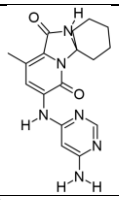
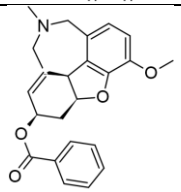
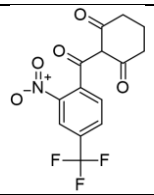
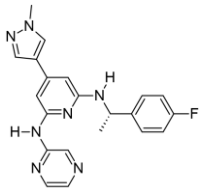
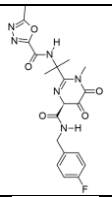
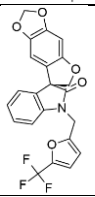
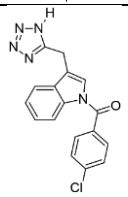
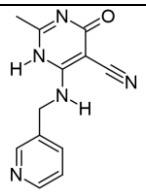
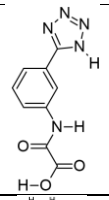
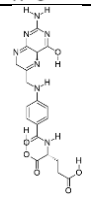
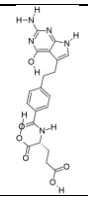
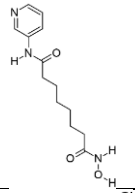
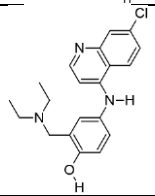
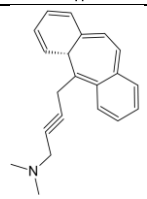
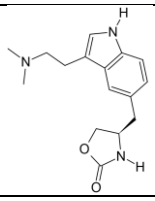
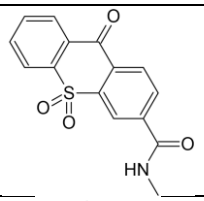
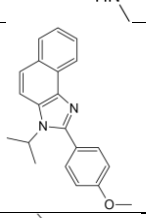
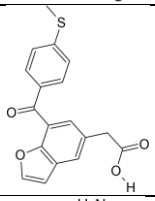
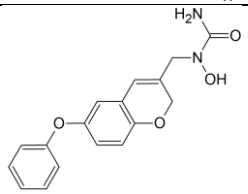
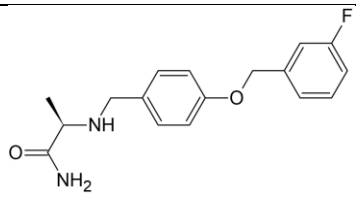
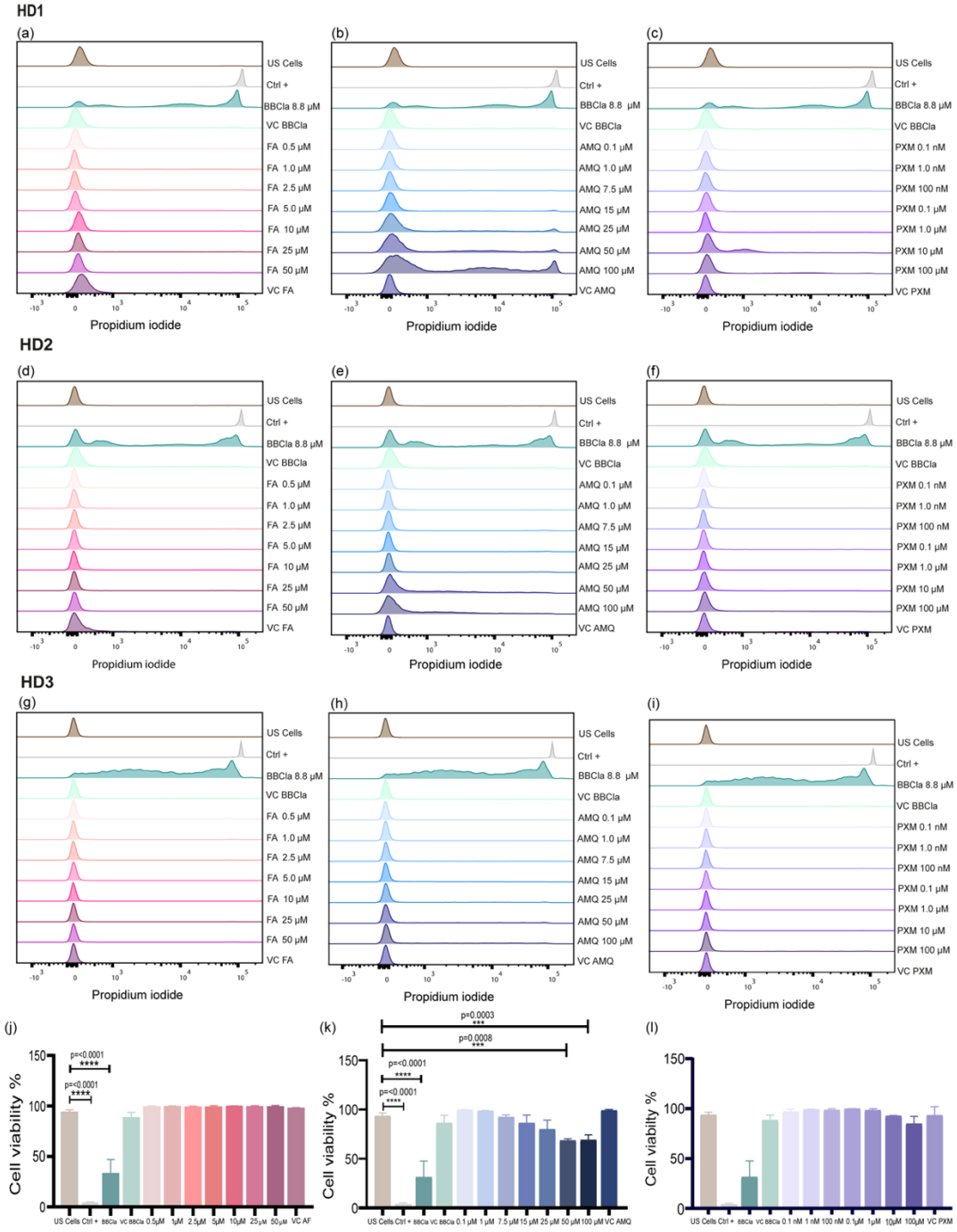
Repositioning new PAD4 inhibitors identified by computer aided simulations, in vitro and ex vivo evaluations

Table 1 Best ranked compounds

Compound	Structure	Name	Binding free energy (kcal/mol)
1		Tomivosertib (Metastatic triple negative breast cancer, Hepatocellular carcinoma) MAPK1,2 inhibitor	-7.8
2		Galantamine analog (AD, ach inhibitor)	-7.4
3		Nitisinone (hydroxyphenylpyruvate dioxygenase inhibitor, treatment of hereditary tyrosinemia type 1	-7.4
4		Ilginatinib (trials studying the treatment of Primary Myelofibrosis, Post-Polycythemia Vera Myelofibrosis, jak2 inhibitor)	-7.3
5		Raltegravir (HIV infections, inhibits HIV integrase)	-7.3
6		Funapide (Postherpetic Neuralgia, and Osteoarthritis of the Knee, Sodium channel protein type 9 subunit alpha)	-7.2
7		Itrazole (anti inflamatory)	-7.1

8		Pelrinone (Phosphodiesterase III inhibitor)	-7.1
9		Acitazanolast (zeppelin) (Active metabolite of tazanolast and anti-allergic drug)	-7.1
10		Folic acid (Indicated to prevent neural tube defects and support the prevention of certain types of cancer)	-7.1
11		Pemetrexed (Folate analog used to treat mesothelioma).	-7
12		Pyroxamide (Treatment of Leukemia, Lymphoma, Small Intestine Cancer, HDAC1 inhibitor)	-7
13		Amodiaquine (Antimalarial and an anti-inflammatory agent)	-7
14		Intriptyline (Tricyclic antidepressant agent)	-7
15		Zolmitriptan (Acute migraines)	-7

16		BW-616U (MAO-A inhibitor)	-7
17		Tomoxiprole (Analgesic and anti-inflamatory agent)	-7
18		Tifurac (Analgesic, anti-inflamatory and antipyretic agent)	-7
19		HA-1004 (PKA, PKC, cGKI and MYLK inhibitor, calcium channel protein inhibitor)	-7
20		Safinamide mesylate (Small molecule drug clinical trial phase IV indicated for Parkinson disease)	-7



Supplementary figure 1. Viability of mononuclear cells. The effect of the compounds was evaluated against untreated human blood cells obtained from a healthy donor (HD). The results represent the percentage relative to the negative control and correspond to the average of three independent experiments. Histograms (a), (d), and (g) represent cells stimulated with folic acid; (b), (e), and (h) show cells in the presence of amodiaquine; and histograms (c), (f), and (i) correspond to cells stimulated with pyroxamide. Bar graphs (j) and (k) show the mean and standard deviation of cell viability with folic acid, amodiaquine, and pyroxamide. The one-way ANOVA statistical test was used, Tukey's Dunn's comparison test was used as a post hoc test to identify pairwise differences between groups.