06	-	18.56	-	-	0.21	7.58	1	-	-	1	1	1	1
Sotalol	14690.00	Li et al.	0.38	0.17	16.59	0.11	0	0.36	7.53	1	0.37	-55	1	1	1	1
Sparfloxacin	1766.00	Kramer et al.	1.95	-	8.71	-	-	0.07	12.51	1	-	-	1	1	1	1
Sparfloxacin	1900.00	Ando et al.	2.09	-	7.92	-	-	0.07	11.63	1	-	-	1	1	1	1
Sunitinib	13.00	Kramer et al.	0.02	-	1.07	-	-	0.02	92.31	1	-	-	2	1	0	0
Tamoxifen	18.00	Ando et al.	0.00	-	2.26	-	-	0.00	43.17	0	-	-	2	1	0	0
Tedisamil	85.00	Mirams et al.	0.00	-	3.29	-	-	0.42	29.41	1	-	-	0	0	0	0
Telbivudine	19720.00	Kramer et al.	2.69	-	4.46	-	-	1.77	21.44	0	-	-	0	0	0	0
Terfenadine	9.00	Kramer et al.	0.02	-	10.49	-	-	0.01	5.56	1	-	-	1	1	1	1
Terfenadine	9.00	Mirams et al.	2.34	-	50.28	-	-	0.92	0.99	1	-	-	1	1	1	1
Terfenadine	9.00	Okada et al.	0.01	0	5.66	0	0	11.39	10.95	1	0	-	1	1	1	1
Terfenadine	4.00	Li et al.	2.62	0	25.93	0.32	0.6	0.08	5.75	1	3.56	-77	1	1	1	1
Terfenadine	9.50	Ando et al.	1.01	-	15.97	-	-	0.47	5.26	1	-	-	1	1	1	1
Terfenadine	9.00	Crumb et al.	4.53	0	38.98	0.47	0.97	0.19	2.11	1	4.49	-	1	1	1	1
Terodiline	240.00	Ando et al.	4.76	-	26.97	-	-	3.14	2.71	1	-	-	0	0	0	0
Terodiline	145.00	Kramer et al.	2.83	-	17.80	-	-	0.79	4.48	1	-	-	0	0	0	0
Thioridazine	45.00	Ando et al.	1.27	-	8.26	-	-	3.11	11.11	1	-	-	1	1	1	1
Thioridazine	980.00	Kramer et al.	15.21	-	65.91	-	-	40.23	0.51	1	-	-	1	1	1	1
Thioridazine	979.00	Mirams et al.	42.96	-	96.74	-	-	34.85	0.03	1	-	-	1	1	1	1
Tolterodine	0.14	Ando et al.	0.10	-	0.82	-	-	0.01	121.43	0	-	-	2	1	0	0
Toremifene	26.30	Crumb et al.	0.00	0	0.75	0	0.65	0.00	133.08	1	0	-	2	1	0	0
Vandetanib	110.00	Ando et al.	0.00	-	21.57	-	-	0.00	3.64	1	-	-	1	1	1	1
Verapamil	45.00	Crumb et al.	16.09	0.85	6.62	0	0.64	0.00	11.09	0	1.04	-	0	0	0	0
Verapamil	81.00	Mirams et al.	44.75	-	36.16	-	-	0.19	1.77	0	-	-	0	0	0	0
Verapamil	88.00	Kramer et al.	34.15	-	28.31	-	-	0.04	2.84	0	-	-	0	0	0	0
Verapamil	87.97	Okada et al.	17.82	0	29.71	0.43	0	3.55	2.29	0	2.51	-	0	0	0	0
Verapamil	92.00	Ando et al.	31.51	-	26.90	-	-	0.28	2.72	0	-	-	0	0	0	0
Verapamil	81.00	Li et al.	26.90	1.01	21.95	0	1.14	0.00	3.56	0	1.65	-100	0	0	0	0
Voriconazole	7563.00	Kramer et al.	1.79	-	1.52	-	-	0.49	64.91	0	-	-	3	0	0	1
Ziprasidone	7.30	Ando et al.	0.00	-	2.95	-	-	0.00	32.88	1	-	-	3	0	0	1

**Table S8.** Merged Dataset. The table reports the block of seven ion channel currents ( $I_{CaV}$ ,  $I_{Kr}$ ,  $I_{K1}$ ,  $I_{Ks}$ ,  $I_{to}$ ,  $I_{Na}$  and  $I_{NaL}$ ) at  $C_{Drug} = EFTPC$ , the maximum EFTPC value of each of the drugs (“EFTPC” column), the reference/source (“Source” column) used to extract the  $IC_{50}$ , Hill coefficients and EFTPC values for the particular drug, the hERG ratio (“Ratio” column), the drug-trapping parameter values for the available drugs (“vtrap” column) and the different risk definition assigned to them (‘target’, ‘CM’, ‘t1’, ‘t2’) columns. target- TdP+:- R1, R2, R3, CH1, CM1 category or label warning, t1- TdP+: Drugs in CM1 and CM2 category, t2- TdP+: - Drugs in CM1 category, t3- TdP+: - Drugs in CM1 and CM3 category.

	<i>EFTPC</i>	<i>Source</i>	<i>I<sub>CaV</sub></i>	<i>I<sub>K1</sub></i>	<i>I<sub>Kr</sub></i>	<i>I<sub>Ks</sub></i>	<i>I<sub>NaL</sub></i>	<i>I<sub>Na</sub></i>	<i>Ratio</i>	<i>target</i>	<i>I<sub>to</sub></i>	<i>vtrap</i>	<i>CMt1</i>	<i>t2</i>	<i>t3</i>	<i>EAD</i>	
Ajmaline	1500.00	Mirams et al.	2.15	-	60.0	-	-	15.98	1.04	1	-	-	0	0	0	0	1
Ajmaline	25.00	Ando et al.	2.15	-	60.0	-	-	15.98	62.40	1	-	-	0	0	0	0	1
Amiodarone	150.00	Ando et al.	40.44	-	60.0	-	-	7.50	8.60	1	-	-	1	1	1	1	0
Amiodarone	0.77	Okada et al.	23.95	0	60.0	0	0	54.49	600.00	1	0	-	1	1	1	1	1
Amiodarone	0.80	Kramer et al.	42.79	-	60.0	-	-	7.81	600.00	1	-	-	1	1	1	1	0
Amiodarone	0.70	Crumb et al.	55.49	0	60.0	24.61	34.27	34.65	600.00	1	42.96	-	1	1	1	1	0
Amiodarone	0.50	Mirams et al.	14.29	-	60.0	-	-	0.93	90.00	1	-	-	1	1	1	1	1
Amitriptyline	36.40	Crumb et al.	80.96	0	60.0	58.61	52.67	48.44	150.82	0	57.64	-	3	0	0	1	0
Amitriptyline	41.00	Mirams et al.	29.78	-	60.0	-	-	19.74	120.00	0	-	-	3	0	0	1	1
Amitriptyline	41.00	Ando et al.	42.86	-	60.0	-	-	84.47	212.20	0	-	-	3	0	0	1	0
Aspirin	7700.00	Ando et al.	0.00	-	60.0	-	-	0.00	600.00	0	-	-	0	0	0	0	1
Astemizole	0.30	Kramer et al.	0.02	-	60.0	-	-	0.00	22.42	1	-	-	1	1	1	1	1
Astemizole	0.29	Okada et al.	0.02	0	60.0	0	0	0.23	123.26	1	0	-	1	1	1	1	1
Astemizole	0.51	Ando et al.	0.54	-	60.0	-	-	0.20	11.76	1	-	-	1	1	1	1	1
Azithromycin	1937.00	Crumb et al.	0.00	0	60.0	18.02	41.92	0.00	82.24	1	57.26	-	1	1	1	1	1
Bepidil	31.50	Crumb et al.	18.37	0	60.0	3.34	5.37	4.59	7.42	1	0	-	1	1	1	1	1
Bepidil	33.00	Mirams et al.	19.00	-	60.0	-	-	1.32	1.50	1	-	-	1	1	1	1	1
Bepidil	35.00	Ando et al.	19.35	-	60.0	-	-	9.45	6.86	1	-	-	1	1	1	1	1
Bepidil	35.00	Kramer et al.	14.73	-	60.0	-	-	5.85	7.25	1	-	-	1	1	1	1	1
Bepidil	33.00	Li et al.	10.46	0	60.0	1.58	1.22	1.28	2.38	1	0	-54.93	1	1	1	1	1
Bepidil	34.63	Okada et al.	0.70	0	60.0	0.18	0	17.79	4.96	1	0.23	-	1	1	1	1	1
Ceftriaxone	23170.00	Kramer et al.	81.30	-	60.0	-	-	54.60	28.85	0	-	-	0	0	0	0	0
Chloroquine	249.50	Crumb et al.	0.00	54.89	60.0	0	16.21	14.48	54.27	1	0	-	1	1	1	1	1
Chlorpheniramine	12.00	Ando et al.	0.00	-	60.0	-	-	0.00	600.00	1	-	-	0	0	0	0	1
Chlorpromazine	38.00	Ando et al.	39.82	-	60.0	-	-	42.86	59.21	1	-	-	1	1	1	1	0
Chlorpromazine	38.00	Mirams et al.	0.00	-	60.0	-	-	33.90	58.03	1	-	-	1	1	1	1	1
Chlorpromazine	38.00	Kramer et al.	28.61	-	60.0	-	-	38.70	52.73	1	-	-	1	1	1	1	1
Chlorpromazine	34.50	Crumb et al.	22.57	23.77	60.0	0	29.74	13.01	50.85	1	2.45	-	1	1	1	1	1
Chlorpromazine	38.00	Li et al.	20.82	22.18	60.0	0	27.38	10.37	40.59	1	2.33	-14	1	1	1	1	1
Cibenzoline	673.00	Crumb et al.	0.00	0	60.0	0	16.94	9.39	4.89	0	0	-	0	0	0	0	1
Cibenzoline	976.00	Mirams et al.	53.05	-	60.0	-	-	81.29	34.73	0	-	-	0	0	0	0	0
Cilostazol	140.00	Ando et al.	18.50	-	60.0	-	-	18.09	147.86	1	-	-	1	1	1	1	1
Cilostazol	128.00	Kramer et al.	19.11	-	60.0	-	-	18.70	168.34	1	-	-	1	1	1	1	1
Cisapride	2.60	Crumb et al.	0.50	2.3	60.0	0.97	0	0.00	6.30	1	13.01	-	1	1	1	1	1
Cisapride	2.60	Ando et al.	0.25	-	60.0	-	-	0.01	11.54	1	-	-	1	1	1	1	1
Cisapride	2.60	Li et al.	0.51	2.4	60.0	1	0	0.00	6.86	1	13.2	-199	1	1	1	1	1
Cisapride	2.58	Okada et al.	0.06	0	60.0	0	0	1.55	7.75	1	0	-	1	1	1	1	1
Cisapride	4.90	Mirams et al.	0.00	-	60.0	-	-	0.07	1.99	1	-	-	1	1	1	1	1
Cisapride	3.00	Kramer et al.	0.25	-	60.0	-	-	0.01	9.85	1	-	-	1	1	1	1	1
Clarithromycin	3300.00	Ando et al.	0.00	-	60.0	-	-	0.00	14.95	1	-	-	1	1	1	1	1
Clozapine	71.00	Kramer et al.	49.25	-	60.0	-	-	15.86	49.20	1	-	-	2	1	0	0	0
Clozapine	320.00	Ando et al.	48.94	-	60.0	-	-	18.60	10.78	1	-	-	2	1	0	0	0
Desipramine	108.00	Mirams et al.	54.96	-	60.0	-	-	57.84	19.31	0	-	-	2	1	0	0	0
Diazepam	29.00	Kramer et al.	69.69	-	60.0	-	-	20.23	600.00	0	-	-	0	0	0	0	0
Diltiazem	122.00	Mirams et al.	98.30	-	60.0	-	-	74.25	212.70	0	-	-	0	0	0	0	0
Diltiazem	122.00	Li et al.	97.47	0	60.0	0	48.98	23.56	169.13	0	8.6	-90	0	0	0	0	0
Diltiazem	127.50	Crumb et al.	96.10	0	60.0	0	38.06	16.47	85.53	0	7.65	-	0	0	0	0	0
Diltiazem	180.00	Ando et al.	96.30	-	60.0	-	-	46.92	110.00	0	-	-	0	0	0	0	0
Diltiazem	122.00	Kramer et al.	97.47	-	60.0	-	-	44.24	153.47	0	-	-	0	0	0	0	0
Diphenhydramine	57.00	Ando et al.	3.31	-	60.0	-	-	15.98	136.84	0	-	-	3	0	0	1	1
Diphenhydramine	34.00	Mirams et al.	3.31	-	60.0	-	-	15.98	229.41	0	-	-	3	0	0	1	1
Disopyramide	750.00	Ando et al.	2.04	-	60.0	-	-	11.37	28.80	1	-	-	1	1	1	1	1
Disopyramide	742.00	Kramer et al.	2.12	-	60.0	-	-	10.02	30.30	1	-	-	1	1	1	1	1

Dofetilide	1.60	Okada et al.	0.06	0	60.0	0	0	6.96	29.35	1	0	-	1	1	1	1	1
Dofetilide	2.00	Ando et al.	0.17	-	60.0	-	-	0.03	22.50	1	-	-	1	1	1	1	1
Dofetilide	2.10	Crumb et al.	0.75	1.42	60.0	0	0	0.00	0.94	1	14.11	-	1	1	1	1	1
Dofetilide	2.00	Li et al.	1.44	4.11	60.0	0	3.08	2.90	3.84	1	32.84	-1	1	1	1	1	1
Dofetilide	2.00	Mirams et al.	0.01	-	60.0	-	-	0.00	3.75	1	-	-	1	1	1	1	1
Dofetilide	2.00	Kramer et al.	0.16	-	60.0	-	-	0.03	21.03	1	-	-	1	1	1	1	1
Dolasetron	360.00	Ando et al.	0.00	-	60.0	-	-	19.02	24.79	1	-	-	2	1	0	0	1
Domperidone	27.00	Ando et al.	0.00	-	60.0	-	-	4.11	8.89	1	-	-	1	1	1	1	1
Donepezil	3.00	Kramer et al.	5.28	-	60.0	-	-	2.68	352.91	1	-	-	1	1	1	1	1
Dosatinib	41.00	Kramer et al.	30.00	-	60.0	-	-	24.52	600.00	0	-	-	2	1	0	0	0
Dronedarone	1.80	Ando et al.	18.12	-	60.0	-	-	11.22	49.17	1	-	-	1	1	1	1	1
Droperidol	16.00	Kramer et al.	0.55	-	60.0	-	-	0.10	5.42	1	-	-	1	1	1	1	1
Droperidol	21.00	Ando et al.	1.17	-	60.0	-	-	0.39	4.29	1	-	-	1	1	1	1	1
Duloxetine	16.00	Kramer et al.	69.89	-	60.0	-	-	49.89	317.94	0	-	-	0	0	0	0	0
E4031	5.67	Okada et al.	1.05	0	60.0	0	0	3.39	5.68	1	0	-	0	0	0	0	1
E4031	8.40	Ando et al.	0.00	-	60.0	-	-	0.00	2.50	1	-	-	0	0	0	0	1
Erythromycin	12000.00	Ando et al.	0.00	-	60.0	-	-	0.00	4.86	1	-	-	1	1	1	1	1
Famotidine	330.00	Ando et al.	0.00	-	60.0	-	-	0.00	45.45	0	-	-	2	1	0	0	1
Flecainide	753.00	Kramer et al.	8.62	-	60.0	-	-	25.11	3.16	1	-	-	1	1	1	1	1
Flecainide	1200.00	Ando et al.	7.67	-	60.0	-	-	26.63	1.88	1	-	-	1	1	1	1	1
Flecainide	752.90	Crumb et al.	1.28	0	60.0	0	15.72	3.41	1.53	1	18.83	-	1	1	1	1	1
Fluvoxamine	377.00	Mirams et al.	48.69	-	60.0	-	-	10.56	12.33	0	-	-	3	0	0	1	0
Gatifloxacin	9000.00	Ando et al.	0.00	-	60.0	-	-	0.00	21.67	1	-	-	1	1	1	1	1
Halofantrine	172.00	Kramer et al.	21.64	-	60.0	-	-	0.16	3.01	1	-	-	1	1	1	1	1
Haloperidol	4.00	Kramer et al.	1.30	-	60.0	-	-	0.11	14.10	1	-	-	1	1	1	1	1
Haloperidol	3.60	Mirams et al.	2.33	-	60.0	-	-	0.58	11.25	1	-	-	1	1	1	1	1
Haloperidol	3.60	Ando et al.	4.41	-	60.0	-	-	1.38	16.67	1	-	-	1	1	1	1	1
Ibutilide	150.00	Ando et al.	0.04	-	60.0	-	-	0.06	0.18	1	-	-	1	1	1	1	1
Ibutilide	140.00	Kramer et al.	0.01	-	60.0	-	-	0.04	0.17	1	-	-	1	1	1	1	1
Imipramine	106.00	Mirams et al.	38.06	-	60.0	-	-	58.62	48.11	0	-	-	2	1	0	0	0
Lamivudine	19540.00	Kramer et al.	97.33	-	60.0	-	-	66.22	157.68	0	-	-	0	0	0	0	0
Levocetirizine	63.00	Ando et al.	0.00	-	60.0	-	-	0.00	600.00	0	-	-	0	0	0	0	1
Lidocaine	2560.00	Crumb et al.	60.00	60	60.0	60	100	60.00	600.00	0	60	-	0	0	0	0	0
Linezolid	59110.00	Kramer et al.	93.25	-	60.0	-	-	39.42	29.11	0	-	-	0	0	0	0	0
Lopinavir	703.70	Crumb et al.	31.72	0	60.0	0	0	0.00	10.30	1	0	-	0	0	0	0	0
Loratadine	0.60	Ando et al.	44.53	-	60.0	-	-	24.05	600.00	0	-	-	0	0	0	0	0
Loratadine	0.40	Kramer et al.	38.36	-	60.0	-	-	11.01	600.00	0	-	-	0	0	0	0	0
Methadone	507.00	Kramer et al.	3.63	-	60.0	-	-	7.82	10.36	1	-	-	1	1	1	1	1
Metoprolol	450.00	Ando et al.	0.00	-	60.0	-	-	84.47	483.33	0	-	-	0	0	0	0	1
Metronidazole	187000.00	Kramer et al.	83.21	-	60.0	-	-	49.23	10.75	0	-	-	0	0	0	0	0
Mexiletine	2503.20	Crumb et al.	75.00	0	60.0	0	97.42	0.00	47.94	0	0	-	0	0	0	0	0
Mexiletine	5400.00	Ando et al.	42.74	-	60.0	-	-	71.06	17.28	0	-	-	0	0	0	0	0
Mexiletine	4129.00	Mirams et al.	42.86	-	60.0	-	-	63.56	18.16	0	-	-	0	0	0	0	0
Mexiletine	4129.00	Li et al.	54.23	0	60.0	0	90.63	0.00	10.98	0	0	-86	0	0	0	0	0
Mibefradil	63.00	Ando et al.	83.33	-	60.0	-	-	31.29	40.48	0	-	-	0	0	0	0	0
Mibefradil	12.00	Mirams et al.	94.54	-	60.0	-	-	73.37	225.00	0	-	-	0	0	0	0	0
Mibefradil	10.60	Crumb et al.	41.75	0	60.0	0	8.14	7.59	45.45	0	0	-	0	0	0	0	0
Mibefradil	12.00	Kramer et al.	89.63	-	60.0	-	-	20.19	190.05	0	-	-	0	0	0	0	0
Mitoxantrone	225.00	Kramer et al.	90.83	-	60.0	-	-	90.60	600.00	0	-	-	0	0	0	0	0
Moxifloxacin	10950.00	Okada et al.	22.59	0	60.0	6.67	0	0.39	19.37	1	15.07	-	1	1	1	1	1
Moxifloxacin	3562.50	Crumb et al.	0.00	0	60.0	78.42	30.76	0.00	51.33	1	0	-	1	1	1	1	1
Moxifloxacin	10960.00	Kramer et al.	43.41	-	60.0	-	-	10.66	12.11	1	-	-	1	1	1	1	0
Moxifloxacin	5600.00	Ando et al.	42.77	-	60.0	-	-	10.42	23.09	1	-	-	1	1	1	1	0
Nifedipine	8.00	Kramer et al.	99.99	-	60.0	-	-	46.60	600.00	0	-	-	0	0	0	0	0



Nifedipine	7.70	Mirams et al.	99.99	-	60.0	-	-	91.77	600.00	0	-	-	0	0	0	0	0
Nifedipine	10.00	Ando et al.	99.98	-	60.0	-	-	42.72	600.00	0	-	-	0	0	0	0	0
Nilotinib	60.40	Crumb et al.	0.00	0	60.0	0	3.11	0.00	2.50	1	0	-	2	1	0	0	1
Nilotinib	172.00	Kramer et al.	8.02	-	60.0	-	-	1.03	8.87	1	-	-	2	1	0	0	1
Nilotinib	170.00	Ando et al.	7.89	-	60.0	-	-	10.14	8.82	1	-	-	2	1	0	0	1
Nitrendipine	3.02	Mirams et al.	100.00	-	60.0	-	-	29.41	600.00	0	-	-	0	0	0	0	0
Nitrendipine	3.00	Ando et al.	99.93	-	60.0	-	-	63.08	600.00	0	-	-	0	0	0	0	0
Nitrendipine	3.00	Kramer et al.	99.69	-	60.0	-	-	68.58	600.00	0	-	-	0	0	0	0	0
Ondansetron	358.50	Crumb et al.	13.61	0	60.0	2.03	10.45	3.74	6.24	1	0.22	-	1	1	1	1	1
Ondansetron	77.00	Ando et al.	9.05	-	60.0	-	-	10.11	29.22	1	-	-	1	1	1	1	1
Ondansetron	139.00	Li et al.	12.90	0	60.0	1.92	9.75	3.47	14.90	1	0.2	-82	1	1	1	1	1
Paliperidone	69.00	Kramer et al.	0.60	-	60.0	-	-	0.24	16.89	1	-	-	2	1	0	0	1
Paliperidone	30.00	Ando et al.	0.60	-	60.0	-	-	1.06	39.00	1	-	-	2	1	0	0	1
Paroxetine	14.00	Kramer et al.	36.53	-	60.0	-	-	14.59	187.23	0	-	-	3	0	0	1	0
Pentobarbital	5171.00	Kramer et al.	93.84	-	60.0	-	-	44.47	415.94	0	-	-	0	0	0	0	0
Phenytoin	4360.00	Kramer et al.	90.77	-	60.0	-	-	76.50	50.57	0	-	-	0	0	0	0	0
Phenytoin	4500.00	Mirams et al.	59.29	-	60.0	-	-	75.38	33.33	0	-	-	0	0	0	0	0
Pimozide	0.50	Kramer et al.	10.44	-	60.0	-	-	4.26	113.47	1	-	-	1	1	1	1	1
Pimozide	0.43	Ando et al.	20.00	-	60.0	-	-	5.17	139.53	1	-	-	1	1	1	1	1
Pimozide	1.00	Mirams et al.	15.62	-	60.0	-	-	35.71	30.00	1	-	-	1	1	1	1	1
Piperacillin	1378000.00	Kramer et al.	80.64	-	60.0	-	-	67.73	3.71	0	-	-	3	0	0	1	0
Prenylamine	3.50	Ando et al.	7.51	-	60.0	-	-	3.75	27.86	1	-	-	0	0	0	0	1
Prenylamine	17.00	Mirams et al.	7.29	-	60.0	-	-	3.72	5.74	1	-	-	0	0	0	0	1
Procainamide	52000.00	Ando et al.	51.20	-	60.0	-	-	35.37	7.86	1	-	-	1	1	1	1	0
Procainamide	54180.00	Kramer et al.	50.99	-	60.0	-	-	35.37	7.54	1	-	-	1	1	1	1	0
Propafenone	241.00	Mirams et al.	26.83	-	60.0	-	-	35.68	2.74	1	-	-	0	0	0	0	1
Propafenone	131.00	Crumb et al.	35.50	0	60.0	0	18.87	17.05	6.10	1	0	-	0	0	0	0	0
Propranolol	26.00	Mirams et al.	19.07	-	60.0	-	-	66.89	163.15	0	-	-	0	0	0	0	1
Quetiapine	33.00	Mirams et al.	45.55	-	60.0	-	-	33.98	263.64	0	-	-	3	0	0	1	0
Quinidine	3200.00	Ando et al.	14.44	-	60.0	-	-	6.89	0.34	1	-	-	1	1	1	1	1
Quinidine	3237.00	Li et al.	11.24	1.74	60.0	17.85	9.39	4.65	0.51	1	27.38	-64.7	1	1	1	1	1
Quinidine	842.90	Crumb et al.	0.99	1.1	60.0	4.09	5.18	0.85	0.61	1	7.67	-	1	1	1	1	1
Quinidine	3237.00	Kramer et al.	22.70	-	60.0	-	-	3.90	0.33	1	-	-	1	1	1	1	1
Quinidine	3235.00	Okada et al.	15.13	0	60.0	0.3	0	1.42	0.29	1	30.33	-	1	1	1	1	1
Quinidine	3237.00	Mirams et al.	2.80	-	60.0	-	-	2.64	0.14	1	-	-	1	1	1	1	1
Quinine	4300.00	Ando et al.	81.89	-	60.0	-	-	78.05	14.72	1	-	-	3	0	0	1	0
Quinine	3956.70	Crumb et al.	22.20	0	60.0	15.03	46.46	22.28	1.96	1	8.91	-	3	0	0	1	1
Raltegravir	7000.00	Kramer et al.	82.64	-	60.0	-	-	58.23	167.74	0	-	-	0	0	0	0	0
Ranolazine	2310.00	Okada et al.	7.35	0	60.0	0	12.01	16.73	3.01	0	0.45	-	3	0	0	1	1
Ranolazine	1948.20	Li et al.	0.00	0	60.0	1.86	61.03	8.83	6.66	0	0	-94	3	0	0	1	1
Ranolazine	2300.00	Ando et al.	5.51	-	60.0	-	-	5.54	7.50	0	-	-	3	0	0	1	1
Ranolazine	1948.20	Crumb et al.	0.00	0	60.0	1.7	56.98	0.00	5.53	0	0	-	3	0	0	1	1
Ribavirin	27880.00	Kramer et al.	69.97	-	60.0	-	-	32.61	52.03	0	-	-	0	0	0	0	0
Risperidone	2.00	Kramer et al.	2.84	-	60.0	-	-	0.98	195.80	1	-	-	2	1	0	0	1
Risperidone	1.81	Mirams et al.	0.31	-	60.0	-	-	0.22	124.31	1	-	-	2	1	0	0	1
Risperidone	15.00	Ando et al.	1.13	-	60.0	-	-	0.89	26.00	1	-	-	2	1	0	0	1
Ritonavir	436.90	Crumb et al.	48.00	0	60.0	0	51.32	31.27	17.71	1	0	-	3	0	0	1	0
Rufinamide	83126.90	Crumb et al.	100.0060		60.0	60	60	60.00	600.00	0	60	-	0	0	0	0	0
Saquinavir	130.00	Kramer et al.	94.18	-	60.0	-	-	79.14	164.56	1	-	-	2	1	0	0	0
Saquinavir	417.20	Crumb et al.	66.84	0	60.0	0	40.9	21.21	12.50	1	0	-	2	1	0	0	0
Sematilide	4400.00	Ando et al.	0.00	-	60.0	-	-	0.00	8.52	1	-	-	0	0	0	0	1
Sertindole	1.59	Mirams et al.	0.24	-	60.0	-	-	0.90	13.21	1	-	-	2	1	0	0	1
Sertindole	1.60	Ando et al.	0.78	-	60.0	-	-	0.71	30.94	1	-	-	2	1	0	0	1
Sertindole	2.00	Kramer et al.	0.17	-	60.0	-	-	0.25	22.82	1	-	-	2	1	0	0	1

Sertindole	1.60	Crumb et al.	0.00	0	60.0	0	0	0.00	11.41	1	0	-	2	1	0	0	1
Sitagliptin	442.00	Kramer et al.	64.05	-	60.0	-	-	17.67	592.87	0	-	-	0	0	0	0	0
Solifenacin	3.00	Kramer et al.	3.38	-	60.0	-	-	16.51	146.45	1	-	-	3	0	0	1	1
Sotalol	14680.00	Okada et al.	0.00	0	60.0	0	0	0.00	36.09	1	0	-	1	1	1	1	1
Sotalol	13000.00	Ando et al.	46.37	-	60.0	-	-	2.33	12.85	1	-	-	1	1	1	1	0
Sotalol	14686.40	Crumb et al.	2.77	2.33	60.0	1.59	0	1.08	9.23	1	1.74	-	1	1	1	1	1
Sotalol	14690.00	Kramer et al.	50.11	-	60.0	-	-	2.69	13.22	1	-	-	1	1	1	1	0
Sotalol	14690.00	Li et al.	3.61	3.32	60.0	2.27	0	1.25	12.50	1	2.14	-55	1	1	1	1	1
Sparfloxacin	1766.00	Kramer et al.	27.79	-	60.0	-	-	1.32	19.35	1	-	-	1	1	1	1	1
Sparfloxacin	1900.00	Ando et al.	27.18	-	60.0	-	-	1.28	17.45	1	-	-	1	1	1	1	1
Sunitinib	13.00	Kramer et al.	3.98	-	60.0	-	-	6.28	138.46	1	-	-	2	1	0	0	1
Tamoxifen	18.00	Ando et al.	0.00	-	60.0	-	-	0.00	64.75	0	-	-	2	1	0	0	1
Tedisamil	85.00	Mirams et al.	0.00	-	60.0	-	-	15.79	44.12	1	-	-	0	0	0	0	1
Telbivudine	19720.00	Kramer et al.	47.04	-	60.0	-	-	36.67	32.15	0	-	-	0	0	0	0	0
Terfenadine	9.00	Kramer et al.	0.92	-	60.0	-	-	0.23	7.68	1	-	-	1	1	1	1	1
Terfenadine	9.00	Mirams et al.	3.44	-	60.0	-	-	1.36	1.48	1	-	-	1	1	1	1	1
Terfenadine	9.00	Okada et al.	2.16	0	60.0	0	0	34.55	15.45	1	0	-	1	1	1	1	1
Terfenadine	4.00	Li et al.	12.81	0	60.0	1.05	2.52	0.93	11.30	1	7.09	-77	1	1	1	1	1
Terfenadine	9.50	Ando et al.	7.46	-	60.0	-	-	3.61	7.89	1	-	-	1	1	1	1	1
Terfenadine	9.00	Crumb et al.	11.39	0	60.0	0.96	2.25	0.77	4.15	1	6.72	-	1	1	1	1	1
Terodiline	240.00	Ando et al.	16.88	-	60.0	-	-	11.64	4.06	1	-	-	0	0	0	0	1
Terodiline	145.00	Kramer et al.	16.55	-	60.0	-	-	7.57	6.67	1	-	-	0	0	0	0	1
Thioridazine	45.00	Ando et al.	17.65	-	60.0	-	-	34.88	16.67	1	-	-	1	1	1	1	1
Thioridazine	980.00	Kramer et al.	11.22	-	60.0	-	-	33.55	0.77	1	-	-	1	1	1	1	1
Thioridazine	979.00	Mirams et al.	3.67	-	60.0	-	-	2.63	0.05	1	-	-	1	1	1	1	1
Tolterodine	0.14	Ando et al.	15.13	-	60.0	-	-	2.49	182.14	0	-	-	2	1	0	0	1
Toremifene	26.30	Crumb et al.	0.00	0	60.0	0	56.76	0.00	199.62	1	0	-	2	1	0	0	1
Vandetanib	110.00	Ando et al.	0.00	-	60.0	-	-	0.00	5.45	1	-	-	1	1	1	1	1
Verapamil	45.00	Crumb et al.	80.22	1.93	60.0	0	9.31	0.00	16.03	0	8.79	-	0	0	0	0	0
Verapamil	81.00	Mirams et al.	68.20	-	60.0	-	-	0.51	2.65	0	-	-	0	0	0	0	0
Verapamil	88.00	Kramer et al.	63.25	-	60.0	-	-	0.28	4.48	0	-	-	0	0	0	0	0
Verapamil	87.97	Okada et al.	46.74	0	60.0	1.34	0	9.40	3.38	0	7.92	-	0	0	0	0	0
Verapamil	92.00	Ando et al.	65.22	-	60.0	-	-	1.14	4.08	0	-	-	0	0	0	0	0
Verapamil	81.00	Li et al.	69.88	1.66	60.0	0	5.79	0.00	5.33	0	6.01	-100	0	0	0	0	0
Voriconazole	7563.00	Kramer et al.	64.00	-	60.0	-	-	32.20	97.36	0	-	-	3	0	0	1	0
Ziprasidone	7.30	Ando et al.	0.00	-	60.0	-	-	0.21	49.32	1	-	-	3	0	0	1	1

**Table S9.** Merged Dataset. The table reports the block of seven ion channel currents ( $I_{CaV}$ ,  $I_{Kr}$ ,  $I_{K1}$ ,  $I_{Ks}$ ,  $I_{to}$ ,  $I_{Na}$  and  $I_{NaL}$ ) at  $C_{Drug} = IC_{60,hERG}$ , the maximum EFTPC value of each of the drugs (“EFTPC” column), the reference/source (“Source” column) used to extract the  $IC_{50}$ , Hill coefficient and EFTPC values for the particular drug, the hERG ratio (“Ratio” column), the drug-trapping parameter values for the available drugs (“vtrap” column) and the different risk definition assigned to them (‘target’, ‘CM’, ‘t1’, ‘t2’) columns. target- TdP+:- R1, R2, R3, CH1, CM1 category or label warning, t1- TdP+: Drugs in CM1 and CM2 category, t2- TdP+: Drugs in CM1 category, t3- TdP+: Drugs in CM1 and CM3 category.



67 **Dataset 9: Drugs in Fermini et al. 2016** A working group under the CiPA initiative led by FDA have  
68 recently categorized 28 drugs into tertiary risk categories (Fermini et al., 2016). Twelve of the twenty eight  
69 drugs are common to the Dataset 5 and 7. We extract *in-vitro* assay data for these drugs from Datasets 1, 2,  
70 3, 5, 6 and 7. We used the mean value of the block for a particular channel if the information for the drug  
71 was present in more than one dataset. No information was available for two (Azimilide and Loratidine) of  
72 the 28 drugs in Datasets 1, 2, 3, 5, 6 and 7 and hence a final dataset of 26 drugs was obtained. If the value  
73 is not available it was available for particular ion channels in any of the datasets described here, it was set  
74 to zero. Drug-trapping parameter for 12 of these drugs reported in Dataset 7 was also added to one of  
75 the columns of the dataset.



76 **1.2 Binary Risk Definition assigned**

	CredibleMeds	Redfern et al. 2013	Champeroux et al. 2005	label	target
Ajmaline	0	0	1	-	1
Amiodarone	1	1	0	-	1
Amitriptyline	3	4	0	QT	0
Aspirin	0	0	3	na	0
Astemizole	1	2	1	-	1
Azithromycin	1	0	2	-	1
Bepidil	1	3	1	-	1
Ceftriaxone	0	0	0	na	0
Chloroquine	1	0	2	-	1
Chlorpheniramine	0	5	1	-	1
Chlorpromazine	1	0	0	-	1
Cibenzoline	0	5	0	na	0
Cilostazol	1	0	0	-	1
Cisapride	1	2	1	-	1
Clarithromycin	1	4	2	-	1
Clozapine	2	0	2	TdP+QT	1
Desipramine	2	4	0	QT	0
Diazepam	0	0	3	na	0
Diltiazem	0	5	3	na	0
Diphenhydramine	3	4	0	na	0
Disopyramide	1	1	1	-	1
Dofetilide	1	1	1	-	1
Dolasetron	2	0	0	TdP+QT	1
Domperidone	1	4	0	-	1
Donepezil	1	0	0	-	1
Dosatinib	2	0	0	QT	0
Dronedarone	1	0	0	-	1
Droperidol	1	0	1	-	1
Duloxetine	0	0	0	na	0
E4031	0	0	0	-	1
Erythromycin	1	3	1	-	1
Famotidine	2	0	0	na	0
Flecainide	1	3	0	-	1
Fluvoxamine	3	0	0	TdP	0
Gatifloxacin	1	0	0	-	1
Halofantrine	1	0	1	-	1
Haloperidol	1	3	0	-	1
Ibutilide	1	1	0	-	1
Imipramine	2	4	1	CYP2D6inhibition	0
Lamivudine	0	0	0	na	0
Levocetirizine	0	0	0	na	0
Lidocaine	0	0	0	na	0
Linezolid	0	0	0	na	0
Lopinavir	0	0	0	TdP+QT	1
Loratadine	0	5	0	na	0
Methadone	1	0	0	TdP+QT	1
Metoprolol	0	0	0	na	0
Metronidazole	0	0	0	na	0
Mexiletine	0	0	0	na	0
Mibefradil	0	4	0	na	0
Mitoxantrone	0	0	0	na	0
Moxifloxacin	1	0	2	-	1
Nifedipine	0	4	0	na	0
Nilotinib	2	0	0	TdP+QT	1
Nitrendipine	0	5	0	na	0
Ondansetron	1	0	2	-	1
Paliperidone	2	0	0	TdP+QT	1
Paroxetine	3	0	0	CYP2D6inhibition	0
Pentobarbital	0	0	0	na	0
Phenytoin	0	5	3	na	0
Pimozide	1	3	1	-	1
Piperacillin	3	0	0	na	0
Prenylamine	0	0	1	-	1
Procainamide	1	1	0	-	1
Propafenone	0	4	1	-	1
Propranolol	0	0	3	na	0
Quetiapine	3	0	0	na	0
Quinidine	1	1	1	-	1
Quinine	3	0	0	TdP+QT	1
Raltegravir	0	0	0	na	0
Ranolazine	3	0	0	QT	0
Ribavirin	0	0	0	na	0
Risperidone	2	5	2	TdP+QT	1
Ritonavir	3	0	0	TdP+QT	1
Rufinamide	0	0	0	QTshort	0
Saquinavir	2	0	0	TdP+QT	1
Sematilide	0	1	0	-	1
Sertindole	2	2	1	-	1
Sitagliptin	0	0	0	na	0
Solifenacin	3	0	0	TdP+QT	1
Sotalol	1	1	1	-	1
Sparfloxacin	1	4	1	-	1
Sunitinib	2	0	0	TdP+QT	1
Tamoxifen	2	5	0	QT	0
Tedisamil	0	1	0	-	1
Telbivudine	0	0	0	na	0
Terfenadine	1	2	0	-	1
Terodiline	0	2	0	-	1
Thioridazine	1	3	1	-	1
Tolterodine	2	0	0	QT	0
Toremifene	2	0	0	TdP+QT	1
Vandetanib	1	0	0	-	1
Verapamil	0	5	2	na	0
Voriconazole	3	0	0	na	0
Ziprasidone	3	0	0	TdP+QT	1

**Table S11.** Binary risk definition assigned to the drugs. **CredibleMeds column:** 0: Drug not analyzed in CredibleMeds or not assigned to any category, 1: CM1, 2: CM2, 3: CM3. **Redfern et al. column:** 0: drug absent from the list of drugs reported in Redfern et al., 1: R1, 2: R2, 3: R3, 4: R4, 5: R5. **Champeroux et al. column:** 0: drug absent in the list of drugs reported in Champeroux et al., 1: CH1, 2: CH2, 3: CH3. **Target column-** Final risk assigned to the drugs in this study. 1: TdP+, 0: TdP-

## 77 1.3 Drugs included in more than one dataset

	Source	% block $I_{Kr}$	% block $I_{CaV}$	% block $I_{Na,peak}$	$\frac{IC_{60,hERG}}{EFTPC}$	Risk(O)	Risk	Prediction	EAD
Ajmaline	Mirams et al.	60.0	2.15	15.98	1.04	1	1	1	1
Ajmaline	Ando et al.	60.0	2.15	15.98	62.40	0	1	1	1
Amiodarone	Kramer et al.	60.0	42.79	7.81	1559.41	1	1	0	0
Amiodarone	Ando et al.	60.0	40.44	7.50	8.60	1	1	1	0
Amiodarone	Mirams et al.	60.0	14.29	0.93	90.00	1	1	1	1
Amiodarone	Okada et al.	60.0	23.95	54.49	1602.42	0	1	0	0
Amiodarone	Crumb et al.	60.0	55.49	34.65	2642.27	-	1	0	0
Amitriptyline	Mirams et al.	60.0	29.78	19.74	120.00	0	0	1	1
Amitriptyline	Ando et al.	60.0	42.86	84.47	212.20	0	0	0	0
Amitriptyline	Crumb et al.	60.0	80.96	48.44	150.82	-	0	0	0
Astemizole	Okada et al.	60.0	0.02	0.23	123.26	1	1	1	1
Astemizole	Ando et al.	60.0	0.54	0.20	11.76	1	1	1	1
Astemizole	Kramer et al.	60.0	0.02	0.00	22.42	1	1	1	1
Bepridil	Li et al.	60.0	10.46	1.28	2.38	1	1	1	1
Bepridil	Mirams et al.	60.0	19.00	1.32	1.50	1	1	1	1
Bepridil	Okada et al.	60.0	0.70	17.79	4.96	1	1	1	1
Bepridil	Crumb et al.	60.0	18.37	4.59	7.42	-	1	1	1
Bepridil	Ando et al.	60.0	19.35	9.45	6.86	1	1	1	1
Bepridil	Kramer et al.	60.0	14.73	5.85	7.25	1	1	1	1
Chlorpromazine	Mirams et al.	60.0	0.00	33.90	58.03	1	1	1	1
Chlorpromazine	Crumb et al.	60.0	22.57	13.01	50.85	-	1	1	1
Chlorpromazine	Ando et al.	60.0	39.82	42.86	59.21	1	1	1	0
Chlorpromazine	Li et al.	60.0	20.82	10.37	40.59	0	1	1	1
Chlorpromazine	Kramer et al.	60.0	28.61	38.70	52.73	1	1	1	1
Cibenzoline	Mirams et al.	60.0	53.05	81.29	34.73	0	0	0	0
Cibenzoline	Crumb et al.	60.0	0.00	9.39	4.89	-	0	1	1
Cilostazol	Ando et al.	60.0	18.50	18.09	147.86	1	1	1	1
Cilostazol	Kramer et al.	60.0	19.11	18.70	168.34	1	1	0	0
Cisapride	Okada et al.	60.0	0.06	1.55	7.75	1	1	1	1
Cisapride	Mirams et al.	60.0	0.00	0.07	1.99	1	1	1	1
Cisapride	Crumb et al.	60.0	0.50	0.00	6.30	-	1	1	1
Cisapride	Ando et al.	60.0	0.25	0.01	11.54	1	1	1	1
Cisapride	Li et al.	60.0	0.51	0.00	6.86	0	1	1	1
Cisapride	Kramer et al.	60.0	0.25	0.01	9.85	1	1	1	1
Clozapine	Ando et al.	60.0	48.94	18.60	10.78	0	1	0	0
Clozapine	Kramer et al.	60.0	49.25	15.86	49.20	1	1	0	0
Diltiazem	Mirams et al.	60.0	98.30	74.25	212.70	0	0	0	0
Diltiazem	Crumb et al.	60.0	96.10	16.47	85.53	-	0	0	0
Diltiazem	Ando et al.	60.0	96.30	46.92	110.00	0	0	0	0
Diltiazem	Li et al.	60.0	97.47	23.56	169.13	0	0	0	0

Diltiazem	Kramer et al.	60.0	97.47	44.24	153.47	0	0	0	0
Diphenhydramine	Ando et al.	60.0	3.31	15.98	136.84	0	0	1	1
Diphenhydramine	Mirams et al.	60.0	3.31	15.98	229.41	0	0	0	0
Disopyramide	Ando et al.	60.0	2.04	11.37	28.80	1	1	1	1
Disopyramide	Kramer et al.	60.0	2.12	10.02	30.30	1	1	1	1
Dofetilide	Crumb et al.	60.0	0.75	0.00	0.94	-	1	1	1
Dofetilide	Okada et al.	60.0	0.06	6.96	29.35	1	1	1	1
Dofetilide	Mirams et al.	60.0	0.01	0.00	3.75	1	1	1	1
Dofetilide	Li et al.	60.0	1.44	2.90	3.84	1	1	1	1
Dofetilide	Ando et al.	60.0	0.17	0.03	22.50	1	1	1	1
Dofetilide	Kramer et al.	60.0	0.16	0.03	21.03	1	1	1	1
Droperidol	Ando et al.	60.0	1.17	0.39	4.29	1	1	1	1
Droperidol	Kramer et al.	60.0	0.55	0.10	5.42	1	1	1	1
E4031	Okada et al.	60.0	1.05	3.39	5.68	1	1	1	1
E4031	Ando et al.	60.0	0.00	0.00	2.50	1	1	1	1
Flecainide	Ando et al.	60.0	7.67	26.63	1.88	1	1	1	1
Flecainide	Crumb et al.	60.0	1.28	3.41	1.53	-	1	1	1
Flecainide	Kramer et al.	60.0	8.62	25.11	3.16	1	1	1	1
Haloperidol	Kramer et al.	60.0	1.30	0.11	14.10	1	1	1	1
Haloperidol	Ando et al.	60.0	4.41	1.38	16.67	1	1	1	1
Haloperidol	Mirams et al.	60.0	2.33	0.58	11.25	1	1	1	1
Ibutilide	Ando et al.	60.0	0.04	0.06	0.18	1	1	1	1
Ibutilide	Kramer et al.	60.0	0.01	0.04	0.17	1	1	1	1
Imipramine	Lanacster and Sobie	60.0	38.06	58.62	48.11	1	0	1	0
Imipramine	Mirams et al.	60.0	38.06	58.62	48.11	0	0	1	0
Loratadine	Ando et al.	60.0	44.53	24.05	15250.00	0	0	0	0
Loratadine	Kramer et al.	60.0	38.36	11.01	20209.49	0	0	0	0
Mexiletine	Ando et al.	60.0	42.74	71.06	17.28	0	0	1	0
Mexiletine	Mirams et al.	60.0	42.86	63.56	18.16	0	0	1	0
Mexiletine	Li et al.	60.0	54.23	0.00	10.98	0	0	0	0
Mexiletine	Crumb et al.	60.0	75.00	0.00	47.94	-	0	0	0
Mibefradil	Kramer et al.	60.0	89.63	20.19	190.05	0	0	0	0
Mibefradil	Ando et al.	60.0	83.33	31.29	40.48	0	0	0	0
Mibefradil	Mirams et al.	60.0	94.54	73.37	225.00	0	0	0	0
Mibefradil	Crumb et al.	60.0	41.75	7.59	45.45	-	0	1	0
Moxifloxacin	Crumb et al.	60.0	0.00	0.00	51.33	-	1	1	1
Moxifloxacin	Ando et al.	60.0	42.77	10.42	23.09	1	1	1	0
Moxifloxacin	Kramer et al.	60.0	43.41	10.66	12.11	1	1	1	0
Moxifloxacin	Okada et al.	60.0	22.59	0.39	19.37	0	1	1	1
Nifedipine	Kramer et al.	60.0	99.99	46.60	9130.13	0	0	0	0

Nifedipine	Ando et al.	60.0	99.98	42.72	6600.00	0	0	0	0
Nifedipine	Mirams et al.	60.0	99.99	91.77	53571.43	0	0	0	0
Nilotinib	Ando et al.	60.0	7.89	10.14	8.82	0	1	1	1
Nilotinib	Kramer et al.	60.0	8.02	1.03	8.87	1	1	1	1
Nilotinib	Crumb et al.	60.0	0.00	0.00	2.50	-	1	1	1
Nitrendipine	Ando et al.	60.0	99.93	63.08	12300.00	0	0	0	0
Nitrendipine	Kramer et al.	60.0	99.69	68.58	13444.95	0	0	0	0
Nitrendipine	Mirams et al.	60.0	100.00	29.41	4966.89	0	0	0	0
Ondansetron	Crumb et al.	60.0	13.61	3.74	6.24	-	1	1	1
Ondansetron	Li et al.	60.0	12.90	3.47	14.90	0	1	1	1
Ondansetron	Ando et al.	60.0	9.05	10.11	29.22	1	1	1	1
Paliperidone	Ando et al.	60.0	0.60	1.06	39.00	0	1	1	1
Paliperidone	Kramer et al.	60.0	0.60	0.24	16.89	1	1	1	1
Phenytoin	Kramer et al.	60.0	90.77	76.50	50.57	0	0	0	0
Phenytoin	Mirams et al.	60.0	59.29	75.38	33.33	0	0	0	0
Pimozide	Kramer et al.	60.0	10.44	4.26	113.47	1	1	1	1
Pimozide	Mirams et al.	60.0	15.62	35.71	30.00	1	1	1	1
Pimozide	Ando et al.	60.0	20.00	5.17	139.53	1	1	1	1
Prenylamine	Ando et al.	60.0	7.51	3.75	27.86	1	1	1	1
Prenylamine	Mirams et al.	60.0	7.29	3.72	5.74	1	1	1	1
Procainamide	Kramer et al.	60.0	50.99	35.37	7.54	1	1	0	0
Procainamide	Ando et al.	60.0	51.20	35.37	7.86	1	1	0	0
Propafenone	Lanacster and Sobie	60.0	26.83	35.68	2.74	1	1	1	1
Propafenone	Mirams et al.	60.0	26.83	35.68	2.74	0	1	1	1
Propafenone	Crumb et al.	60.0	35.50	17.05	6.10	-	1	1	0
Quinidine	Ando et al.	60.0	14.44	6.89	0.34	1	1	1	1
Quinidine	Okada et al.	60.0	15.13	1.42	0.29	1	1	1	1
Quinidine	Li et al.	60.0	11.24	4.65	0.51	1	1	1	1
Quinidine	Mirams et al.	60.0	2.80	2.64	0.14	1	1	1	1
Quinidine	Kramer et al.	60.0	22.70	3.90	0.33	1	1	1	1
Quinidine	Crumb et al.	60.0	0.99	0.85	0.61	-	1	1	1
Quinine	Ando et al.	60.0	81.89	78.05	14.72	0	1	0	0
Quinine	Crumb et al.	60.0	22.20	22.28	1.96	-	1	1	1
Ranolazine	Okada et al.	60.0	7.35	16.73	3.01	0	0	1	1
Ranolazine	Crumb et al.	60.0	0.00	0.00	5.53	-	0	1	1
Ranolazine	Li et al.	60.0	0.00	8.83	6.66	0	0	1	1
Ranolazine	Ando et al.	60.0	5.51	5.54	7.50	0	0	1	1
Risperidone	Lanacster and Sobie	60.0	0.31	0.22	124.31	1	1	1	1
Risperidone	Kramer et al.	60.0	2.84	0.98	195.80	1	1	0	0
Risperidone	Mirams et al.	60.0	0.31	0.22	124.31	0	1	1	1

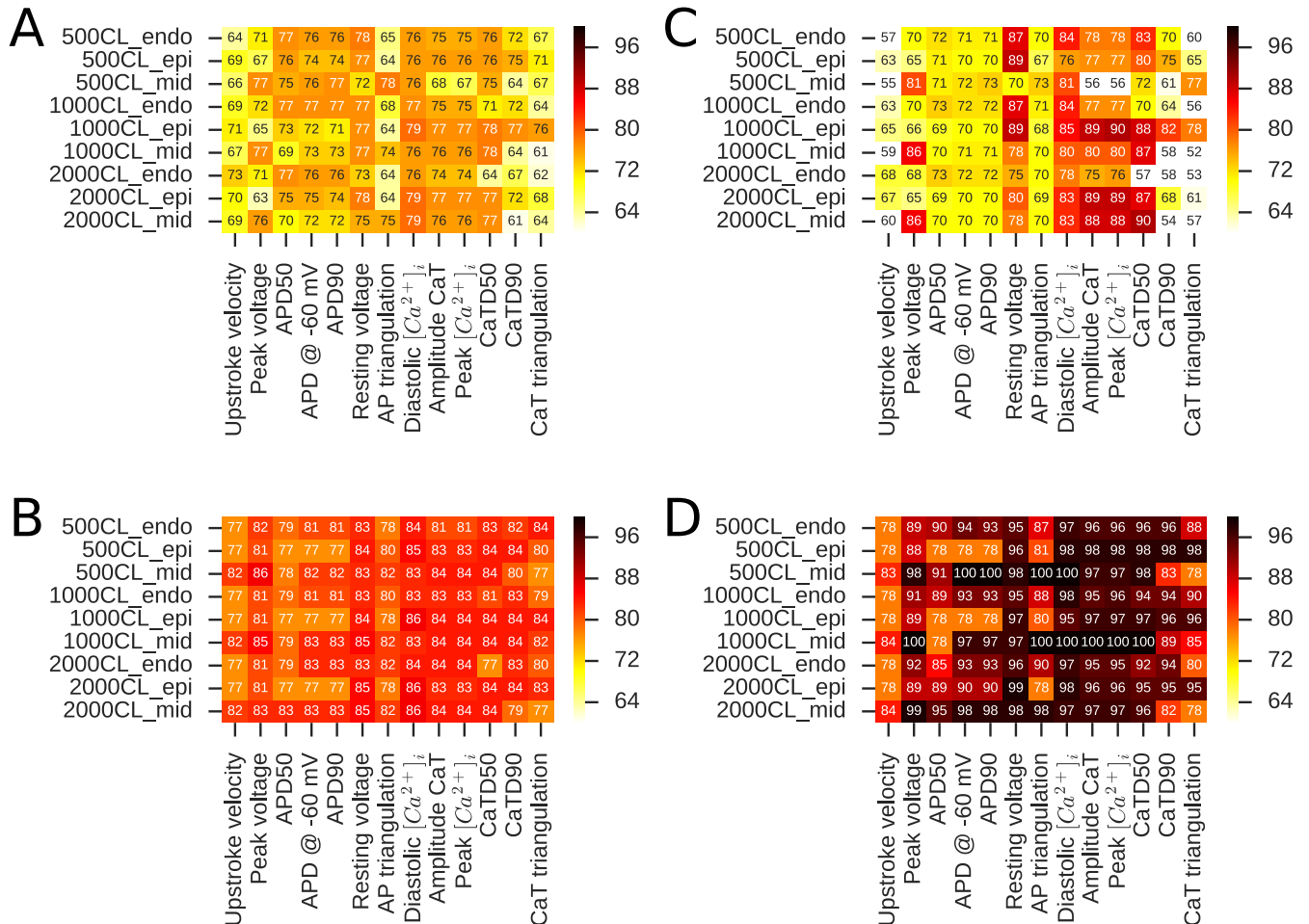
Risperidone	Ando et al.	60.0	1.13	0.89	26.00	0	1	1	1
Saquinavir	Crumb et al.	60.0	66.84	21.21	12.50	-	1	0	0
Saquinavir	Kramer et al.	60.0	94.18	79.14	164.56	0	1	0	0
Sertindole	Kramer et al.	60.0	0.17	0.25	22.82	1	1	1	1
Sertindole	Mirams et al.	60.0	0.24	0.90	13.21	1	1	1	1
Sertindole	Ando et al.	60.0	0.78	0.71	30.94	0	1	1	1
Sertindole	Crumb et al.	60.0	0.00	0.00	11.41	-	1	1	1
Sotalol	Li et al.	60.0	3.61	1.25	12.50	1	1	1	1
Sotalol	Crumb et al.	60.0	2.77	1.08	9.23	-	1	1	1
Sotalol	Ando et al.	60.0	46.37	2.33	12.85	1	1	0	0
Sotalol	Kramer et al.	60.0	50.11	2.69	13.22	1	1	0	0
Sotalol	Okada et al.	60.0	0.00	0.00	36.09	1	1	1	1
Sparfloxacin	Kramer et al.	60.0	27.79	1.32	19.35	1	1	1	1
Sparfloxacin	Ando et al.	60.0	27.18	1.28	17.45	1	1	1	1
Terfenadine	Li et al.	60.0	12.81	0.93	11.30	0	1	1	1
Terfenadine	Okada et al.	60.0	2.16	34.55	15.45	1	1	1	1
Terfenadine	Crumb et al.	60.0	11.39	0.77	4.15	-	1	1	1
Terfenadine	Kramer et al.	60.0	0.92	0.23	7.68	1	1	1	1
Terfenadine	Ando et al.	60.0	7.46	3.61	7.89	1	1	1	1
Terfenadine	Mirams et al.	60.0	3.44	1.36	1.48	1	1	1	1
Terodiline	Ando et al.	60.0	16.88	11.64	4.06	1	1	1	1
Terodiline	Kramer et al.	60.0	16.55	7.57	6.67	1	1	1	1
Thioridazine	Kramer et al.	60.0	11.22	33.55	0.77	1	1	1	1
Thioridazine	Mirams et al.	60.0	3.67	2.63	0.05	1	1	1	1
Thioridazine	Ando et al.	60.0	17.65	34.88	16.67	1	1	1	1
Verapamil	Kramer et al.	60.0	63.25	0.28	4.48	0	0	0	0
Verapamil	Crumb et al.	60.0	80.22	0.00	16.03	-	0	0	0
Verapamil	Ando et al.	60.0	65.22	1.14	4.08	0	0	0	0
Verapamil	Mirams et al.	60.0	68.20	0.51	2.65	0	0	0	0
Verapamil	Okada et al.	60.0	46.74	9.40	3.38	0	0	0	0
Verapamil	Li et al.	60.0	69.88	0.00	5.33	0	0	0	0

**Table S12.** Common drugs: 46 drugs were common across more than one datasets. Here, we list the % block of  $IC_{CaV}$ ,  $I_{Na,peak}$  for these drugs at drug concentrations equal to  $IC_{60,hERG}$  to highlight the differences across the datasets. Moreover, we list the risk category each drug was assigned to in the original datasets (“Risk (O)” column) as well the risk category (“Risk”) assigned here to analyze the merged dataset. “Prediction” column highlights whether a drug is classified as TdP+ (1) or TdP (0) for the merged dataset using the direct features. We also highlight whether a drug results in EAD or not at  $C_{drug} = IC_{60,hERG}$  in the “EAD” column. Drugs which ended up with different predictions are highlighted in gray.



## 2 METHODS AND RESULTS

### 79 2.1 Classification accuracy based on the derived Features taking into account the 80 drug-induced block of all the available ion-channels for a particular drug



(A,B) TdP risk classification accuracy using the derived Features

(C,D) Accuracy of prediction of pause-induced EADs using the derived features

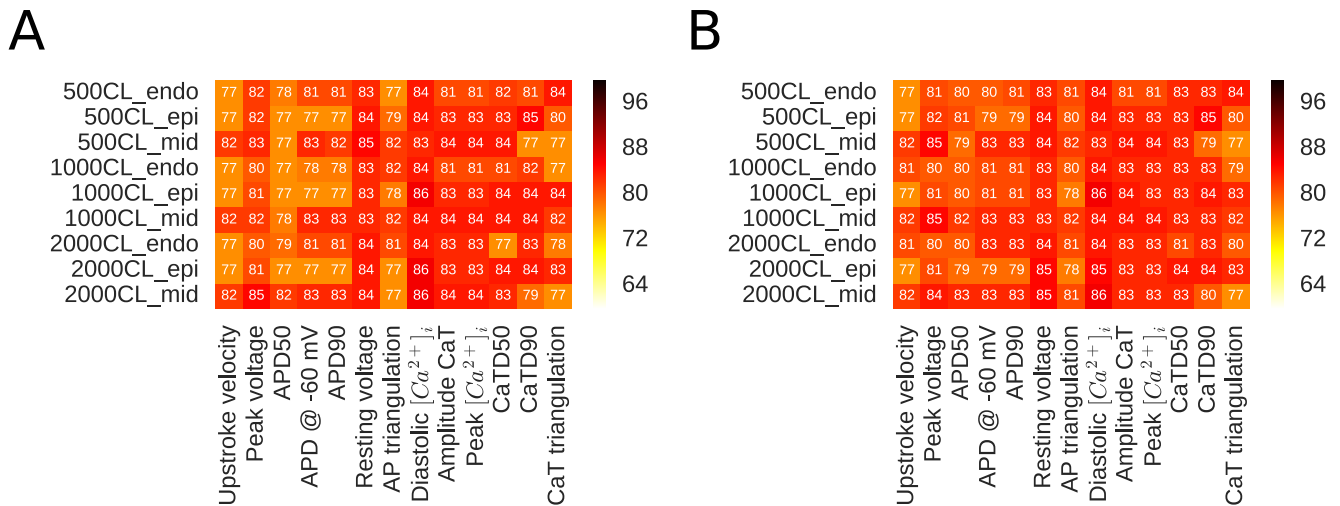
**Figure S1.** Heat maps of leave-one-out cross validation scores for logistic regression classifiers built on 13 features extracted from the APs and  $Ca^{2+}$  transients in OHR model simulations. Drug-induced multi-channel block evaluated in the mid, endo and epi cell type at 500, 1000 and 2000ms pacing rates. TdP risk classification at (A) EFTPC drug concentrations and (B) drug concentrations equal to hERG  $IC_{50}$ . Classification by EAD induction at (C) EFTPC drug concentrations (D) drug concentrations equal to hERG  $IC_{50}$ .

	$\beta_{intercept}$	$\beta_{cav}$	$\beta_{nal}$	Figure/Table	$Coe.f_{nal}$ $= \beta_{nal}/\beta_{cav}$	Threshold Y-axis $= \beta_{nal}/\beta_{intercept}$
Dataset1	4.473618	-0.195135	-	<b>Figure 3 and Table 4</b>	-	22.925721
Dataset2	5.571355	-0.097846	-	<b>Figure 3 and Table 4</b>	-	56.940049
Dataset3 [cav]	2.879890	-0.146161	-	<b>Figure 3 and Table 4</b>	-	19.703524
Dataset3 [cav nal]	22.949021	-1.036844	-1.64362	<b>Figure 3 and Table 4</b>	1.58522	22.133535
Dataset4	2.827687	-0.063619	-	<b>Figure 3 and Table 4</b>	-	44.447431
Dataset5 [cav]	2.300028	-0.042746	-	<b>Figure 4A and Table 4</b>	-	53.806997
Dataset5 [cav nal]	2.771003	-0.038716	-0.0197162	<b>Figure 4B and Table 4</b>	0.509248	71.571871
Dataset6	1.607803	-0.037014	-	<b>Figure 3 and Table 4</b>	-	43.437807
Dataset7 [cav]	2.548515	-0.075452	-	<b>Figure 3 and Table 4</b>	-	33.776838
Dataset7 [cav nal]	41.795781	-0.640847	-0.804278	<b>Figure 3 and Table 4</b>	1.25502	65.219578
Dataset8	1.471547	-0.032359	-	<b>Figure 3 and Table 4</b>	-	45.476341
Dataset5 [cav] [target2]	1.221071	-0.047759	-	<b>Figure 4C</b>	-	25.567424
Dataset3 [cav nal] [target2]	2.188419	-0.053652	-0.0263147	<b>Figure 4D</b>	0.490471	40.789300

**Table S13.** Beta coefficients for Logistic Regression. Figure/Table column lists the corresponding figure and table number in the main article for which the regression coefficients and the thresholds are listed here.

81 **2.2 Classification results using SVM and Neural Network**

82 TdP classifiers from the direct features built using SVM and Neural networks yielded identical  
 83 classification accuracy (85%) for the merged dataset as compared to logistic regression models.  
 84 Classification accuracies obtained using SVM and Neural networks on derived features are shown in  
 85 Figure S2 and resulted in maximum classification accuracy of 86%, as for the Logistic regression classifier.  
 86 For the limited data with insignificant nonlinearities the choice of the classifier had not significant impact  
 87 on the observed accuracies.



(A,B) TdP risk classification accuracy using the derived Features

**Figure S2.** Heat maps of leave-one-out cross validation scores for logistic regression classifiers from 13 features of the APs and  $Ca^{2+}$  transients in OHR model simulations using 1) Support Vector machine 2) Feed forward neural network with 13 hidden units. Drug-induced multi-channel block evaluated in the mid, endo and epi cell type at 500, 1000 and 2000 ms pacing rates. TdP risk classification at drug concentrations equal to hERG  $IC_{50}$ .

## 88 2.3 GPU implementation

89 EAD simulations with fixed time step of 0.001 ms take approximately 2 mins per simulation (Intel Xeon  
90 E5-2660 v4, 2.00 GHz CPU). Hence, the 1000 simulations to generate the EAD space in Figure 2 (main  
91 article) result in approximately 2000 mins (33 hours) if executed serially. We parallelized the models using  
92 Python's PyCUDA package which allows access to NVIDIA's CUDA GPUs (8GB DDR5 graphics card  
93 with 2048 CUDA cores, Quadro M5000). The parallelization allowed execution of the 1000 simulations in  
94 approximately 8 hours providing a 4x improvement in the performance. However, the numerical methods  
95 and number of simulations will greatly affect these timings.

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