



**Figure S1.** Dose-response curves of the six positive hits. *klpmr1Δ* cells were grown for 24h in the presence of different concentrations of the indicated compounds, then cells were challenged for further 24h with either menadione or H<sub>2</sub>O<sub>2</sub>, depending on the ability of each compound to allow the growth of *klpmr1Δ* cells using enadione or H<sub>2</sub>O<sub>2</sub> as selective agents, as reported in Figure1. For Kaempferol only the dose-curve response in the presence of H<sub>2</sub>O<sub>2</sub> is shown since its effect on cell growth in H<sub>2</sub>O<sub>2</sub> was much stronger than that observed in menadione treated cells Figure1 The optical density was determined and normalized to OD<sub>600</sub> of untreated cells.

**Table S1.** The collection of 131 natural compounds utilized in the screening. Asterisks indicate molecules that resulted toxic.

S1973	Cyclocytidine HCl	S2314	Kaempferol	S2370	Ursolic acid (Malol)
S2250	(-)-Epigallocatechin gallate	S2316	Kinetin (6-Furfuryladenine)	S2371	Vanillylacetone
S2252	(+)-Usniacin (D-Usnic acid)	S2317	L (+)-Rhamnose Monohydrate	S2372	Xanthone (Genicide)
S2253	3-Indolebutyric acid (IBA)	S2319	Limonin	S2373	Yohimbine hydrochloride (Antagonil)
S2256	4-Methylumbelliferone (4-MU)	S2320	Luteolin	S2374	5-hydroxytryptophan (5-HTP)
S2258	Aesculin (Esculin)	S2321	*Magnolol	S2375	Aloin (Barbaloin)
S2260	*Amygdalin	S2322	Matrine ((+)-Matrine)	S2376	Ammonium Glycyrrhizinate (AMGZ)
S2261	Andrographolide	S2323	Methyl-Hesperidin	S2377	*Biochanin A (4-Methylgenistein)
S2262	Apigenin	S2325	Morin hydrate (Aurantica)	S2378	Butylscopolamine bromide
S2263	Arbutin (Uva, p-Arbutin)	S2326	Myricetin (Cannabiscetin)	S2379	Dioscin (Collettiside III)
S2265	Artesunate	S2327	Myricitrin (Myricitrine)	S2380	Diosmetin (Luteolin 4-methyl ether)
S2266	Asiatic acid	S2328	Nalidixic acid (NegGram)	S2381	D-Mannitol (Osmitrol)
S2267	Azomycin (2-Nitroimidazole)	S2329	Naringin (Naringoside)	S2383	Gastrodin (Gastrodine)
S2268	*Baicalein	S2331	Neohesperidin dihydrochalcone (Nhdc)	S2384	Hematoxylin (Hydroxybrazilin)
S2269	Baicalin	S2332	Neohesperidin	S2385	Hordenine
S2270	Bergenin (Cuscutin)	S2333	Nobiletin (Hexamethoxyflavone)	S2386	Indirubin
S2271	*Berberine Hydrochloride	S2334	Oleanolic Acid (Caryophyllin)	S2387	Lappaconite Hydrobromide
S2273	β-Sitosterol	S2335	Oridonin (Isodonol)	S2389	Naringin Dihydrochalcone (Naringin DC)
S2276	Bilobalide	S2336	Orotic acid (6-Carboxyuracil)	S2390	Polydatin(Piceid)
S2277	Caffeic acid	S2337	Osthole (Osthol)	S2391	Quercetin (Sophoretin)
S2280	Chlorogenic acid	S2338	Oxymatrine (Matrine N-oxide)	S2392	Sesamin (Fagarol)
S2281	*Chrysin	S2339	Paeonol (Peonol)	S2393	Sorbitol (Glucitol)
S2282	Cinchonidine	S2341	*Parthenolide ((-)-Parthenolide)	S2394	Naringenin
S2285	Cryptotanshinone	S2342	Phloretin (Dihydronaringenin)	S2395	Rheochrysidin (Physcione)
S2286	Cyclosporin A (Cyclosporine A)	S2343	Phlorizin (Phloridzin)	S2396	Salidroside (Rhodioloside)
S2287	Cytisine (Baphitoxine, Sophorine)	S2344	Piperine (1-Piperoylpiperidine)	S2397	Palmatine chloride
S2290	Dihydroartemisinin (DHA)	S2346	Puerarin (Kakonein)	S2399	Dihydromyricetin (Ampeloptin)

S2292	Diosmin	S2347	Quercetin dihydrate (Sophoretin)	S2401	Sodium Danshensu
S2293	DL-Carnitine hydrochloride	S2349	Rutaecarpine (Rutecarpine)	S2403	Tetrandrine (Fanchinine)
S2295	Emodin	S2350	Rutin (Rutoside)	S2404	*Isoliquiritigenin
S2296	Enoxolone (Glycyrrhetin)	S2351	Salicin (Salicoside, Salicine)	S2405	Sophocarpine
S2298	Fisetin (Fustel)	S2354	Sclareol	S2406	Chrysophanic acid (Chrysophanol)
S2299	Formononetin (Formononetol)	S2355	Sclareolide (Norambreinolide)	S2407	Curcumol
S2300	Fumalic acid (Ferulic acid)	S2356	Shikimic acid (Shikimate)	S2415	Astragaloside A
S2302	Glycyrrhizic acid	S2357	Silibinin (Silybin)	S2422	Ipriflavone
S2303	Gossypol	S2358	Silymarin (Silybin B)	S2423	10-Hydroxycamptothecin
S2304	Gramine	S2359	Sinomenine (Cucoline)	S2424	Hypoxanthine
S2306	Gynostemma Extract	S2362	Synephrine (Oxedrine)	S2425	Apocynin (Acetovanillone)
S2308	Hesperetin	S2363	Tangeretin (Tangeritin)	S2437	Rotundine
S2309	Hesperidin	S2364	Tanshinone I	S2439	Guanosine
S2310	*Honokiol	S2365	Tanshinone IIA (Tanshinone B)	S2442	Inosine
S2311	Hyodeoxycholic acid (HDCA)	S2366	Taxifolin (Dihydroquercetin)	S3071	Vanillin
S2312	Icariin	S2367	Tetrahydropapaverine hydrochloride	S3604	Triptolide
S2313	Indole-3-carbinol	S2369	Troloxerutin		

**Table S2.** Summary of the *klpmr1Δ* phenotypes analyzed to screen the natural product library.

Compounds	menadione	H <sub>2</sub> O <sub>2</sub>	EGTA	CFW	DASPMI
S2387 (Lappaconite)	++	-	-	++	++
S2267 (Azomycin)	++	+	-	++	-
S2386 (Indirubin)	+	-	++	++	++
S2328 (Nalidixic acid)	+	-	-	+++	-
S1973 (Cyclocytidine)	-	++	++	++	-
S2314 (Kaempferol)	+	++	-	++	+++

\*(+++)= Totally o strongly recovered; (++) = partialy recovered; (+) = slightly recovered; (-) = not recovered