

IN-SILICO CARDIAC LIABILITY, EXPLAINED IN ONE PAGE

The mechanism read: a ranked cause, the risk class, and the one experiment that settles it.

A fast answer to which ion current drove a repolarization signal, scored on a published human iPSC-cardiomyocyte model, with the confirming experiment you would run next.

The loss is on the page. On the public 28-drug CiPA panel, a free hERG-only margin built from two published numbers classifies torsade risk more accurately than our simulation does, 18 of 28 against 17 of 28. Every row, including the misses, is published at perturb.bio/benchmark.

01 WHAT THE READ RETURNS

Ranked ion-current mechanisms. A short list of causes with the distance between them measured, so you see when rank 1 wins by a factor of three versus by a hair.

Dose-response and APD90. Block and repolarization against multiples of free Cmax, the curve the risk class is a threshold on.

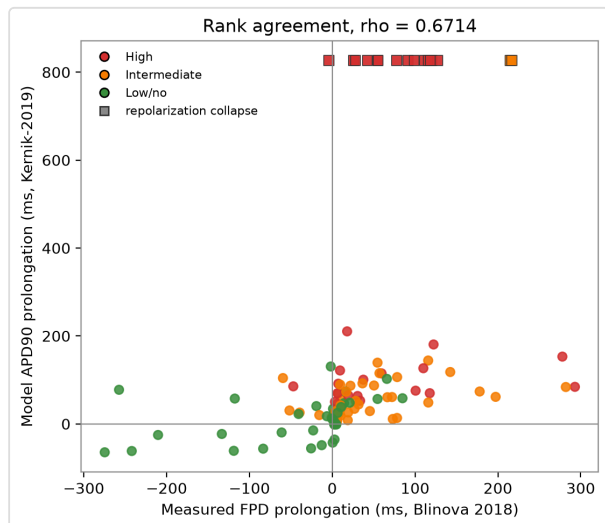
Risk class. Low, Intermediate or High on the CiPA TdP scale, from frozen thresholds.

One confirming experiment. The single assay that separates the surviving hypotheses, on the same cell type your assay uses.

Stated limits. Which currents resolve, which the model leaves out, and where the report says "unclear".

02 THE TWO-DATASET VALIDATION

Two independent measured datasets agree with the model's direction and rank.



Blinova et al. 2018: 112 matched drug-dose points, Spearman rank 0.67, direction agreement 89%.

Against Lee et al. 2025, direction agrees on 9 of 10 anchored drugs. The preprint is at perturb.bio/writing/two-dataset-validation.

Free first read

On a published or non-confidential compound, in the identical report format. Judge the work before paying. Never invoiced.

03 A WORKED EXAMPLE · VERAPAMIL

Verapamil blocks calcium hard enough to offset its own repolarization delay, so the hERG-only margin misses it by two classes (calls it High). The mechanism read ranks the competing hypotheses, stays one class off (Intermediate, clinically Low), and names the calcium readout that would confirm the cause.

current	IC50 (nM)	block 1x	enters sim
Cav1.2 / ICaL	202	26.8%	yes
hERG / IKr	288	22.8%	yes
late Na / INaL	7.03e3	1.0%	recorded

APD90 +5.7% / +9.8% / +13.9% / +18.8% at 1x-4x free Cmax.

04 HOW IT COMPARES

The read sits before the three standard routes: the free CiPA in-silico model, the licensed simulator (Certara CSS), and the wet CRO. Each returns a class or a license; the read returns the ranked cause and the confirming experiment a margin cannot give. On the risk-label task the free margin wins, and that is published.

05 WHERE IT STANDS

The model is a single cell, short of tissue and a whole heart. Its one structural gap, the missing late-sodium current, is stated in every limits section, and compounds whose margin depends on INaL read too dangerous.

17/28

OUR 3-CLASS CALL,
BLIND + TRAIN

18/28

FREE HERG MARGIN

0.67

SPEARMAN RANK VS
BLINOVA

Paid mechanism read

On your proprietary data. Ranked mechanisms, dose curve, risk class, confirming experiment, stated limits. 1-2 weeks, from \$12,000.