Figure S1

Kondo et al.

a

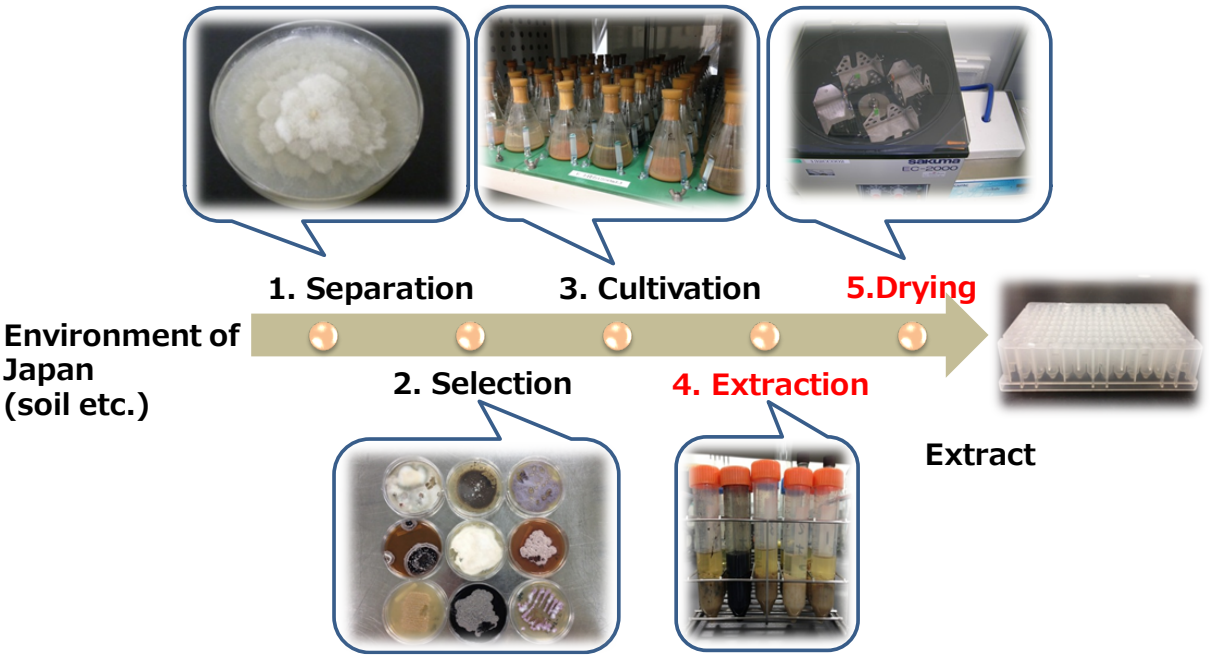

Figure S1

Schema of isolation culture of microbiota

Figure S2

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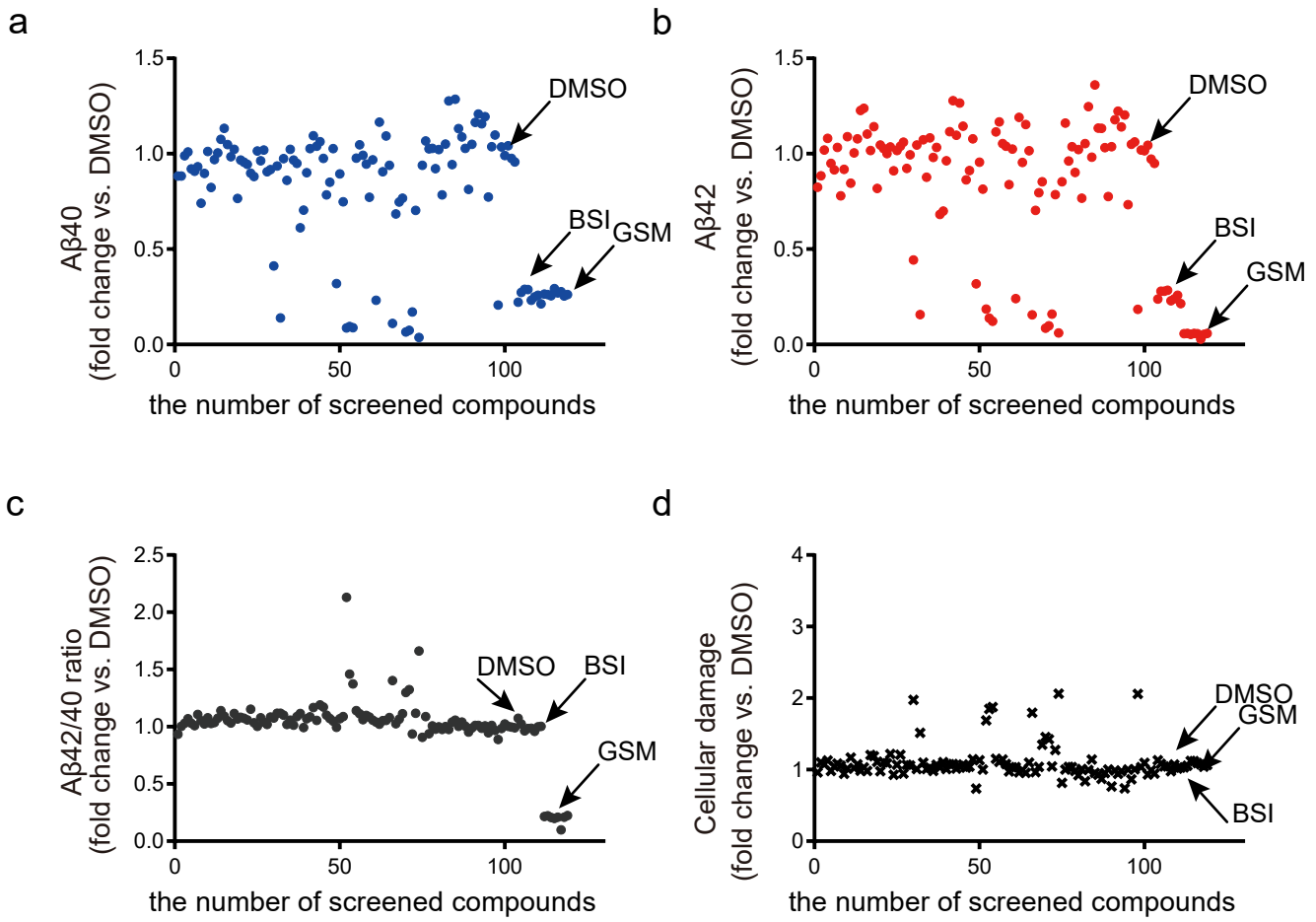


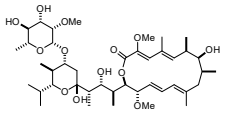
Figure S2

Primary screen results by using cortical neurons of familial Alzheimer's disease

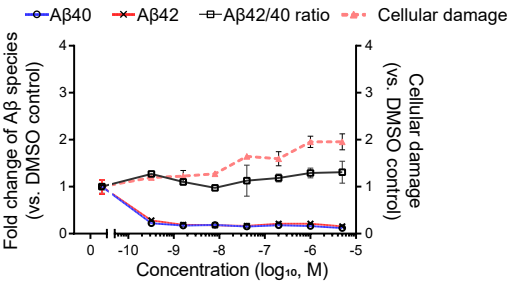
Scatter plot graph of (a) Aβ40 (blue round), (b) Aβ42 (red round), (c) Aβ42/40 ratio (black round), and (d) cellular damage (black x-mark). Fold change compared with DMSO control was plotted after adding compounds at a concentration of 50 nM. DMSO: dimethyl sulfoxide (negative control); BSI: β-secretase inhibitor (β-secretase inhibitor IV, positive control for Aβ40); GSM: γ-secretase modulator (JNJ-40418677, positive control for Aβ42 and Aβ42/40 ratio).

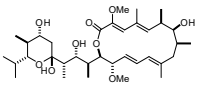
Figure S3

Kondo et al.

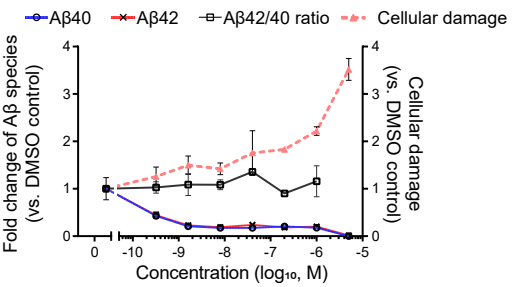


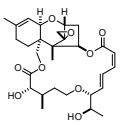
leucanicidin



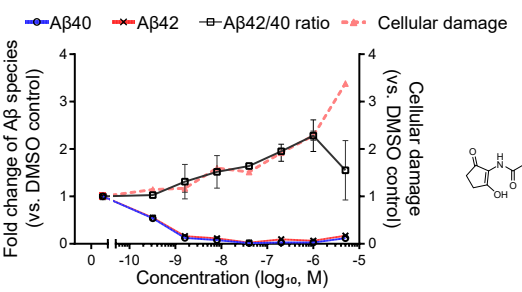


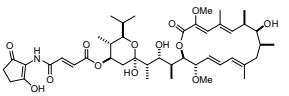
bafilomycin A1



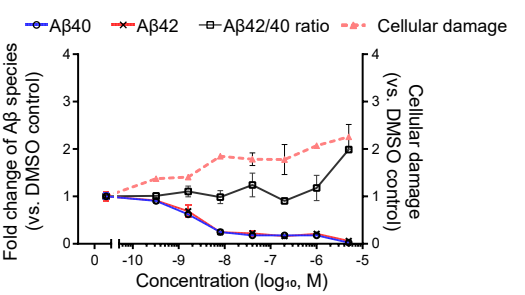


roridin A





bafilomycin B1



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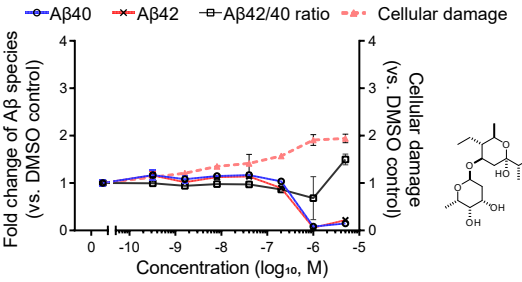
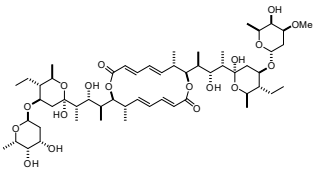
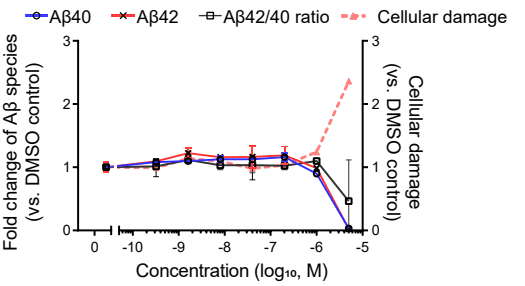
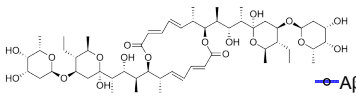




efomycin A





elaiophylin

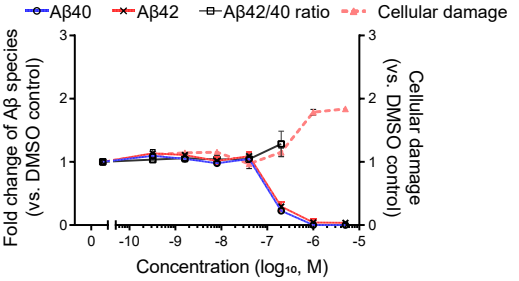


Figure S3

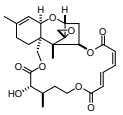
Evaluation of dose-dependent effect of hit compounds from the screening assay by using iPSCs of a patient with sporadic AD.

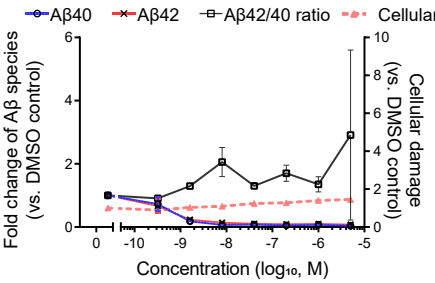
The effect on Aβ40 (blue line), Aβ42 (red line), Aβ42/40 ratio (black line), and cellular damage (dash line) was shown for each compound. Data represent mean ± SD (n = 3 per clone).

Figure S4

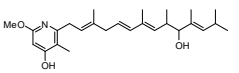
Kondo et al.

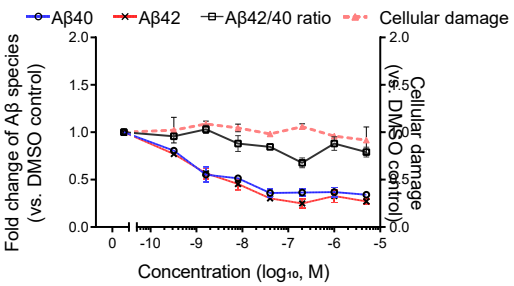
Verrucarin A



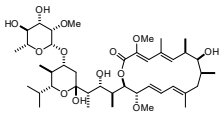


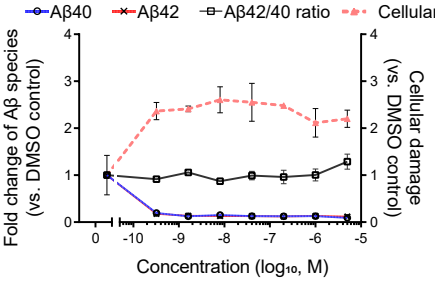
Mer-A2026A



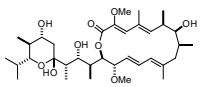


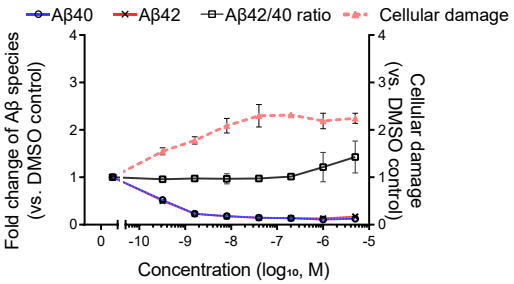
leucanicidin



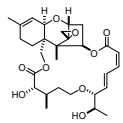


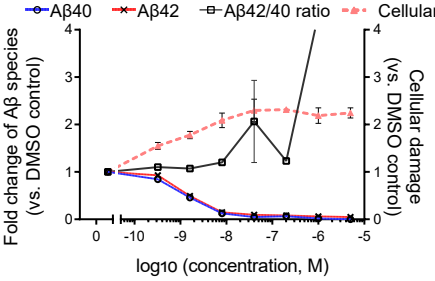
bafilomycin A1



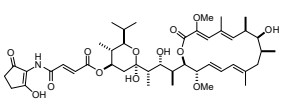


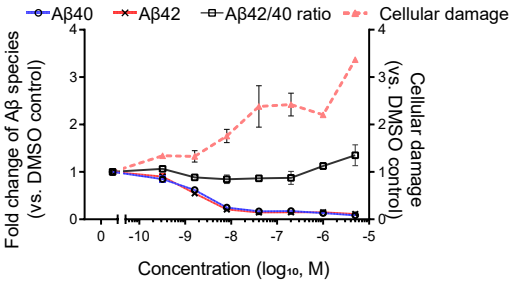
roridin A



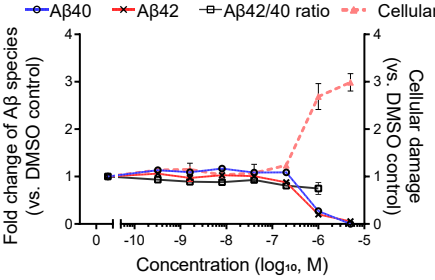


bafilomycin B1

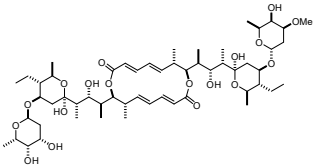


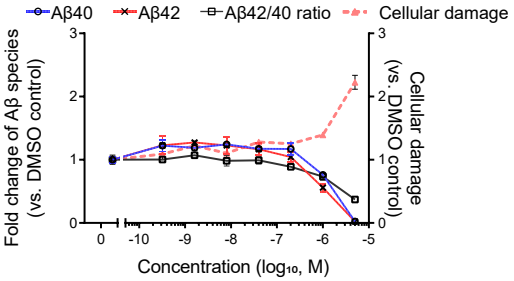


kalafungin

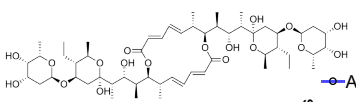


efomycin A





elaiophylin



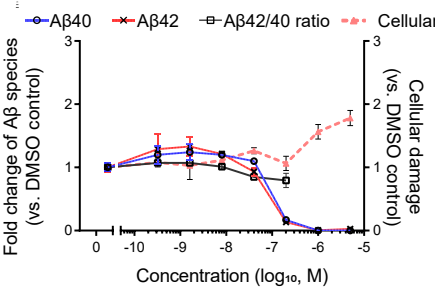


Figure S4

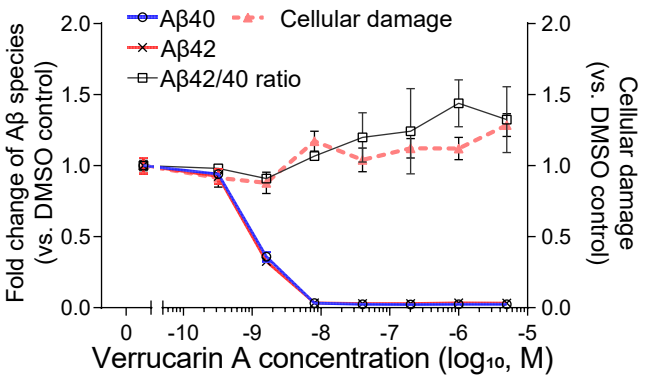
Evaluation of dose-dependent effect of hit compounds from the screening assay by using iPSCs of a patient with familial AD bearing *PSEN1* G384A mutation.

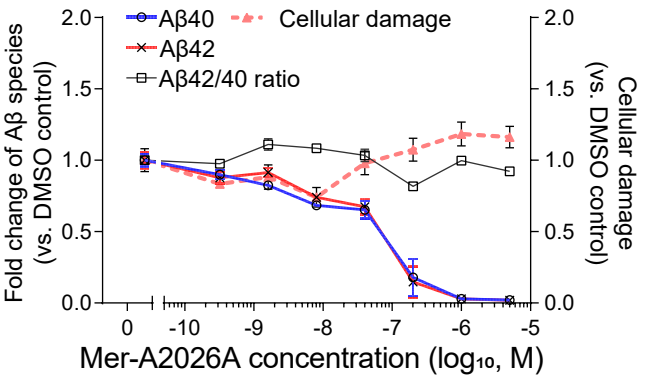
The effect on Aβ40 (blue line), Aβ42 (red line), Aβ42/40 ratio (black line), and cellular damage (dash line) was shown for each compound. Data represent mean ± SD (n = 3 per clone).

Figure S5

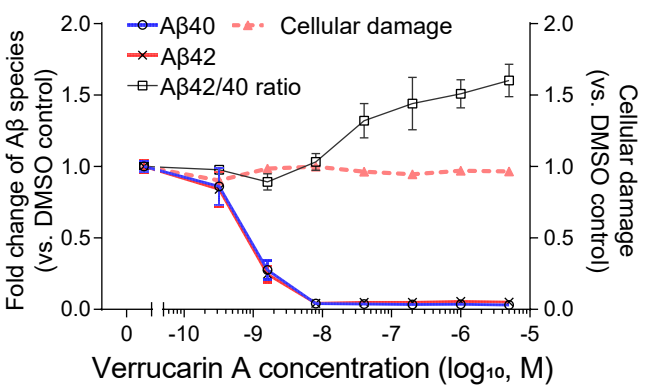
Kondo et al.

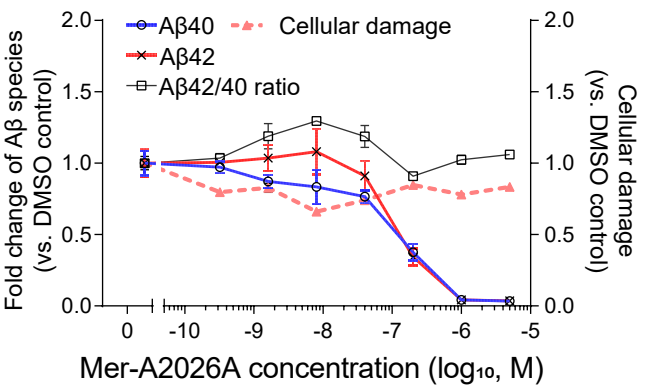
Healthy control 1



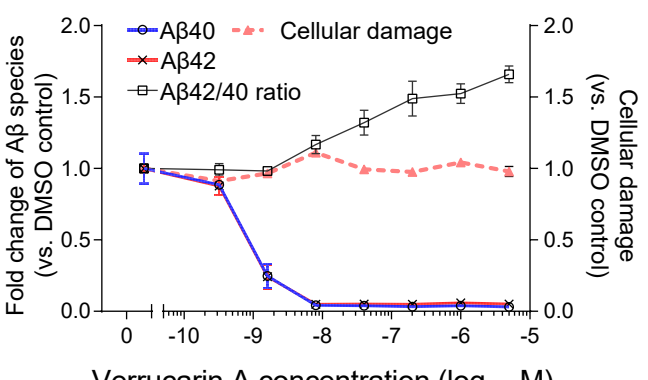


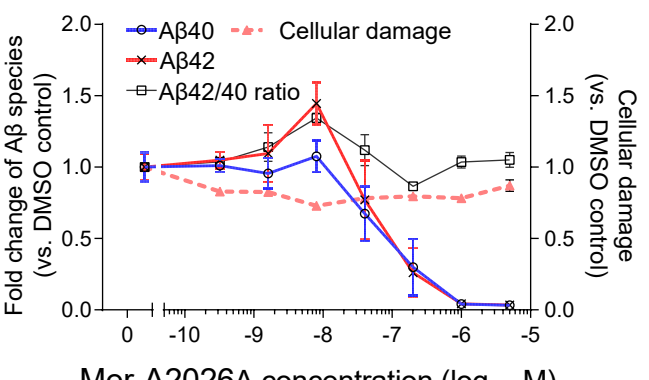
Healthy control 2



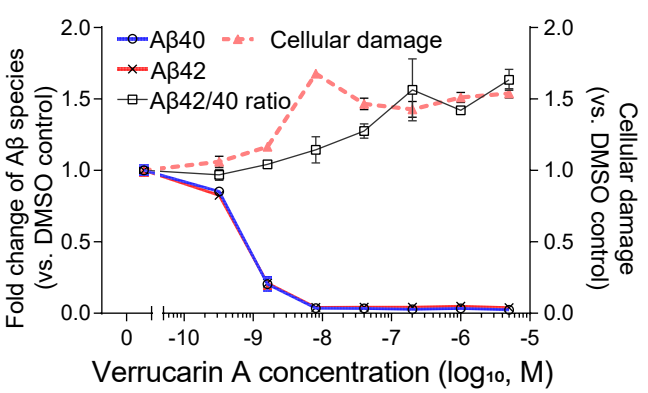


SAD patient 2





FAD patient 2



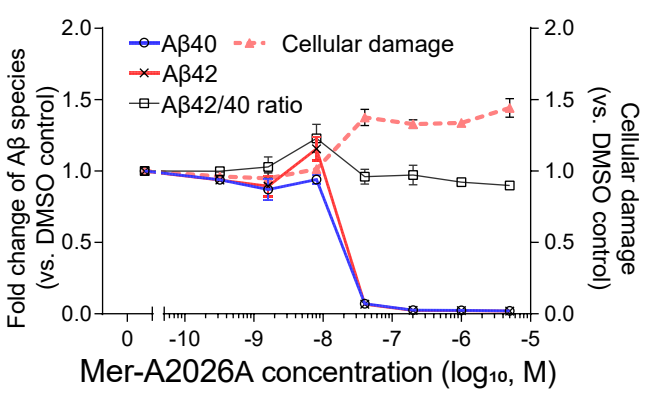


Figure S5

Evaluation of dose-dependent effect of Verrucarin A and Mer-A2026A by using iPSCs of healthy controls (Healthy control 1 and Healthy control 2), another patient of sporadic AD (SAD patient 2), and another patient of familial AD bearing *APP* V717L mutation (FAD patient 2)

The effect on Aβ40 (blue line), Aβ42 (red line), Aβ42/40 ratio (black line), and cellular damage (dash line) was shown for each compound. Data represent mean ± SD (n = 3 per clone).

Supplementary table S1: Results of the first screening based on neurons with SAD

No.	Compound	Aβ40	Aβ42	Aβ42/40 ratio	toxicity	Hit criteria
1	desmycosin	0.919	0.751	0.818	0.886	-
2	izenamicin B3	0.907	0.913	1.007	0.980	-
3	23-O-demycinosyltylosin	0.860	0.822	0.956	0.995	-
4	tylosin	0.829	0.735	0.887	1.084	-
5	5-O-mycaminosyltylonolide	0.956	0.870	0.910	1.003	-
6	demethylmacrocin	0.943	0.831	0.881	1.105	-
7	macrocin	0.835	0.793	0.949	0.970	-
8	carbomycin B	0.708	0.594	0.839	1.041	-
9	3-O-acetyltylosin	0.885	0.871	0.984	0.941	-
10	cytochalasin A	0.929	0.903	0.972	1.137	-
11	cytochalasin B	0.573	0.573	1.000	1.216	-
12	chaetoglobosin A	0.655	0.563	0.859	1.120	-
13	chaetoglobosin B	0.848	0.807	0.952	1.107	-
14	chaetoglobosin C	0.949	0.933	0.983	1.170	-
15	chaetoglobosin D	0.507	0.455	0.897	1.401	-
16	chaetoglobosin E	0.863	0.792	0.917	1.265	-
17	chaetoglobosin F	0.863	0.797	0.924	1.296	-
18	chaetoglobosin J	0.864	0.753	0.871	1.228	-
19	polyoxin D	0.706	0.717	1.015	1.060	-
20	polyoxin L	0.879	0.885	1.007	0.812	-
21	guanidylfungin A	0.928	1.022	1.101	1.055	-
22	Mer-WF5027	0.988	0.766	0.776	1.158	-
23	wortmannin	0.868	0.957	1.102	1.349	-
24	toyocamycin	**0.234**	**0.226**	0.965	**1.570**	-
25	amastatin	0.952	1.006	1.057	1.040	-
26	griseolutein B	0.539	0.516	0.957	**1.738**	-
27	relomycin	0.961	1.036	1.077	1.082	-
28	calbistrin A	0.845	0.825	0.977	1.112	-
29	neoviridogrisein II	0.879	0.901	1.025	1.198	-
30	chrysomycin A	**0.115**	**0.127**	1.100	**2.103**	-
31	gancidin W	0.788	0.815	1.035	0.942	-
32	salinomycin	**0.066**	**0.067**	1.022	**1.626**	-
33	leupeptin	0.894	0.946	1.058	1.068	-
34	deferoxamine mesylate	0.801	0.756	0.944	0.896	-
35	pepstatin A	1.097	1.051	0.958	1.113	-
36	chymostatin	1.015	1.057	1.041	1.071	-
37	neoaspergillic acid	0.952	0.933	0.980	1.152	-
38	brefeldin A	**0.056**	**0.069**	1.225	**2.398**	-
39	dehydrorabelomycin	0.433	0.438	1.011	1.190	-
40	tenuazonic acid	0.797	0.741	0.930	0.783	-
41	funiculosin	**0.234**	**0.212**	0.905	**1.871**	-
42	leucomycin U	0.959	0.968	1.009	0.887	-
43	3-O-acetyl-4"-O-isovaleryltylosin	0.988	0.988	1.001	1.091	-
44	leucomycin A1	1.024	1.117	1.092	0.973	-
45	angolamycin	0.958	1.002	1.046	1.095	-
46	Mer-NF5003 E	0.633	0.628	0.993	1.009	-
47	stachybotrydial	0.835	0.776	0.930	0.921	-
48	Mer-NF8054 A	1.000	1.000	1.000	1.036	-
49	Mer-A2026 B	**0.211**	**0.195**	0.920	**1.579**	-
50	propioxatin A	0.969	0.974	1.005	1.189	-
51	cytomycin	0.629	0.610	0.970	1.023	-
52	bafilomycin A1	**0.074**	**0.123**	**1.677**	**1.531**	**1**
53	leucanicidin	**0.074**	**0.137**	**1.866**	**1.709**	**1**
54	bafilomycin B1	**0.079**	**0.120**	**1.518**	**2.071**	**1**
55	bafilomycin D	0.496	0.442	0.891	1.014	-
56	phenylacetic acid	0.955	0.929	0.973	1.111	-
57	eupenifeldin	0.869	0.800	0.920	1.052	-
58	α-MAPI	1.087	1.042	0.958	1.010	-
59	papulacandin E	0.646	0.643	0.996	1.038	-
60	bacilycin	0.785	0.781	0.995	0.964	-
61	antibiotic SF 2487	**0.043**	**0.036**	0.843	**1.592**	-
62	β-MAPI	0.982	1.001	1.019	1.039	-
63	FK 506	0.889	1.040	1.170	0.904	-
64	hikizimycin	0.954	0.986	1.034	1.080	-
65	mithramycin	**0.134**	**0.113**	0.842	**2.053**	-
66	concanamycin A	**0.067**	**0.083**	1.246	**1.991**	-
67	bredinin	0.464	0.484	1.044	0.881	-
68	fungichromin	0.723	0.713	0.986	0.950	-

69	zincophorin	0.540	0.544	1.008	1.230	-
70	verrucarin A	**0.062**	**0.070**	1.129	1.329	**2**
71	roridin A	**0.058**	**0.094**	**1.620**	1.301	**1**
72	Mer-A2026 A	**0.150**	**0.157**	1.052	0.953	**2**
73	efomycin A	**0.209**	**0.187**	0.893	1.165	**2**
74	boromycin	**0.018**	**0.018**	1.033	**1.884**	-
75	pyridoxatin	0.997	0.889	0.892	0.788	-
76	complestatin	1.136	1.156	1.018	0.926	-
77	kalafungin	**0.076**	**0.043**	**0.564**	**3.036**	**1**
78	blasticidin S	0.683	0.597	0.874	1.100	-
79	gliotoxin G	0.671	0.574	0.856	1.010	-
80	elaiophylin	**0.010**	**0.011**	1.141	1.119	**2**
81	efomycin G	**0.029**	**0.000**	**0.000**	**2.423**	-
82	medermycin	1.019	1.087	1.067	0.756	-
83	oosporein	0.827	0.847	1.025	1.057	-
84	staurosporine	0.316	0.351	1.112	**2.045**	-
85	citrinin	1.033	1.016	0.983	0.960	-
86	spiculisporic acid	0.972	0.994	1.023	0.902	-
87	calbistrin B	0.607	0.525	0.864	0.970	-
88	5'-deoxytoyocamycin	0.943	0.930	0.986	0.896	-
89	aspergillin	0.882	0.847	0.960	0.928	-
90	chrysomycin B	0.434	0.406	0.935	**1.955**	-
91	cephamycin C	1.004	0.990	0.987	1.025	-
92	gliotoxin	0.964	0.953	0.989	0.961	-
93	streptothricin F	1.063	1.015	0.955	0.991	-
94	penicillic acid	1.034	0.981	0.949	0.901	-
95	streptothricin A	0.889	0.850	0.956	0.971	-
96	thiopeptin A1a	0.595	0.590	0.992	0.887	-
97	novobiocin	0.995	1.042	1.047	0.833	-
98	actinomycin D	**0.129**	**0.132**	1.023	**2.310**	-
NA	DMSO (negative control)	1.007	1.035	0.988	1.045	-
NA	DMSO (negative control)	1.006	1.013	1.007	1.029	-
NA	DMSO (negative control)	1.001	1.004	1.003	0.982	-
NA	DMSO (negative control)	0.952	0.928	0.975	0.948	-
NA	DMSO (negative control)	0.994	1.020	1.026	0.997	-
NA	BACE inhibitor IV (BSI)	**0.205**	**0.210**	1.023	0.979	-
NA	BACE inhibitor IV (BSI)	**0.238**	**0.219**	0.921	0.969	-
NA	BACE inhibitor IV (BSI)	**0.250**	**0.248**	0.992	0.985	-
NA	BACE inhibitor IV (BSI)	**0.228**	**0.227**	0.996	0.995	-
NA	BACE inhibitor IV (BSI)	**0.279**	**0.248**	0.891	0.963	-
NA	BACE inhibitor IV (BSI)	**0.206**	**0.171**	0.833	0.982	-
NA	BACE inhibitor IV (BSI)	**0.226**	**0.201**	0.893	0.936	-
NA	BACE inhibitor IV (BSI)	**0.214**	**0.201**	0.939	0.990	-
NA	JNJ-40418677 (GSM)	**0.285**	**0.059**	**0.209**	1.007	-
NA	JNJ-40418677 (GSM)	**0.276**	**0.056**	**0.201**	1.000	-
NA	JNJ-40418677 (GSM)	**0.273**	**0.059**	**0.218**	1.012	-
NA	JNJ-40418677 (GSM)	**0.265**	**0.057**	**0.215**	0.989	-
NA	JNJ-40418677 (GSM)	**0.282**	**0.059**	**0.208**	0.960	-
NA	JNJ-40418677 (GSM)	**0.273**	**0.061**	**0.222**	0.993	-
NA	JNJ-40418677 (GSM)	**0.280**	**0.064**	**0.228**	0.975	-
NA	JNJ-40418677 (GSM)	**0.260**	**0.058**	**0.222**	0.963	-