

Supplementary Information

Identification of D-amino acid oxidase and propiverine interaction partners and their potential role in the propiverine-mediated nephropathy

Maier, Marcia Y.^{1,2*}, Luks, Lisanne^{1*}, Baudendistel, Oliver R.^{2,3}, Wittmann, Valentin^{2,3} and Dietrich, Daniel R.^{1,2§}

¹Human and Environmental Toxicology, Department of Biology, University of Konstanz

²Konstanz Research School Chemical Biology (KoRS-CB), University of Konstanz

³Organic Chemistry/Bioorganic Chemistry, Department of Chemistry, University of Konstanz

[§]Corresponding author; Daniel R. Dietrich, Universitätsstrasse 10, 78457 Konstanz, Germany; phone: +49 7531 883518, E-mail: daniel.dietrich@uni-konstanz.de, orcid.org/0000-0003-0416-3811

*These authors contributed equally to this work

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Table S1: Primary antibodies for immunohistochemistry.

Primary antibody	Concentration	Supplier	Cat#
anti-MFE2	1:100	Proteintech	15116-AP
anti-DAAO	1:100	Santa Cruz Biotechnology	sc-26077
anti-catalase	1:100	Santa Cruz Biotechnology	sc-50508
anti-ACOX1	1:100	Atlas Antibodies	HPA028759
anti-EHHADH	1:50	Biorbyt	orb39323
anti-PEX5	1:200	Atlas Antibodies	HPA039260
anti-ACAA1	1:200	Abcam	ab210961
anti-AGPS	1:100	Santa Cruz Biotechnology	sc-374201
anti-PEX7	1:100	Biorbyt	orb214380
anti-PMP70	1:100	Atlas Antibodies	HPA032027
anti-PEX19	1:100	Thermo Fisher	PA5-22129
anti-PEX16	1:200	Novus Biologicals	NBP1-85828
anti-PEX3	1:50	Santa Cruz Biotechnology	sc-515149
anti-TCP1	1:100	Abcam	ab109184
anti-HSC70	1:100	Santa Cruz Biotechnology	sc-7298
anti-DnaJB1	1:200	Novus Biologicals	NB100-91818
anti-HSP90	1:100	Santa Cruz Biotechnology	sc-515081

Table S2: rDAAO interaction partners in HEK293 cells. Identified interaction partners of EYFP-tagged rat DAAO (EYFP-rDAAO) deriving from nano-LC-ESI-MS/MS analysis are listed in order of abundance (LFQ intensity). Note that proteins might be listed twice when detected both in DAAO_{perox} (indicated as perox) and DAAO_{cyt} (indicated as cyt) subtypes.

Protein IDs	Protein names	Sequence coverage (%)	Mol. weight (kDa)	Score	LFQ intensity	DAAO subtype	
1	P49368	T-complex protein 1 subunit gamma	52.3	60.533	237.07	8723700.0	perox
2	P17987	T-complex protein 1 subunit alpha	57.6	60.343	323.31	8156100.0	perox
3	P50990	T-complex protein 1 subunit theta	64.2	59.62	323.01	7751100.0	perox
4	Q99832	T-complex protein 1 subunit eta	46	59.366	263.38	4979700.0	perox
5	P50990	T-complex protein 1 subunit theta	64.2	59.62	323.01	3663200.0	cyt
6	P17987	T-complex protein 1 subunit alpha	57.6	60.343	323.31	3189300.0	cyt
7	P49368	T-complex protein 1 subunit gamma	52.3	60.533	237.07	2615800.0	cyt
8	Q99832	T-complex protein 1 subunit eta	46	59.366	263.38	923690.0	cyt
9	P51659	Peroxisomal multifunctional enzyme type 2	23.2	79.685	99.255	863160.0	perox
10	P04040	Catalase	8.5	59.755	18.947	265230.0	perox
11	Q71UM5;P42677	40S ribosomal protein S27; S27-like	25	9.4771	12.838	203340.0	cyt
12	Q9BVA1;Q13885	Tubulin beta-2B chain; beta-2A chain	50.8	49.953	18.237	200610.0	perox
13	Q71UM5;P42677	40S ribosomal protein S27;S27-like	25	9.4771	12.838	189800.0	perox
14	Q9BVA1;Q13885	Tubulin beta-2B chain;Tubulin beta-2A chain	50.8	49.953	18.237	178130.0	cyt
15	P07197	Neurofilament medium polypeptide	18.8	102.47	107.05	158090.0	cyt
16	P31689	DnaJ homolog subfamily A member 1	12.3	44.868	22.063	154610.0	perox
17	P07900	Heat shock protein HSP 90-alpha	15.7	84.659	61.529	138260.0	cyt
18	P31689	DnaJ homolog subfamily A member 1	12.3	44.868	22.063	124000.0	cyt
19	P31943; P55795	Heterogeneous nuclear ribonucleoprotein H; N-terminally processed; H2	11.1	49.229	50.992	103440.0	perox
20	Q02978	Mitochondrial 2-oxoglutarate/malate carrier protein	8	34.061	25.47	88570.0	cyt
21	P57088	Transmembrane protein 33	8.9	27.978	14.104	85178.0	cyt
22	P07900	Heat shock protein HSP 90-alpha	15.7	84.659	61.529	80975.0	perox
23	Q15366	Poly(rC)-binding protein 2	6.6	38.58	12.496	75436.0	perox
24	O15523;O00571	ATP-dependent RNA helicase DDX3Y; DDX3X	6.7	73.153	23.302	74960.0	cyt
25	P62937	Peptidyl-prolyl cis-trans isomerase A; N-terminally processed	20.6	18.012	17.075	74654.0	perox
26	P05023	Sodium/potassium-transporting ATPase subunit alpha-1	5	112.89	29.469	71560.0	cyt
27	O15523;O00571	ATP-dependent RNA helicase DDX3Y; DDX3X	6.7	73.153	23.302	63792.0	perox
28	Q02978	Mitochondrial 2-oxoglutarate/malate carrier protein	8	34.061	25.47	62446.0	perox
29	Q15366	Poly(rC)-binding protein 2	6.6	38.58	12.496	62330.0	cyt
30	P52907	F-actin-capping protein subunit alpha-1	33.2	32.922	32.807	61309.0	perox
31	Q9Y265	RuvB-like 1	11	50.227	26.329	60125.0	cyt
32	O75521	Enoyl-CoA delta isomerase 2, mitochondrial	16.8	43.585	44.45	58761.0	perox
33	P07196	Neurofilament light polypeptide	35.9	61.516	141.95	55377.0	cyt
34	P62879;Q9HAV0	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2; subunit beta-4	25.9	37.331	48.548	48028.0	perox
35	P35613	Basigin	7	42.2	13.276	47705.0	cyt
36	Q99615	DnaJ homolog subfamily C member 7	8.9	56.44	38.086	47657.0	cyt
37	P05023	Sodium/potassium-transporting ATPase subunit alpha-1	5	112.89	29.469	45984.0	perox
38	Q9Y265	RuvB-like 1	11	50.227	26.329	43495.0	perox
39	Q99615	DnaJ homolog subfamily C member 7	8.9	56.44	38.086	42589.0	perox
40	P31948	Stress-induced-phosphoprotein 1	3.5	62.639	14.546	40601.0	cyt
41	P35613	Basigin	7	42.2	13.276	37001.0	perox
42	P40939	Trifunctional enzyme subunit alpha, mitochondrial	12.1	82.999	37.297	36525.0	perox
43	Q9UL15	BAG family molecular chaperone regulator 5	9.2	51.199	27.972	34095.0	cyt

44	Q3ZCQ8	Mitochondrial import inner membrane translocase subunit TIM50	9.3	39.646	11.216	28381.0	cyt
45	Q9NZ01	Very-long-chain enoyl-CoA reductase	9.4	36.034	18.243	28076.0	cyt
46	P07196	Neurofilament light polypeptide	35.9	61.516	141.95	27840.0	perox
47	P50402	Emerin	15.4	28.994	16.289	27504.0	perox
48	P13639	Elongation factor 2	2.3	95.337	11.553	25424.0	perox
49	P09651;Q32P51	Heterogeneous nuclear ribonucleoprotein A1;N-terminally processed; A1-like 2	17.2	38.746	28.892	24807.0	perox
50	Q9NZ01	Very-long-chain enoyl-CoA reductase	9.4	36.034	18.243	24362.0	perox
51	P31040	Succinate dehydrogenase [ubiquinone] flavoprotein subunit	3.3	72.691	11.08	23803.0	perox
52	P12814;O43707	Alpha-actinin-1;Alpha-actinin-4	3.8	103.06	21.666	23667.0	perox
53	P31948	Stress-induced-phosphoprotein 1	3.5	62.639	14.546	22796.0	perox
54	Q9UNE7	E3 ubiquitin-protein ligase CHIP	7.3	34.856	13.527	17951.0	cyt
55	P22626	Heterogeneous nuclear ribonucleoproteins A2/B1	7.4	37.429	36.362	10936.0	perox
56	P59998	Actin-related protein 2/3 complex subunit 4	11.3	19.667	11.699	4461.7	perox
57	P78371	T-complex protein 1 subunit beta	65.6	57.488	323.31	377.0	perox
58	P48643	T-complex protein 1 subunit epsilon	59.1	59.67	204.51	243.3	perox
59	P40227	T-complex protein 1 subunit zeta	45	58.024	186.92	208.0	perox
60	P78371	T-complex protein 1 subunit beta	65.6	57.488	323.31	96.6	cyt
61	P50991	T-complex protein 1 subunit delta	36.7	57.924	207.04	58.4	perox
62	P48643	T-complex protein 1 subunit epsilon	59.1	59.67	204.51	38.1	cyt
63	P40227	T-complex protein 1 subunit zeta	45	58.024	186.92	36.1	cyt
64	P08238	Heat shock protein HSP 90-beta	21	83.263	151.65	26.3	cyt
65	P50991	T-complex protein 1 subunit delta	36.7	57.924	207.04	13.6	cyt
66	P08238	Heat shock protein HSP 90-beta	21	83.263	151.65	12.8	perox
67	P07437	Tubulin beta chain	53.6	49.67	323.31	11.5	perox
68	P68363;P68366	Tubulin alpha-1B chain; alpha-4A chain	63	50.151	323.31	10.3	perox
69	P68363;P68366	Tubulin alpha-1B chain; alpha-4A chain	63	50.151	323.31	7.6	cyt
70	P07437	Tubulin beta chain	53.6	49.67	323.31	7.4	cyt
71	P68371	Tubulin beta-4B chain	59.3	49.83	94.686	5.7	perox
72	P45880	Voltage-dependent anion-selective channel protein 2	42.2	31.566	55.117	4.7	perox
73	P25705	ATP synthase subunit alpha, mitochondrial	15.7	59.75	105.37	4.5	cyt
74	P05141	ADP/ATP translocase 2;ADP/ATP translocase 2, N-terminally processed	26.5	32.852	69.639	4.1	perox
75	P68371	Tubulin beta-4B chain	59.3	49.83	94.686	4.1	cyt
76	P05141	ADP/ATP translocase 2;ADP/ATP translocase 2, N-terminally processed	26.5	32.852	69.639	3.8	cyt
77	Q9Y230	RuvB-like 2	24.6	51.156	62.364	3.8	cyt
78	Q5VTE0;P68104; Q05639	Putative elongation factor 1-alpha-like 3; 1-alpha 1; 1-alpha 2	35.9	50.184	66.882	3.7	cyt
79	Q5VTE0;P68104; Q05639	Putative elongation factor 1-alpha-like 3; 1-alpha 1; 1-alpha 2	35.9	50.184	66.882	3.5	perox
80	P12236;P12235	ADP/ATP translocase 3; N-terminally processed; 1	23.5	32.866	34.411	3.4	cyt
81	Q00325	Phosphate carrier protein, mitochondrial	9.4	40.094	32.016	3.1	cyt
82	Q9Y230	RuvB-like 2	24.6	51.156	62.364	3.1	perox
83	P12236;P12235	ADP/ATP translocase 3;N-terminally processed;1	23.5	32.866	34.411	2.8	perox
84	P10809	60 kDa heat shock protein, mitochondrial	14.7	61.054	39.02	2.8	cyt
85	P23396	40S ribosomal protein S3	41.6	26.688	64.881	2.7	cyt
86	Q00325	Phosphate carrier protein, mitochondrial	9.4	40.094	32.016	2.6	perox
87	P10809	60 kDa heat shock protein, mitochondrial	14.7	61.054	39.02	2.3	perox
98	Q9NV17;Q5T2N8; Q5T9A4	ATPase family AAA domain-containing protein 3A; 3C; 3B	7.7	71.368	30.746	2.2	perox
99	P49411	Elongation factor Tu, mitochondrial	11.3	49.541	33.188	2.0	cyt

Table S3: hDAAO interaction partners in HEK293 cells. Identified interaction partners of EYFP-tagged human DAAO (EYFP-hDAAO) deriving from nano-LC-ESI-MS/MS analysis are listed in order of abundance (LFQ intensity). Note that proteins might be listed twice when detected both in DAAO_{perox} (indicated as perox) and DAAO_{cyt} (indicated as cyt) subtypes.

	Protein IDs	Protein names	Sequence coverage (%)	Mol. weight (kDa)	Score	LFQ intensity	DAAO subtype
1	P17987	T-complex protein 1 subunit alpha	57.6	60.343	323.31	2146500.0	cyt
2	P50990	T-complex protein 1 subunit theta	64.2	59.62	323.01	2068900.0	cyt
3	P49368	T-complex protein 1 subunit gamma	52.3	60.533	237.07	1933800.0	cyt
4	P17987	T-complex protein 1 subunit alpha	57.6	60.343	323.31	1907600.0	perox
5	P50990	T-complex protein 1 subunit theta	64.2	59.62	323.01	1879200.0	perox
6	Q99832	T-complex protein 1 subunit eta	46	59.366	263.38	1766900.0	cyt
7	P49368	T-complex protein 1 subunit gamma	52.3	60.533	237.07	1535300.0	perox
8	P51659	Peroxisomal multifunctional enzyme type 2	23.2	79.685	99.255	998350.0	perox
9	Q9BVA1;Q13885	Tubulin beta-2B chain;Tubulin beta-2A chain	50.8	49.953	18.237	544270.0	cyt
10	Q99832	T-complex protein 1 subunit eta	46	59.366	263.38	467510.0	perox
11	O75521	Enoyl-CoA delta isomerase 2, mitochondrial	16.8	43.585	44.45	440940.0	cyt
12	Q71UM5;P42677	40S ribosomal protein S27-like;40S ribosomal protein S27	25	9.4771	12.838	277000.0	cyt
13	P07900	Heat shock protein HSP 90-alpha	15.7	84.659	61.529	240490.0	cyt
14	Q71UM5;P42677	40S ribosomal protein S27-like;40S ribosomal protein S27	25	9.4771	12.838	231150.0	perox
15	P07900	Heat shock protein HSP 90-alpha	15.7	84.659	61.529	215260.0	perox
16	Q9Y265	RuvB-like 1	11	50.227	26.329	196550.0	cyt
17	Q99615	DnaJ homolog subfamily C member 7	8.9	56.44	38.086	176680.0	cyt
18	P31943;P55795	Heterogeneous nuclear ribonucleoprotein H; N-terminally processed; H2	11.1	49.229	50.992	169860.0	cyt
19	P35613	Basigin	7	42.2	13.276	161310.0	cyt
20	P31689	DnaJ homolog subfamily A member 1	12.3	44.868	22.063	155200.0	cyt
21	P31689	DnaJ homolog subfamily A member 1	12.3	44.868	22.063	154220.0	perox
22	P07197	Neurofilament medium polypeptide	18.8	102.47	107.05	150620.0	cyt
23	P43307	Translocon-associated protein subunit alpha	9.1	32.235	19.075	135900.0	cyt
24	P57088	Transmembrane protein 33	8.9	27.978	14.104	134760.0	cyt
25	O75521	Enoyl-CoA delta isomerase 2, mitochondrial	16.8	43.585	44.45	130880.0	perox
26	Q02978	Mitochondrial 2-oxoglutarate/malate carrier protein	8	34.061	25.47	130500.0	cyt
27	P31943;P55795	Heterogeneous nuclear ribonucleoprotein H; N-terminally processed; H2	11.1	49.229	50.992	112510.0	perox
28	P05023	Sodium/potassium-transporting ATPase subunit alpha-1	5	112.89	29.469	111930.0	cyt
29	P31948	Stress-induced-phosphoprotein 1	3.5	62.639	14.546	104570.0	cyt
30	Q9ULI0	ATPase family AAA domain-containing protein 2B	2.7	164.91	10.956	103420.0	cyt
31	Q9UL15	BAG family molecular chaperone regulator 5	9.2	51.199	27.972	92171.0	cyt
32	P04040	Catalase	8.5	59.755	18.947	90547.0	perox
33	Q9UNE7	E3 ubiquitin-protein ligase CHIP	7.3	34.856	13.527	82370.0	cyt
34	O43175	D-3-phosphoglycerate dehydrogenase	4.9	56.65	13.235	73200.0	cyt
35	Q3ZC08	Mitochondrial import inner membrane translocase subunit TIM50	9.3	39.646	11.216	71950.0	cyt
36	Q15366	Poly(rC)-binding protein 2	6.6	38.58	12.496	69471.0	perox
37	Q15366	Poly(rC)-binding protein 2	6.6	38.58	12.496	62400.0	cyt
38	P07910	Heterogeneous nuclear ribonucleoproteins C1/C2	8.8	33.67	12.559	60771.0	cyt
39	P05023	Sodium/potassium-transporting ATPase subunit alpha-1	5	112.89	29.469	60419.0	perox
40	Q9NZ01	Very-long-chain enoyl-CoA reductase	9.4	36.034	18.243	56970.0	cyt
41	Q99615	DnaJ homolog subfamily C member 7	8.9	56.44	38.086	53352.0	perox
42	P43307	Translocon-associated protein subunit alpha	9.1	32.235	19.075	53225.0	perox
43	P52907	F-actin-capping protein subunit alpha-1	33.2	32.922	32.807	52491.0	cyt
44	P62937	Peptidyl-prolyl cis-trans isomerase A; N-terminally processed	20.6	18.012	17.075	49160.0	perox
45	P07196	Neurofilament light polypeptide	35.9	61.516	141.95	47396.0	cyt
46	P62879;Q9HAV0	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2; subunit beta-4	25.9	37.331	48.548	45318.0	cyt
47	P35613	Basigin	7	42.2	13.276	42718.0	perox
48	Q9Y265	RuvB-like 1	11	50.227	26.329	42624.0	perox
49	P31948	Stress-induced-phosphoprotein 1	3.5	62.639	14.546	39691.0	perox
50	P62879;Q9HAV0	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2; subunit beta-4	25.9	37.331	48.548	34905.0	perox
51	P31040	Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial	3.3	72.691	11.08	31865.0	cyt
52	P09651;Q32P51	Heterogeneous nuclear ribonucleoprotein A1; N-terminally processed; A1-like 2	17.2	38.746	28.892	30679.0	cyt
53	P31040	Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial	3.3	72.691	11.08	30602.0	perox
54	P62269	40S ribosomal protein S18	17.1	17.718	16.425	26496.0	cyt
55	P13639	Elongation factor 2	2.3	95.337	11.553	26170.0	perox
56	Q3ZC08	Mitochondrial import inner membrane translocase subunit TIM50	9.3	39.646	11.216	25961.0	perox
57	Q15233	Non-POU domain-containing octamer-binding protein	8.3	54.231	20.587	24979.0	cyt
58	P40939	Trifunctional enzyme subunit alpha, mitochondrial	12.1	82.999	37.297	23976.0	cyt
59	P13639	Elongation factor 2	2.3	95.337	11.553	22504.0	cyt
60	P51659	Peroxisomal multifunctional enzyme type 2	23.2	79.685	99.255	21110.0	cyt
61	P50402	Emerin	15.4	28.994	16.289	20524.0	cyt

62	P62834;P61224; A6NIZ1	Ras-related protein Rap-1A; Rap-1b; Rap-1b-like protein	12.5	20.987	16.774	17336.0	cyt
63	P17844;Q92841	Probable ATP-dependent RNA helicase DDX5; DDX17	5.5	69.147	11.664	17140.0	cyt
64	Q9UNE7	E3 ubiquitin-protein ligase CHIP	7.3	34.856	13.527	15264.0	perox
65	P22626	Heterogeneous nuclear ribonucleoproteins A2/B1	7.4	37.429	36.362	11553.0	cyt
66	P78371	T-complex protein 1 subunit beta	65.6	57.488	323.31	58.4	cyt
67	P08238	Heat shock protein HSP 90-beta	21	83.263	151.65	38.9	cyt
68	P08238	Heat shock protein HSP 90-beta	21	83.263	151.65	27.7	perox
69	P48643	T-complex protein 1 subunit epsilon	59.1	59.67	204.51	24.5	cyt
70	P40227	T-complex protein 1 subunit zeta	45	58.024	186.92	23.7	cyt
71	Q00325	Phosphate carrier protein, mitochondrial	9.4	40.094	32.016	23.5	cyt
72	P40227	T-complex protein 1 subunit zeta	45	58.024	186.92	21.6	perox
73	P48643	T-complex protein 1 subunit epsilon	59.1	59.67	204.51	21.4	perox
74	Q9Y230	RuvB-like 2	24.6	51.156	62.364	21.4	cyt
75	P78371	T-complex protein 1 subunit beta	65.6	57.488	323.31	19.6	perox
76	P68363;P68366	Tubulin alpha-1B chain;Tubulin alpha-4A chain	63	50.151	323.31	13.5	cyt
77	P12236;P12235	ADP/ATP translocase 3;N-terminally processed; 1	23.5	32.866	34.411	12.9	cyt
78	P07437	Tubulin beta chain	53.6	49.67	323.31	12.6	cyt
79	P50991	T-complex protein 1 subunit delta	36.7	57.924	207.04	12.1	cyt
80	P05141	ADP/ATP translocase 2;ADP/ATP translocase 2, N-terminally processed	26.5	32.852	69.639	11.3	cyt
81	P84077;P61204; P84085	ADP-ribosylation factor 1; 3; 5	27.6	20.697	28.835	9.7	cyt
82	P25705	ATP synthase subunit alpha, mitochondrial	15.7	59.75	105.37	9.2	cyt
83	P50991	T-complex protein 1 subunit delta	36.7	57.924	207.04	9.1	perox
84	P68371	Tubulin beta-4B chain	59.3	49.83	94.686	8.4	cyt
85	P07437	Tubulin beta chain	53.6	49.67	323.31	8.3	perox
86	P68363;P68366	Tubulin alpha-1B chain; alpha-4A chain	63	50.151	323.31	7.5	perox
87	P05141	ADP/ATP translocase 2; N-terminally processed	26.5	32.852	69.639	7.5	perox
88	P68371	Tubulin beta-4B chain	59.3	49.83	94.686	7.1	perox
89	P06576	ATP synthase subunit beta, mitochondrial	5.3	56.559	11.808	6.7	cyt
90	P23396	40S ribosomal protein S3	41.6	26.688	64.881	5.8	cyt
91	P62826	GTP-binding nuclear protein Ran	14.8	24.423	22.418	5.5	cyt
92	Q5VTE0;P68104; Q05639	Putative elongation factor 1-alpha-like 3; 1-alpha 1; 1-alpha 2	35.9	50.184	66.882	5.2	cyt
93	P12236;P12235	ADP/ATP translocase 3;N-terminally processed; 1	23.5	32.866	34.411	5.0	perox
94	Q9Y230	RuvB-like 2	24.6	51.156	62.364	3.4	perox
95	P25705	ATP synthase subunit alpha, mitochondrial	15.7	59.75	105.37	3.3	perox
96	P49411	Elongation factor Tu, mitochondrial	11.3	49.541	33.188	3.1	cyt
97	Q00325	Phosphate carrier protein, mitochondrial	9.4	40.094	32.016	2.5	perox
98	Q5VTE0;P68104; Q05639	Putative elongation factor 1-alpha-like 3; 1-alpha 1; 1-alpha 2	35.9	50.184	66.882	2.4	perox
99	P49411	Elongation factor Tu, mitochondrial	11.3	49.541	33.188	2.1	perox
100	P10809	60 kDa heat shock protein, mitochondrial	14.7	61.054	39.02	2.1	perox
101	P11142	Heat shock cognate 71 kDa protein (HSC70)	50.2	70.897	323.31	2.1	cyt
102	Q06830	Peroxiredoxin-1	33.7	22.11	62.681	2.1	cyt
103	P10809	60 kDa heat shock protein, mitochondrial	14.7	61.054	39.02	2.1	cyt

Table S4: Rat and human DAAO specific interaction partners identified from HEK293 cells. Protein species-specific interaction partners are listed according to their abundance. Mutual binding partners are specified in Tables S2 and S3.

	Protein ID	Protein names
rDAAO	1 O15523; O00571	ATP-dependent RNA helicase DDX3Y; DDX3X ¹
	2 P12814; O43707	Alpha-actinin-1; -4
	3 P59998	Actin-related protein 2/3 complex subunit 4
	4 P45880	Voltage-dependent anion-selective channel protein 2
	5 Q9NV17; Q5T2N8; Q5T9A4	ATPase family AAA domain-containing protein 3A; 3C; 3B ¹
hDAAO	1 P43307	Translocon-associated protein subunit alpha
	2 Q06830	Peroxisome oxidoreductin-1
	3 P84077; P61204; P84085	ADP-ribosylation factor 1; 3; 5
	4 P06576	ATP synthase subunit beta, mitochondrial ²
	5 Q15233	Non-POU domain-containing octamer-binding protein
	6 P62834; P61224; A6NIZ1	Ras-related protein Rap-1A; -1b; -1b-like protein
	7 P62269	40S ribosomal protein S18
	8 O43175	D-3-phosphoglycerate dehydrogenase
	9 P07910	Heterogeneous nuclear ribonucleoproteins C1/C2
	10 P17844; Q92841	Probable ATP-dependent RNA helicase DDX5; DDX17 ¹
	11 Q9ULI0	ATPase family AAA domain-containing protein 2B ¹
	12 P62826	GTP-binding nuclear protein Ran
	13 P11142	Heat shock cognate 71 kDa protein (HSC70)

¹Note that a different protein subtype of this protein class was identified specifically for the respective other DAAO species

²Note that both, rDAAO and hDAAO bind to the subunit alpha of ATP synthase

Table S5: Interaction partners of biotin-linked propiverine in rat kidney cortex. Biotinylated propiverine was added to streptavidin-coated magnetic beads, incubated with lysate from rat kidney cortex sections and analyzed via nano-LC-ESI-MS/MS. Potential interaction partners are listed in order of abundance (LFQ intensity) and grouped as either weak or strong binders based on elution strength.

	Uniprot IDs	Protein names	Sequence coverage (%)	Mol. weight (kDa)	Score	LFQ intensity	Potential binding affinity
1	P63326	40S ribosomal protein S10	14,5	18,916	12,770	1571900,0	strong
2	P62804	Histone H4	31,1	11,367	25,475	1449800,0	weak
3	Q9WUW9	Sulfotransferase 1C2A	39,2	34,859	172,96	1428000,0	strong
4	P15684	Aminopeptidase N	9,1	109,45	79,712	1399400,0	strong
5	P09895	60S ribosomal protein L5	19,9	34,458	35,671	1381700,0	weak
6	Q6MG61	Chloride intracellular channel protein 1	15,8	26,980	21,289	1362000,0	strong
7	B0BNE5	S-formylglutathione hydrolase	26,6	31,363	45,041	1195800,0	weak
8	Q63716	Peroxiredoxin-1	16,1	22,109	23,234	1118100,0	strong
9	M0RC99	Ras-related protein Rab-5A	9,8	23,624	13,947	1062800,0	strong
10	Q9EQV6	Tripeptidyl-peptidase 1	6,2	61,332	11,340	958030,0	strong
11	Q02253	Methylmalonate-semialdehyde dehydrogenase [acylating]	16,6	57,807	54,677	918020,0	weak
12	P13437	3-Ketoacyl-CoA thiolase	27	41,870	70,735	878440,0	strong
13	P69897	Tubulin beta-5 chain	39	49,670	12,812	844580,0	strong
14	P19945	60S acidic ribosomal protein P0	39,7	34,215	69,772	771270,0	strong
15	Q9JLJ3	4-trimethylaminobutylaldehyde dehydrogenase	10,7	53,652	51,363	709900,0	weak
16	P52873	Pyruvate carboxylase	35,7	129,78	323,31	702350,0	weak
17	Q64230	Meprin A subunit alpha	2,8	85,122	13,191	697050,0	strong
18	O35078	D-amino-acid oxidase	12,7	38,820	34,320	692740,0	weak
19	Q4FZ79	26S proteasome non-ATPase regulatory subunit 2	3,3	100,19	12,750	663050,0	strong
20	PODMW1;PODMW0	Heat shock 70 kDa protein 1B; -1A	13,9	70,184	33,34	646700,0	weak
21	P31977	Ezrin	12,3	69,390	51,912	638120,0	strong
22	P86252	Transcriptional activator protein Pur-alpha	23,2	15,322	12,802	598550,0	weak
23	Q63617	Hypoxia up-regulated protein 1	3,5	111,29	25,725	533650,0	strong
24	P32232	Cystathionine beta-synthase	9,6	61,454	18,402	530500,0	strong
25	P68182;P27791	cAMP-dependent protein kinase catalytic subunit beta; -alpha	9,4	40,707	22,372	502900,0	strong
26	Q6P7B0	Tryptophan-tRNA ligase	13,3	54,143	29,958	501680,0	strong
27	P85108;Q3KRE8	Tubulin beta-2A chain; beta-2B chain	42,9	49,906	46,023	478470,0	weak
28	P51647	Retinal dehydrogenase 1	14,6	54,458	39,697	472030,0	weak
29	O88761	26S proteasome non-ATPase regulatory subunit 1	7,8	105,75	36,456	464890,0	strong
30	P15178	Aspartate-tRNA ligase	5	57,126	12,316	462720,0	strong
31	Q9WU50	Adenylate kinase 4	33,2	25,203	37,779	462270,0	strong
32	P08503	Medium-chain specific acyl-CoA dehydrogenase	11,6	46,555	29,188	459130,0	strong
33	Q62871	Cytoplasmic dynein 1 intermediate chain 2	8	71,177	12,526	454670,0	strong
34	P07340	Sodium/potassium-transporting ATPase subunit beta-1	16,4	35,201	34,267	454250,0	strong
35	Q99J82	Integrin-linked protein kinase	10,6	51,373	29,946	447270,0	strong
36	Q922L0	Voltage-dependent anion-selective channel protein 1	21,6	30,755	45,882	391500,0	strong
37	Q3T1L0	Aldehyde dehydrogenase family 16 member A1	4,1	85,413	13,339	385110,0	strong
38	Q68F54	Cytosol aminopeptidase	4,6	56,149	15,598	375090,0	strong
39	Q6PCU2	V-type proton ATPase subunit E 1	10,6	26,128	13,639	366730,0	strong
40	P61589;P62747	Transforming protein RhoA;Rho-related GTP-binding protein RhoB	16,6	21,782	16,618	362490,0	strong
41	P38918	Aflatoxin B1 aldehyde reductase member 3	13,1	36,747	20,868	356760,0	weak
42	P63036	DnaJ homolog subfamily A member 1	9,3	44,868	22,857	356320,0	strong
43	P63039	60 kDa heat shock protein	13,3	60,955	38,705	340180,0	strong
44	Q56150	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 10	5,9	40,493	13,966	329030,0	strong
45	O88370	Phosphatidylinositol 5-phosphate 4-kinase type-2 gamma	6,7	47,048	13,673	314920,0	strong
46	Q8R431	Monoglyceride lipase	8,3	33,499	12,118	313090,0	strong
47	P63331;P62716	Serine/threonine-protein phosphatase 2A catalytic subunit alpha isoform; beta isoform	8,1	35,608	11,634	308090,0	strong
48	POC2X9	Delta-1-pyrroline-5-carboxylate dehydrogenase	7,8	61,868	41,058	306500,0	weak
49	Q8CFN2	Cell division control protein 42 homolog	16,2	21,258	14,575	297150,0	strong
50	P11442	Clathrin heavy chain 1	27,3	191,6	323,31	291970,0	strong
51	Q99NA5	Isocitrate dehydrogenase [NAD] subunit alpha	6	39,613	13,707	291040,0	strong
52	Q920P0	L-xylulose reductase	24,6	25,719	33,593	285700,0	strong
53	Q62812	Myosin-9	15,3	226,34	212,88	277660,0	strong
54	P46844	Biliverdin reductase A	10,5	33,565	12,431	272030,0	strong
55	Q80W57	ATP-binding cassette sub-family G member 2	5,8	72,960	19,143	270230,0	weak
56	O88267;O55171	Acyl-coenzyme A thioesterase 1; -2	8,8	46,013	18,330	267890,0	strong
57	Q922F5;Q9EQH5	C-terminal-binding protein 1; -2	5,1	46,628	14,387	267660,0	strong
58	P51635	Alcohol dehydrogenase [NADP(+)]	7,7	36,505	17,388	256460,0	strong
59	P11980	Pyruvate kinase PKM	7,9	57,817	23,624	253380,0	strong
60	P54313;P54311;O35353	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2; -beta-1; -beta-4	8,8	37,331	11,460	247850,0	strong
61	P12928	Pyruvate kinase PKLR	6,8	62,200	15,591	246010,0	strong
62	Q6XQN1	Nicotinate phosphoribosyltransferase	15,8	58,564	55,213	238340,0	strong
63	P04906	Glutathione S-transferase P	17,1	23,439	18,174	231650,0	strong
64	Q07523	Hydroxyacid oxidase 2	7,9	39,201	25,360	227060,0	strong
65	P07379	Phosphoenolpyruvate carboxykinase, cytosolic [GTP]	4,8	69,415	12,314	225320,0	strong
66	Q63530	Phosphotriesterase-related protein	8,6	39,145	14,289	216790,0	strong

67	Q66HD0	Endoplasmin	3,5	92,770	12,870	205450,0	weak
68	Q5U2R0	Methionine adenosyltransferase 2 subunit beta	11,1	37,374	14,031	196200,0	strong
69	P85515	Alpha-centractin	6,6	42,613	11,869	195910,0	strong
70	P62142	Serine/threonine-protein phosphatase PP1-beta catalytic subunit	8	37,186	16,303	190910,0	strong
71	P35565	Calnexin	4,4	67,254	12,206	182080,0	weak
72	P21533	60S ribosomal protein L6	5,7	33,561	16,978	177330,0	weak
73	Q9QUL6	Vesicle-fusing ATPase	4,6	82,652	18,383	174540,0	strong
74	Q9Z0W7	Chloride intracellular channel protein 4	10,3	28,633	13,198	163240,0	strong
75	Q35824	DnaJ homolog subfamily A member 2	6,8	45,765	13,369	161230,0	strong
76	P62083	40S ribosomal protein S7	10,3	22,127	12,469	141340,0	strong
77	O88600	Heat shock 70 kDa protein 4	3,2	94,055	16,879	131850,0	strong
78	P97852	Peroxisomal multifunctional enzyme type 2	3,8	79,427	11,931	123770,0	strong
79	Q9WVB1	Ras-related protein Rab-6A	10,6	23,590	11,751	76347,0	strong
80	Q66HF1	NADH-ubiquinone oxidoreductase 75 kDa subunit	4,4	79,411	25,364	61625,0	strong

Table S6: Clustered interaction partners of biotin-linked propiverine. Propiverine-specific interaction partners (see Table S5) were clustered based on joint cellular pathways, protein class or sub-cellular destination and are listed with their corresponding protein ID.

Protein homeostasis	
Degradation	
P15684	Aminopeptidase N
Q9EQV6	Tripeptidyl-peptidase 1
Q64230	Meprin A subunit alpha
Q4FZT9	26S proteasome non-ATPase regulatory subunit 2
O88761	26S proteasome non-ATPase regulatory subunit 1
Q68F54	Cytosol aminopeptidase
Chaperones	
PODMW1;PODMW0	Heat shock 70 kDa protein 1B; 1A
O35824	DnaJ homolog subfamily A member 2
P63036	DnaJ homolog subfamily A member 1
O88600	Heat shock 70 kDa protein 4
P63039	60 kDa heat shock protein, mitochondrial
Q66HDO	Endoplasmic
P35565	Calnexin
Q63617	Hypoxia up-regulated protein 1
Protein biosynthesis	
P21533	60S ribosomal protein L6
P63326	40S ribosomal protein S10
P19945	60S acidic ribosomal protein P0
P62083	40S ribosomal protein S7
P09895	60S ribosomal protein L5
Q6P7B0	Tryptophan-tRNA ligase, cytoplasmic;T1-TrpRS;T2-TrpRS
P15178	Aspartate-tRNA ligase, cytoplasmic
P86252	Transcriptional activator protein Pur-alpha
Q9Z2F5;Q9EQH5	C-terminal-binding protein 1;C-terminal-binding protein 2
Q9JLJ3	4-trimethylaminobutyraldehyde dehydrogenase
P62804	Histone H4;Osteogenic growth peptide
Q6XQN1	Nicotinate phosphoribosyltransferase
Oxidoreductases	
O35078	D-amino-acid oxidase
P97852	Peroxisomal multifunctional enzyme type 2
Q07523	Hydroxyacid oxidase 2
P08503	Medium-chain specific acyl-CoA dehydrogenase, mitochondrial
Q02253	Methylmalonate-semialdehyde dehydrogenase [acylating], mitochondrial
POC2X9	Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial
Q66HF1	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial
Q99NA5	Isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial
Q56150	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 10, mitochondrial
Q9JLJ3	4-trimethylaminobutyraldehyde dehydrogenase
P51635	Alcohol dehydrogenase [NADP(+)]
P38918	Aflatoxin B1 aldehyde reductase member 3
Q63716	Peroxioredoxin-1
P51647	Retinal dehydrogenase 1
Q3T1L0	Aldehyde dehydrogenase family 16 member A1
P46844	Biliverdin reductase A
Q920P0	L-xylulose reductase
Q9Z2F5;Q9EQH5	C-terminal-binding protein 1;C-terminal-binding protein 2
Mitochondrial proteins	
Q02253	Methylmalonate-semialdehyde dehydrogenase [acylating], mitochondrial
POC2X9	Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial
Q9WUS0	Adenylate kinase 4, mitochondrial
Q66HF1	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial
Q99NA5	Isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial
Q56150	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 10, mitochondrial
P13437	3-ketoacyl-CoA thiolase, mitochondrial
P08503	Medium-chain specific acyl-CoA dehydrogenase, mitochondrial
P52873	Pyruvate carboxylase, mitochondrial
P63039	60 kDa heat shock protein, mitochondrial
Q5U2R0	Methionine adenosyltransferase 2 subunit beta
Cytoskeleton	
P85108;Q3KRE8	Tubulin beta-2A chain;Tubulin beta-2B chain
P69897	Tubulin beta-5 chain
P31977	Ezrin
Q62871	Cytoplasmic dynein 1 intermediate chain 2
Q99J82	Integrin-linked protein kinase
P85515	Alpha-centractin
Q62812	Myosin-9
P61589;P62747	Transforming protein RhoA;Rho-related GTP-binding protein RhoB
Q8CFN2	Cell division control protein 42 homolog
Channels and transporter	

Q80W57	ATP-binding cassette sub-family G member 2
Q6MG61	Chloride intracellular channel protein 1
Q920W7	Chloride intracellular channel protein 4
P54313;P54311;O35353	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2;Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-1;Guanine nucleotide-binding protein subunit beta-4
Q6PCU2	V-type proton ATPase subunit E 1
Q9Z2L0	Voltage-dependent anion-selective channel protein 1
P07340	Sodium/potassium-transporting ATPase subunit beta-1
Fatty acid metabolism	
O88267;O55171	Acyl-coenzyme A thioesterase 1;Acyl-coenzyme A thioesterase 2, mitochondrial
Q8R431	Monoglyceride lipase
P13437	3-ketoacyl-CoA thiolase, mitochondrial
P08503	Medium-chain specific acyl-CoA dehydrogenase, mitochondrial
P52873	Pyruvate carboxylase, mitochondrial
P97852	Peroxisomal multifunctional enzyme type 2;(3R)-hydroxyacyl-CoA dehydrogenase;Enoyl-CoA hydratase 2
Q07523	Hydroxyacid oxidase 2
Metabolizing enzymes and detoxification	
Q9WUW9	Sulfotransferase 1C2A
P04906	Glutathione S-transferase P
P51635	Alcohol dehydrogenase [NADP(+)]
B0BNE5	S-formylglutathione hydrolase
P38918	Aflatoxin B1 aldehyde reductase member 3
Q63716	Peroxioredoxin-1
Amino acid metabolism	
O35078	D-amino-acid oxidase
Q07523	Hydroxyacid oxidase 2
Q02253	Methylmalonate-semialdehyde dehydrogenase [acylating], mitochondrial
POC2X9	Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial
Q9JLJ3	4-trimethylaminobutyraldehyde dehydrogenase
P32232	Cystathionine beta-synthase
Signal transduction	
O88370	Serine/threonine-protein phosphatase PP1-beta catalytic subunit
P62142	Phosphatidylinositol 5-phosphate 4-kinase type-2 gamma
P68182;P27791	cAMP-dependent protein kinase catalytic subunit beta
Q63530	Phosphotriesterase-related protein
P63331;P62716	Serine/threonine-protein phosphatase 2A catalytic subunit alpha isoform;Serine/threonine-protein phosphatase 2A catalytic subunit beta isoform
Carbohydrate metabolism	
P12928	Pyruvate kinase PKLR
P07379	Phosphoenolpyruvate carboxykinase, cytosolic [GTP]
Q920P0	L-xylulose reductase
P11980	Pyruvate kinase PKM
Vesicle-mediated transport	
Q9WVB1	Ras-related protein Rab-6A
Q9QUL6	Vesicle-fusing ATPase
M0RC99	Ras-related protein Rab-5A
P11442	Clathrin heavy chain 1
Peroxisomal proteins	
O35078	D-amino-acid oxidase
P97852	Peroxisomal multifunctional enzyme type 2
Q07523	Hydroxyacid oxidase 2

Table S7 **Clustered interaction partners of biotin-linked propiverine in rat liver.** Propiverine-specific interaction partners (see Table S8) were clustered based on joint cellular pathways, protein class or sub-cellular destination.

Cluster of interaction partner	Number of proteins
Total number of proteins	120
Protein homeostasis	33
chaperones	7
protein degradation	7
Oxidoreductases	25
Mitochondrial proteins	21
Cytoskeleton	3
Channels and transporter	6
Fatty acid metabolism	14
Metabolizing proteins and detoxification	9
Amino acid metabolism	12
Signal transduction	9
Carbohydrate and energy metabolism	11
Vesicle-mediated transport	8
Peroxisomal proteins	4

Table S8 Interaction partners of biotin-linked propiverine in rat liver. Biotinylated propiverine was added to streptavidin-coated magnetic beads, incubated with lysate from rat liver and analyzed via nano-LC-ESI-MS/MS. Potential interaction partners are listed in order of abundance (LFQ intensity) and grouped as either weak or strong binders based on elution strength.

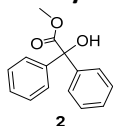
	Uniprot IDs	Protein names	Sequence coverage (%)	Mol. weight (kDa)	Score	LFQ intensity	Potential binding affinity
1	P12785	Fatty acid synthase	19	272,65	323,31	8899500,0	weak
2	P04904	Glutathione S-transferase alpha-3	45,7	25,319	207,84	6598200,0	weak
3	P61354	60S ribosomal protein L27	20,6	15,798	20,208	6506400,0	weak
4	Q03336	Regucalcin	21,7	33,389	30,719	5772500,0	strong
5	P62986; P62982; P0CG51; Q63429	Ubiquitin-60S ribosomal protein L40; Ubiquitin-40S ribosomal protein S27a; Polyubiquitin-B; Polyubiquitin-C	19,5	14,728	88,576	5311900,0	weak
6	P55006; P50169	Retinol dehydrogenase 7; -3	10,1	35,736	83,375	5178800,0	weak
7	P02692	Fatty acid-binding protein	36,2	14,272	187,5	5105200,0	strong
8	P69897	Tubulin beta-5 chain	58,1	49,67	84,341	4839600,0	weak
9	P61805	Dolichyl-diphosphooligosaccharide-protein glycosyltransferase subunit DAD1	19,5	12,497	21,953	4501400,0	weak
10	Q4QQT4	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A beta isoform	5,7	66,006	26,314	3893000,0	strong
11	Q7TMA5	Apolipoprotein B-100; B-48	0,5	536,02	10,797	3798200,0	weak
12	P52845; P49890	Estrogen sulfotransferase, isoform 2; Estrogen sulfotransferase Ste2	46,8	35,364	47,109	3328800,0	strong
13	O35826	Bifunctional UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase	15,2	79,226	190,9	3184400,0	weak
14	P07150	Annexin A1	10,4	38,829	143,51	3076200,0	weak
15	P85834	Elongation factor Tu	27,4	49,522	101,87	3045000,0	weak
16	O88761	26S proteasome non-ATPase regulatory subunit 1	16,1	105,75	171,91	2879700,0	weak
17	P31399	ATP synthase subunit d	56,5	18,763	80,813	2697900,0	strong
18	P57093	Phytanoyl-CoA dioxygenase	22,8	38,588	227,56	2609300,0	weak
19	P11598	Protein disulfide-isomerase A3	22,4	56,623	89,372	2600100,0	strong
20	P02793; Q7TP54	Ferritin light chain 1; Protein FAM65B	25,1	20,748	18,848	2599000,0	strong
21	Q64611	Cysteine sulfinic acid decarboxylase	14,8	55,248	53,847	2546200,0	weak
22	P62804	Histone H4	29,1	11,367	91,56	2428100,0	strong
23	P83732	60S ribosomal protein L24	19,1	17,779	29,037	2363600,0	weak
24	P00481	Ornithine carbamoyltransferase	10,2	39,886	121,73	2324000,0	strong
25	P04636	Malate dehydrogenase	12,4	35,683	64,294	2284000,0	weak
26	P21533	60S ribosomal protein L6	16,1	33,561	28,681	2251300,0	weak
27	Q5I0M2	Nicotinate-nucleotide pyrophosphorylase [carboxylating]	20,1	31,297	28,181	2245900,0	strong
28	P62243	40S ribosomal protein S8	19,2	24,205	129,36	2131600,0	weak
29	P20280	60S ribosomal protein L21	16,2	18,465	14,814	1974500,0	strong
30	P04937	Fibronectin;Anastellin	3,2	272,51	30,848	1919600,0	weak
31	P00406	Cytochrome c oxidase subunit 2	20,3	25,928	19,226	1904200,0	strong
32	Q920L2	Succinate dehydrogenase [ubiquinone] flavoprotein subunit	21,6	71,614	143,95	1860800,0	strong
33	D3ZZL9	GRIP and coiled-coil domain-containing protein 2	2,1	195,08	10,914	1857700,0	strong
34	Q03248	Beta-ureidopropionase	7,6	44,042	13,243	1838200,0	strong
35	Q9JIT3; Q07141	Transducin-like enhancer protein 3; -4	4,1	82,643	11,329	1821000,0	strong
36	Q8VBU2	Protein NDRG2	26,4	40,779	63,501	1792500,0	strong
37	P10860	Glutamate dehydrogenase 1	9,5	61,415	33,849	1777400,0	weak
38	P11980	Pyruvate kinase PKM	9,2	57,817	21,145	1742600,0	strong
39	Q561S0	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 10	25,4	40,493	53,517	1724700,0	strong
40	P12938	Cytochrome P450 2D3	14,8	56,641	21,568	1714000,0	weak
41	P09606	Glutamine synthetase	21,2	42,267	107,96	1655000,0	weak
42	P14046; Q6IE52; Q03626	Alpha-1-inhibitor 3;Murnoglobulin-2;Murnoglobulin-1	3	163,77	26,343	1624400,0	weak
43	P04642	L-lactate dehydrogenase A chain	12	36,45	111,34	1617500,0	strong
44	P49242	40S ribosomal protein S3a;40S ribosomal protein S3b	27,3	29,945	71,04	1617100,0	strong
45	P35704	Peroxiredoxin-2	9,6	21,783	19,305	1610900,0	strong
46	Q9QZU7	Gamma-butyrobetaine dioxygenase	16,5	44,545	28,152	1577900,0	strong
47	P31210	3-oxo-5-beta-steroid 4-dehydrogenase	49,4	37,377	106,44	1573500,0	weak
48	Q5QE80	Aldehyde oxidase 3	7	146,75	57,456	1567500,0	weak
49	Q497B0	Omega-amidase NIT2	8	30,701	30,477	1479600,0	strong
50	Q62636; P62836	Ras-related protein Rap-1b; Rap-1A	29,9	20,798	43,405	1456600,0	strong
51	P32232	Cystathionine beta-synthase	16,6	61,454	43,562	1403600,0	strong
52	Q64573; P10959; Q63108; Q63010	Liver carboxylesterase 4; 1C; 1E; B-1	4,1	62,308	36,925	1376900,0	weak
53	O54753	17-beta-hydroxysteroid dehydrogenase type 6	6,3	36,144	11,428	1372700,0	weak
54	D3ZAF6	ATP synthase subunit f	36,4	10,452	35,358	1360000,0	strong
55	Q64640	Adenosine kinase	29,4	40,133	106,68	1351700,0	weak
56	Q64194	Lysosomal acid lipase/cholesteryl ester hydrolase	8,3	45,185	59,099	1347400,0	strong
57	P62744	AP-2 complex subunit sigma	13,4	17,018	12,341	1311200,0	weak
58	P16232	Corticosteroid 11-beta-dehydrogenase isozyme 1	20,1	31,883	39,941	1297500,0	strong
59	O35244	Peroxiredoxin-6	12,5	24,818	11,63	1283600,0	strong

60	P46953	3-hydroxyanthranilate 3,4-dioxygenase	17,5	32,582	27,994	1235200,0	strong
61	P56571	ES1 protein homolog	13,2	28,172	24,72	1226800,0	strong
62	Q8CG45	Aflatoxin B1 aldehyde reductase member 2	14,7	40,675	28,995	1215400,0	strong
63	P32551	Cytochrome b-c1 complex subunit 2	16,2	48,396	91,903	1208600,0	strong
64	P10111	Peptidyl-prolyl cis-trans isomerase A; Peptidyl-prolyl cis-trans isomerase A, N-terminally processed	18,3	17,874	13,416	1207700,0	strong
65	P16303	Carboxylesterase 1D	6	62,146	19,012	1161900,0	strong
66	P24368	Peptidyl-prolyl cis-trans isomerase B	35,2	23,802	52,197	1141300,0	strong
67	P18418	Calreticulin	4,6	47,995	12,17	1125500,0	weak
68	P62198	26S protease regulatory subunit 8	20,2	45,626	34,464	1101700,0	strong
69	Q9WVK3	Peroxisomal trans-2-enoyl-CoA reductase	36,6	32,433	323,31	1076400,0	strong
70	Q68FT5	S-methylmethionine-homocysteine S-methyltransferase BHMT2	18,7	39,928	21,027	1064400,0	weak
71	P02401	60S acidic ribosomal protein P2	55,7	11,692	23,765	1063900,0	strong
72	P41123	60S ribosomal protein L13	10	24,309	16,74	1039100,0	weak
73	P52759	Ribonuclease UK114	45,3	14,303	271,85	1008500,0	strong
74	P16638	ATP-citrate synthase	8	120,63	36,432	1006700,0	weak
75	Q63507	60S ribosomal protein L14	11,2	23,339	26,735	958770,0	strong
76	P36201	Cysteine-rich protein 2	23,1	22,696	25,4	955090,0	strong
77	Q9Z0T0	Thiopurine S-methyltransferase	37,5	27,691	61,3	940910,0	weak
78	P62275	40S ribosomal protein S29	33,9	6,6767	23,081	920790,0	strong
79	B0K020	CDGSH iron-sulfur domain-containing protein 1	34,3	12,097	18,505	918460,0	strong
80	P04903	Glutathione S-transferase alpha-2	30,6	25,559	18,036	908050,0	strong
81	Q8VIF7	Selenium-binding protein 1	11,9	52,531	36,435	905030,0	strong
82	Q5XIH7	Prohibitin-2	13	33,312	29,557	896220,0	strong
83	A0JPJ7	Obg-like ATPase 1	7,1	44,535	27,484	860040,0	strong
84	P86252	Transcriptional activator protein Pur-alpha	35,5	15,322	12,69	856120,0	strong
85	Q4KLZ6	Bifunctional ATP-dependent dihydroxyacetone kinase/FAD-AMP lyase	7,1	59,443	25,933	853480,0	weak
86	P04785	Protein disulfide-isomerase	8,6	56,951	22,71	822340,0	strong
87	G3V9R8	Heterogeneous nuclear ribonucleoprotein C	9,4	32,857	14,325	814860,0	weak
88	P10760	Adenosylhomocysteinase	16	47,538	50,581	813310,0	strong
89	P15178	Aspartate-tRNA ligase	6,4	57,126	20,987	809640,0	strong
90	P24329	Thiosulfate sulfurtransferase	14,5	33,406	127,77	745980,0	strong
91	P00173	Cytochrome b5	41	15,355	27,517	719240,0	strong
92	P23514	Coatomer subunit beta	3,4	107,01	12,689	691600,0	strong
93	P00507	Aspartate aminotransferase	6,7	47,314	115,36	677850,0	weak
94	Q63448	Peroxisomal acyl-coenzyme A oxidase 3	5,9	78,445	25,996	662780,0	weak
95	P12007	Isovaleryl-CoA dehydrogenase	23,6	46,435	91,028	653660,0	weak
96	Q5BK63	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 9	5,6	42,559	15,169	640440,0	strong
97	P67874	Casein kinase II subunit beta	15,8	24,942	12,243	629520,0	weak
98	Q68FR9	Elongation factor 1-delta	21,4	31,33	101,6	622900,0	strong
99	Q62902	Protein ERGIC-53	6	57,956	27,713	621860,0	strong
100	P62271	40S ribosomal protein S18	19,7	17,718	36,926	586950,0	strong
101	Q9JLA3	UDP-glucose:glycoprotein glucosyltransferase 1	2,8	176,43	17,692	562770,0	weak
102	P38652	Phosphoglucomutase-1	3,9	61,402	10,955	522020,0	weak
103	P62193	26S protease regulatory subunit 4	8,6	49,184	33,911	521550,0	strong
104	Q64126	EH domain-containing protein 1	8,4	60,602	31,074	500380,0	strong
105	P17046	Lysosome-associated membrane glycoprotein 2	4,6	45,155	12,037	466690,0	strong
106	Q77PB1	T-complex protein 1 subunit delta	12,2	58,099	34,096	462050,0	weak
107	P20650; P35815	Protein phosphatase 1A; 1B	6	42,416	17,982	445180,0	strong
108	Q63965	Sideroflexin-1	14,3	35,546	38,685	422950,0	strong
109	Q07523	Hydroxyacid oxidase 2	7,4	39,201	32,589	389920,0	strong
110	Q64057	Alpha-aminoacidipic semialdehyde dehydrogenase	7,8	58,748	20,657	389920,0	weak
111	Q64565	Alanine--glyoxylate aminotransferase 2	4,5	57,2	12,136	386080,0	strong
112	Q8CFN2	Cell division control protein 42 homolog	19,9	21,258	13,45	308190,0	strong
113	Q9WVB1	Ras-related protein Rab-6A	11,1	23,59	12,33	255820,0	strong
114	Q63347	26S protease regulatory subunit 7	6,2	48,574	11,869	254760,0	strong
115	P97612	Fatty-acid amide hydrolase 1	6,9	63,356	13,299	236300,0	strong
116	Q05096	Unconventional myosin-Ib	3,3	131,92	19,968	228310,0	weak
117	Q5XI89	NXPE family member 4	5,4	61,615	13,491	196210,0	weak
118	P60901	Proteasome subunit alpha type-6	8,9	27,399	11,939	183120,0	strong
119	Q4QQW3	Hydroxyacid-oxoacid transhydrogenase	8,6	50,225	16,435	179650,0	strong
120	Q9Z2Q1	Protein transport protein Sec31A	2,6	135,27	13,217	153050,0	strong

Chemical Synthesis

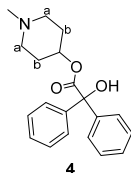
General methods. All chemicals were purchased from *Sigma Aldrich* and used without further purification. D-Biotin was purchased from *Iris Biotech* (LS-1070.0005). Technical solvents were distilled prior to use. All reactions were carried out in dry solvents under nitrogen conditions if not stated otherwise. Reactions were monitored by thin-layer chromatography (TLC) on silica gel 60 F₂₅₄ (*Merck*) with detection by UV light ($\lambda = 254$ nm). Additionally, acidic ethanolic *p*-anisaldehyde or ninhydrin solution followed by gentle heating were used for visualization. Preparative flash column chromatography was performed with a MPLC-Reveleris system from *Grace*. Nuclear magnetic resonance (NMR) spectra were recorded at room temperature on Avance III 400 instruments from *Bruker*. Chemical shifts are reported relative to solvent signals (CDCl₃: $\delta_{\text{H}} = 7.26$ ppm, $\delta_{\text{C}} = 77.16$ ppm; CD₃OD: $\delta_{\text{H}} = 3.31$ ppm, $\delta_{\text{C}} = 49.00$ ppm; (CD₃)₂SO: $\delta_{\text{H}} = 2.50$ ppm, $\delta_{\text{C}} = 39.52$ ppm). Signals were assigned by first-order analysis and two-dimensional ¹H,¹H and ¹H,¹³C correlation spectroscopy (COSY, HMBC and HSQC). High-Resolution mass determination was performed at the Proteomics Center, University of Konstanz, with an Orbitrap Discovery instrument. Samples were dissolved in a mixture of 25% methanol, 25% acetonitril, 48 % water and 2% formic acid and measured by direct infusion with a flow rate of 5 $\mu\text{L}/\text{min}$ at an instrument resolution of 30000.

Methyl 2-hydroxy-2,2-diphenylacetate (**2**)



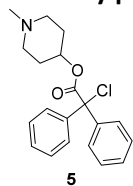
Bencilic acid methyl ester **2** was synthesized according to Dawar *et al.*, 2014 [1] and obtained as white solid (2.16 g, 41% yield). $R_f = 0.29$ (petroleum ether/ethyl acetate 10:1). ¹H NMR (400 MHz, CDCl₃): δ (ppm) = 7.48 - 7.28 (m, 10H, CH_{Ar}), 4.19 (s, 1H, OH), 3.86 (s, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃): δ (ppm) = 175.11 (C_{carbonyl}), 142.07 (C_{quart-Ar}), 128.26, 128.22, 127.51 (C_{Ar}), 81.27 (C_{quart}), 53.69 (CH₃).

1-Methylpiperidin-4-yl 2-hydroxy-2,2-diphenylacetate (**4**)



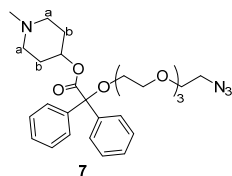
Synthesis of **4** was adapted from Tsukada *et al.*, 2003 [2] using *N*-methyl-4-piperidinol **3**. Briefly, benzene (45 mL), **2** (1.00 g, 4.13 mmol, 1 equiv) and **3** (475 mg, 4.13 mmol, 1 equiv, commercially available) were stirred at 80 °C until completely dissolved. After adding NaOMe (22.3 mg, 0.41 mmol, 0.1 equiv), the reaction was refluxed for 3 h over 4 Å molecular sieves (20 g). After TLC showed no more starting material, the reaction was cooled down to ambient temperature. 1 N HCl (50 mL) was added and extracted three times with Et₂O. The aqueous layer was adjusted to pH 10 with 30% NH₄OH solution and extracted twice with Et₂O and CH₂Cl₂. The combined organic layers were washed once with H₂O, dried over MgSO₄, filtered and concentrated under reduced pressure to obtain **4** as a white solid (686 mg, 51% yield) which was used without further purification. $R_f = 0.32$ (CH₂Cl₂/MeOH 8:1). ¹H NMR (400 MHz, CDCl₃): δ (ppm) = 7.64 - 7.11 (m, 10H, CH_{Ar}), 5.04 - 4.88 (m, 1H, CH), 4.46 (s, 1H, OH), 2.40 - 2.18 (m, 4H, CH_{2 a}), 2.16 (s, 3H, CH₃), 1.93 - 1.80 (m, 2H, H_{2 b}), 1.76 - 1.62 (m, 2H, H_{2 b}). ¹³C NMR (101 MHz, CDCl₃): δ (ppm) = 173.98 (C_{carbonyl}), 142.33 (C_{quart-Ar}), 128.13, 128.05, 127.58 (C_{Ar}), 81.06 (C_{quart}), 72.37 (CH), 52.12 (CH_{2 a}), 46.19 (CH₃), 30.43 (CH_{2 b}). **HRMS (ESI-Orbitrap) m/z:** [M+H]⁺ Calcd for C₂₀H₂₃NO₃: 326.1751; Found 326.1774.

1-Methylpiperidin-4-yl 2-chloro-2,2-diphenylacetate (5)



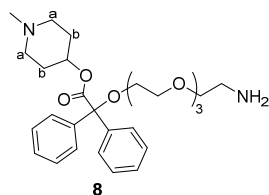
4 (119 mg, 0.37 mmol, 1 equiv) was dissolved in CH_2Cl_2 (3 mL) and pyridine (295 μL , 3.66 mmol, 10 equiv). After adding SOCl_2 (80 μL , 1.10 mmol, 3 equiv) the reaction was allowed to continue at ambient temperature for 3 h. The reaction mixture was then poured into saturated NaHCO_3 (18 mL) and extracted three times with ethyl acetate. The combined organic layers were washed three times with H_2O , dried over MgSO_4 , filtered and concentrated under reduced pressure to obtain **5** as reddish oil (113 mg, 91%, R_f = 0.44 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$ 5:1)) and used directly without further purification for the synthesis of **7**.

1-Methylpiperidin-4-yl 14-azido-2,2-diphenyl-3,6,9,12-tetraoxatetradecanoate (7)



5 (113 mg, 0.33 mmol, 1 equiv) was dissolved in DMF (400 μL) and added to a solution of AgPF_6 (91 mg, 0.36 mmol, 1.1 equiv) in **6** [3] (1 g, 4.93 mmol, 15 equiv). After stirring for 66 h at 100 $^\circ\text{C}$ the reaction was extracted three times with ethyl acetate. The aqueous layer was adjusted to pH 9 with saturated NaHCO_3 solution and extracted three times with ethyl acetate. Finally, the organic layer was washed twice with H_2O , dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue was purified by gradient silica flash chromatography (5-20 % MeOH in ethyl acetate) to obtain **7** as colorless oil (121 mg, 70% yield). R_f = 0.54 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$ 5:1). $^1\text{H NMR}$ (400 MHz, CD_3OD) δ (ppm): = 7.48 - 7.29 (m, 10H, CH_{Ar}), 5.00 - 4.90 (m, 1H, CH), 3.68 - 3.60 (m, 12H, OCH_2), 3.43 (t, J = 5.1 Hz, 2H, CH_2N_3), 3.34 (d, J = 5.0 Hz, 2H, CH_2), 2.41 - 2.23 (m, 4H, CH_2_a), 2.20 (s, 3H, CH_3), 1.88 - 1.77 (m, 2H, CH_2_b), 1.72 - 1.59 (m, 2H, CH_2_b). $^{13}\text{C NMR}$ (101 MHz, CD_3OD) δ (ppm): = 172.23 ($\text{C}_{\text{carbonyl}}$), 141.89 ($\text{C}_{\text{quart-Ar}}$), 129.83 (C_{Ar}), 129.21 (C_{Ar}), 128.94 (C_{Ar}), 88.12 (C_{quart}), 71.63, 71.60, 71.58, 71.52, 71.44 (CH_2), 71.08 (CH), 65.80 ($\text{C}_{\text{quartOCH}_2}$), 52.49 (CH_2_a), 51.74 (CH_2N_3), 46.01 (CH_3), 30.64 (CH_2_b). **HRMS (ESI-Orbitrap) m/z**: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{28}\text{H}_{38}\text{N}_4\text{O}_6$: 527.2864; Found 527.2859.

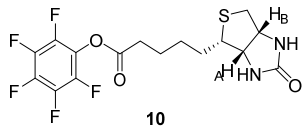
1-Methylpiperidin-4-yl 14-amino-2,2-diphenyl-3,6,9,12-tetraoxatetradecanoate (8)



Azide **7** (89 mg, 0.17 mmol, 1 equiv) and PPh_3 (22 mg, 0.08 mmol, 1.5 equiv) were dissolved in THF/ H_2O (4:1 (v/v), 1.85 mL) and stirred for 18 h at ambient temperature. The crude solution was concentrated and purified by gradient silica flash chromatography (0-10% MeOH in CH_2Cl_2 with 3% Et_3N) to obtain **8** (89 mg, 79% yield). R_f = 0.29 ($\text{CH}_2\text{Cl}_2/\text{MeOH}/\text{Et}_3\text{N}$ 95:5:3). $^1\text{H NMR}$ (400 MHz, CD_3OD): δ (ppm) = 7.72 - 7.13 (m, 10H, CH_{Ar}), 4.99 - 4.91 (m, 1H, CH), 3.69 - 3.60 (m, 12H, CH_2), 3.41 (t, J = 4.9 Hz, 2H, $\text{C}_{\text{quartOCH}_2}$), 3.01 (t, J = 5.1 Hz, 2H, CH_2N_3), 2.40 - 2.20 (m, 4H, CH_2_a), 2.17 (s, 3H, CH_3), 1.88 - 1.75 (m, 2H, CH_2_b), 1.69 - 1.56 (m, 2H, CH_2_b). $^{13}\text{C NMR}$ (101 MHz, CD_3OD): δ (ppm) = 172.55 ($\text{C}(\text{O})\text{O}$), 141.23 ($\text{C}_{\text{quart-Ar}}$), 129.91 (C_{Ar}), 129.38 (C_{Ar}), 129.05 (C_{Ar}), 88.28 (C_{quart}), 71.49, 71.39, 71.35, 71.02, 69.72 (CH_2 and CH), 65.64 ($\text{C}_{\text{quartOCH}_2}$), 52.53 (CH_2_a),

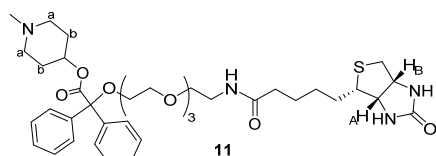
46.10 (CH₃), 41.12 (CH₂N₃), 30.71 (CH₂b). **HRMS (ESI-Orbitrap) m/z:** [M+H]⁺ Calcd for C₂₈H₄₀N₂O₆: 501.2959; Found 501.2947.

Perfluorophenyl 5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanoate (**10**)



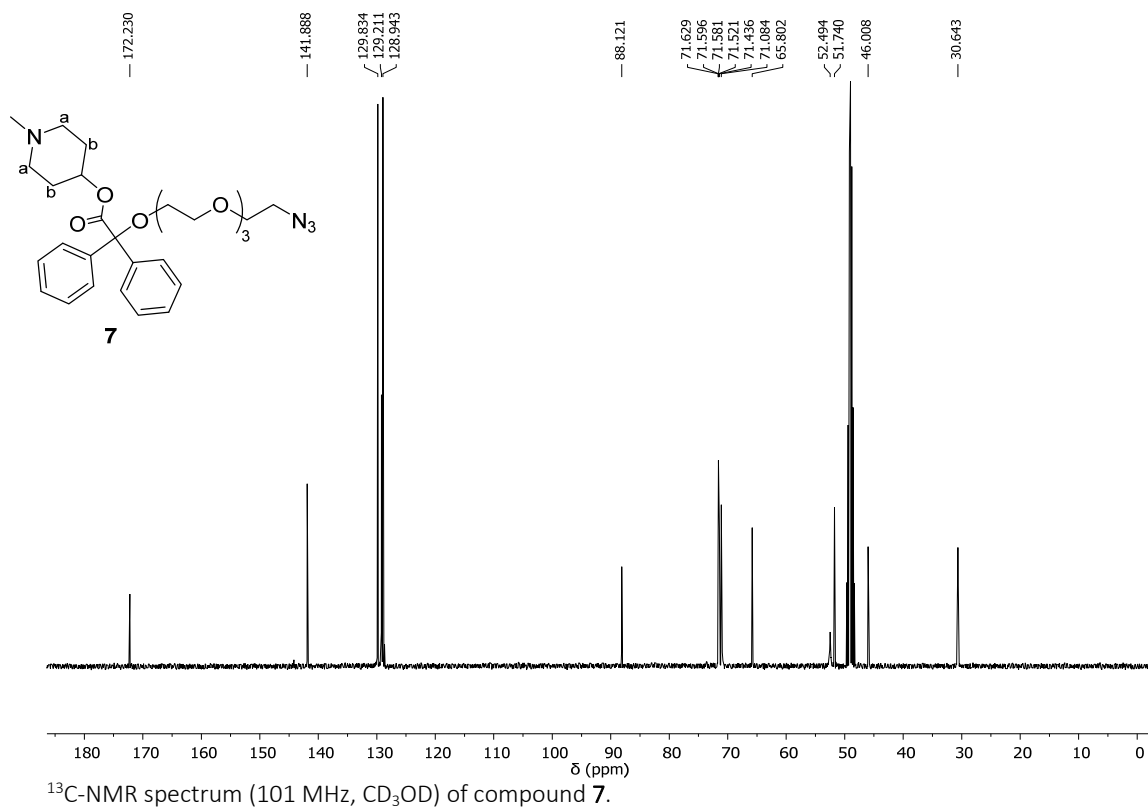
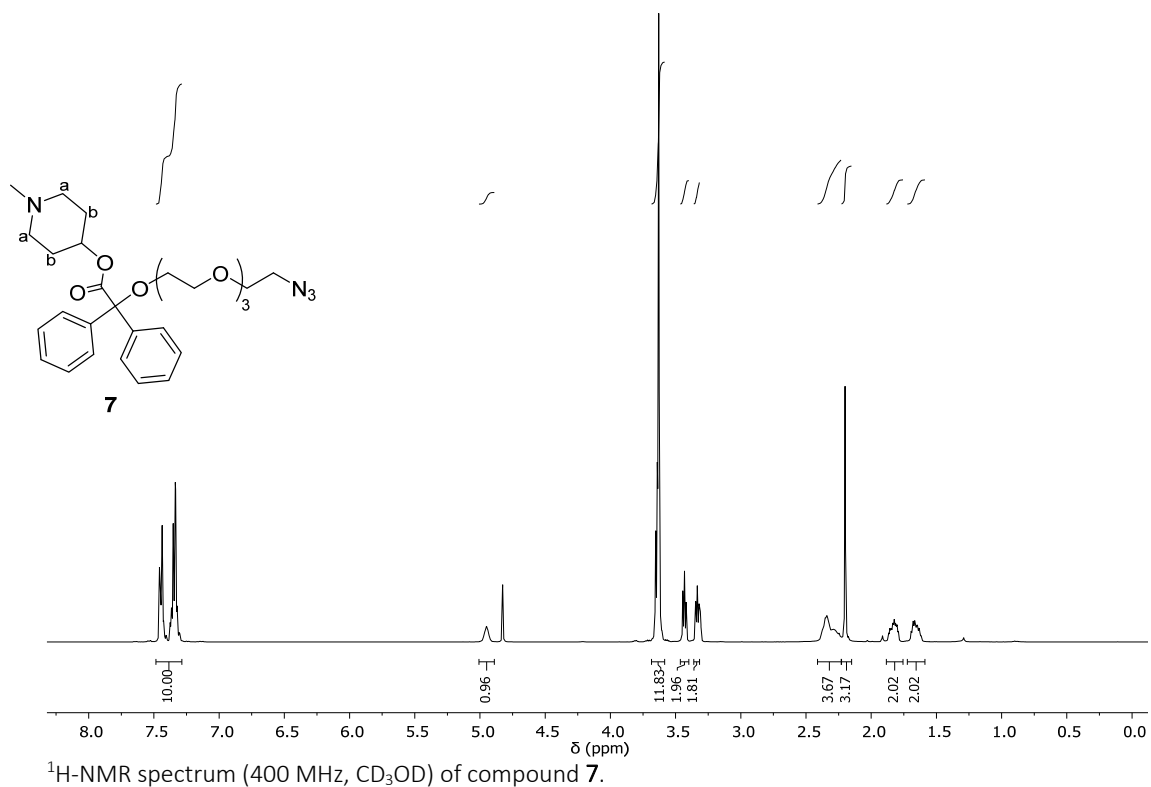
Biotin-pentafluorophenyl (Pfp) ester **10** was synthesized according to Kessler *et al.*, 2009 [4] and was obtained as white solid (335 mg, 80% yield). *R_f* = 0.47 (CH₂Cl₂/MeOH 5:1). ¹H NMR (400 MHz, (CD₃)₂SO): δ (ppm) = 6.43 (s, 1H, NH), 6.35 (s, 1H, NH), 4.36 - 4.26 (m, 1H, HNCH_B), 4.19 - 4.11 (m, 1H, HNCH_A), 3.17 - 3.08 (m, 1H, CHS), 2.84 (dd, *J* = 12.4, 5.1 Hz, 1H, CH₂S), 2.79 (t, *J* = 7.3 Hz, 2H, CH₂ biotin), 2.59 (d, *J* = 12.4 Hz, 1H, CH₂S), 1.78 - 1.35 (m, 6H, CH₂ biotin).

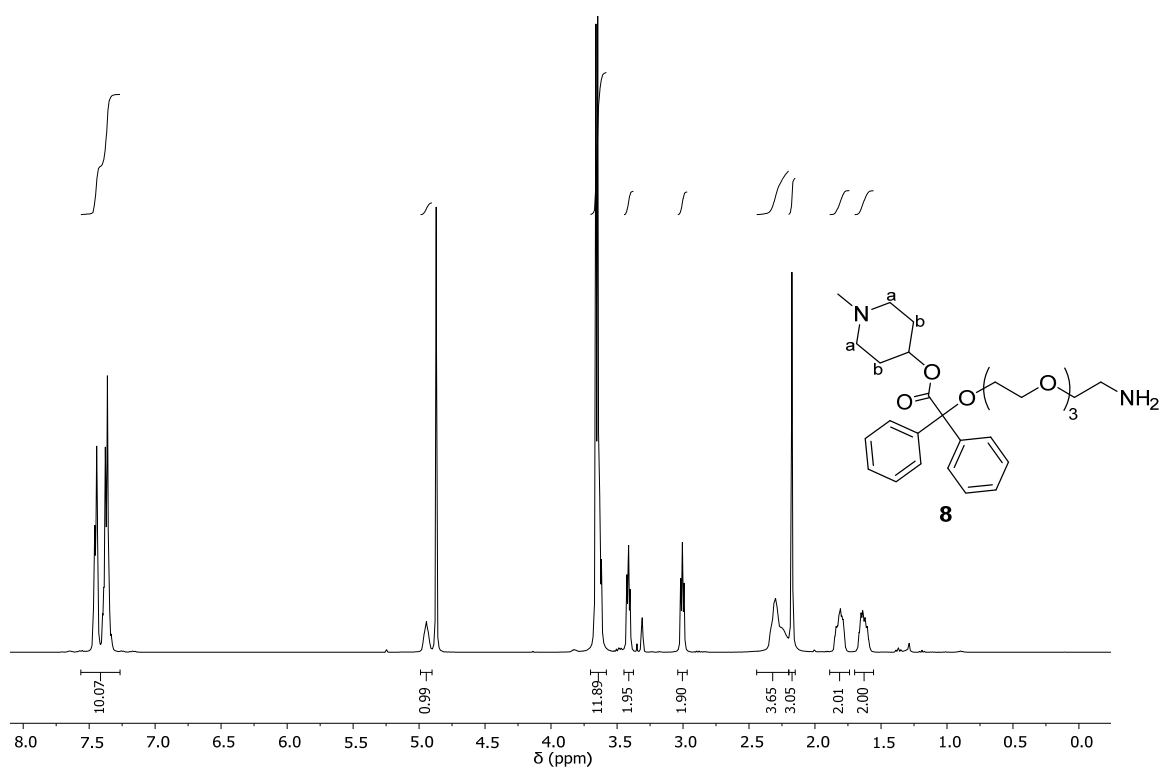
1-Methylpiperidin-4-yl 16-oxo-20-((3aR,4R,6aS)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)-2,2-diphenyl-3,6,9,12-tetraoxa-15-azaicosanoate (**11**)



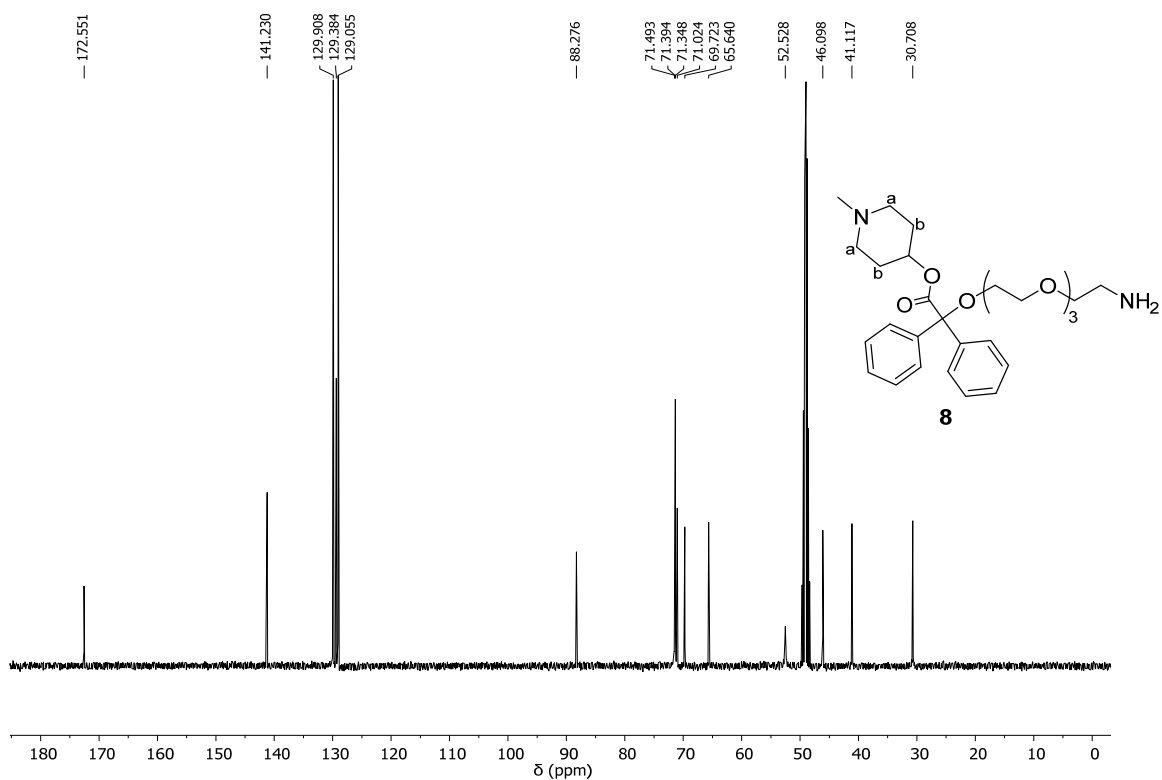
Biotin-Pfp ester **10** (102 mg, 0.25 mmol, 1.4 equiv) was stirred in DMF (800 μL) at 70 °C until completely dissolved and directly transferred into a solution of **8** (89 mg, 0.18 mmol, 1 equiv) in DMF (380 μL). After adding Et₃N (197 μL, 1.42 mmol, 8 equiv) the reaction was allowed to proceed 17 h at ambient temperature. The solvent was evaporated under reduced pressure and the residue purified by gradient silica flash chromatography (0-25% MeOH in CH₂Cl₂). **11** was obtained as white crispy solid (105 mg, 82%). *R_f* = 0.19 (CH₂Cl₂/MeOH 5:1). ¹H NMR (400 MHz, CD₃OD): δ (ppm) = 7.49 - 7.31 (m, 10H, CH_{Ar}), 5.11-5.02 (m, 1H, OCH), 4.52 - 4.44 (m, 1H, HNCH_B), 4.33 - 4.25 (m, 1H, HNCH_A), 3.71 - 3.57 (m, 10H, CH₂ PEG), 3.52 (t, *J* = 5.4 Hz, 2H, CH₂ PEG), 3.44 (t, *J* = 5.0 Hz, 2H, C_{quart}OCH₂), 3.34 (t, *J* = 5.4 Hz, 2H, CONHCH₂), 3.24 - 3.15 (m, 1H, CHS), 2.92 (dd, *J* = 12.7, 5.0 Hz, 1H, CH₂S), 2.85 - 2.75 (m, 2H, CH₂ a), 2.70 (d, *J* = 12.7 Hz, 1H, CH₂S), 2.62 - 2.50 (m, 2H, CH₂ a), 2.49 (s, 3H, CH₃), 2.20 (t, *J* = 7.4 Hz, 2H, CH₂ biotin), 2.02 - 1.90 (m, 2H, CH₂ b), 1.85 - 1.75 (m, 2H, CH₂ b), 1.75 - 1.52 (m, 4H, CH₂ biotin), 1.51 - 1.37 (m, 2H, CH₂ biotin). ¹³C NMR (101 MHz, CD₃OD): δ (ppm) = 176.07 (C_{amide}), 172.07 (C_{carbonyl}), 166.06 (C_{urea}), 141.77 (C_{quart-Ar}), 129.84 (C_{Ar}), 129.40 (C_{Ar}), 129.10 (C_{Ar}), 88.20 (C_{quart}), 71.58 (CH₂ PEG), 71.54 (CH₂ PEG), 71.47 (CH₂ PEG), 71.27 (CH₂ PEG), 70.58 (CH₂ PEG), 69.00 (CH), 65.88 (C_{quart}OCH₂), 63.35 (HNCH_A), 61.61 (HNCH_B), 56.99 (CHS), 51.97 (CH₂ a), 44.83 (CH₃), 41.06 (CH₂S), 40.34 (CONHCH₂), 36.73 (CH₂ biotin), 29.75 (CH₂ biotin), 29.50 (CH₂ biotin), 29.42 (CH₂ b), 26.84 (CH₂ biotin). **HRMS (ESI-Orbitrap) m/z:** [M+H]⁺ Calcd for C₃₈H₅₄N₄O₈S: 727.3735; Found 727.3709.

NMR spectra

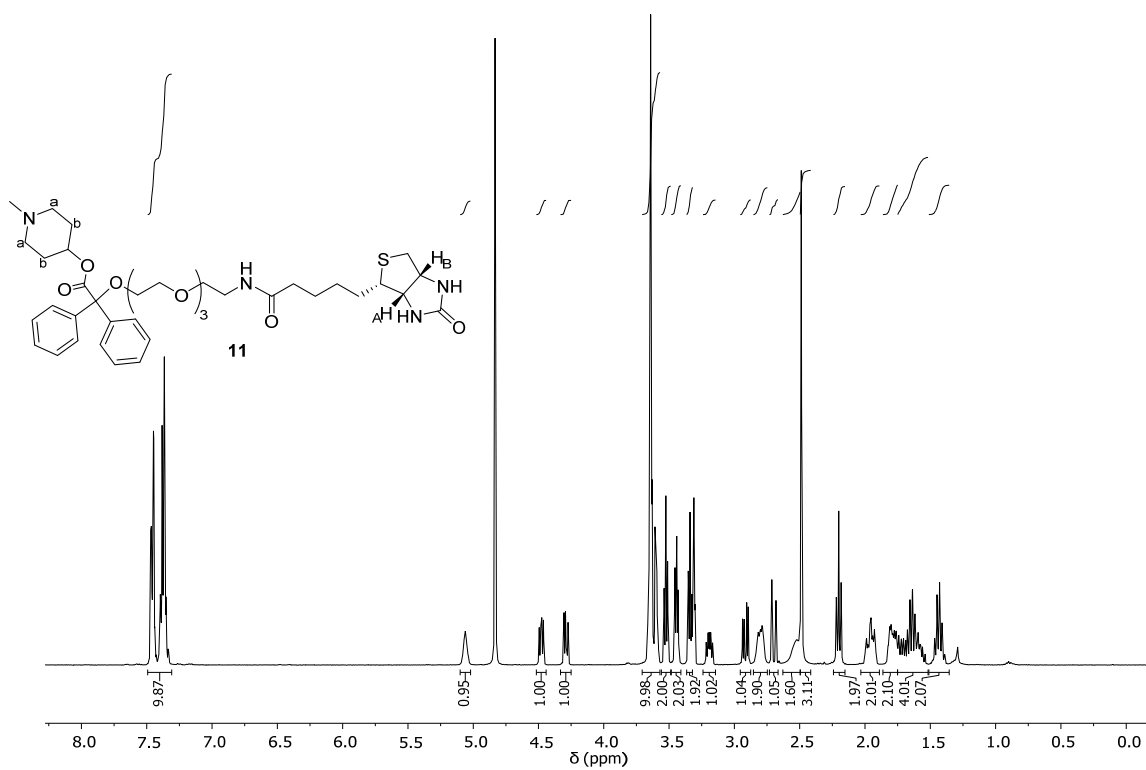




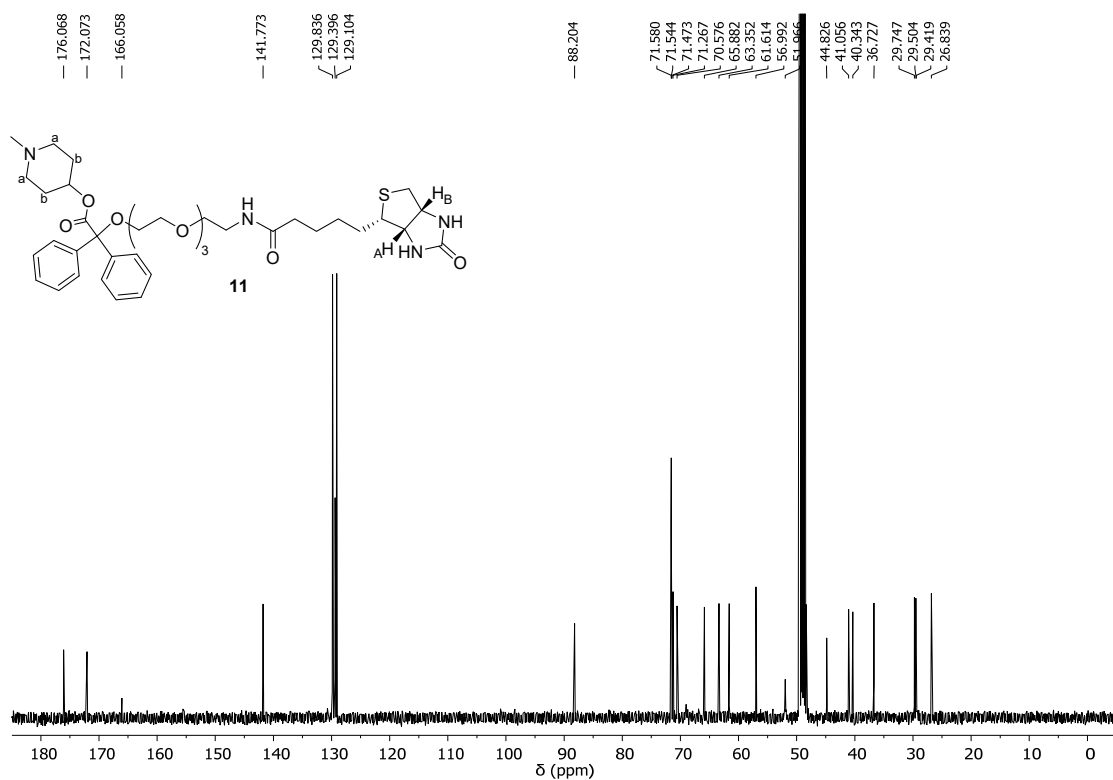
$^1\text{H-NMR}$ spectrum (400 MHz, CD_3OD) of compound **8**.



$^{13}\text{C-NMR}$ spectrum (101 MHz, CD_3OD) of compound **8**.



¹H-NMR spectrum (400 MHz, CD₃OD) of compound **11**.



¹³C-NMR spectrum (101 MHz, CD₃OD) of compound **11**.

Supplementary Bibliography

- [1] P. Dawar, M.B. Raju, R.A. Ramakrishna, One-Pot Esterification and Amide Formation via Acid-Catalyzed Dehydration and Ritter Reactions, *Synthetic Communications*, 44 (2014) 836-846.
- [2] H. Tsukada, K. Sato, S. Nishiyama, N. Harada, Labeled compounds for measuring the function of the muscarinic acetylcholine nervous system, Patent Application Publication, Pub. No. US 2003/0113261 A1 (2003).
- [3] M.S. Cubberley, B.L. Iverson, ¹H NMR Investigation of Solvent Effects in Aromatic Stacking Interactions, *Journal of the American Chemical Society*, 123 (2001) 7560-7563.
- [4] D. Kessler, P.J. Roth, P. Theato, Reactive Surface Coatings Based on Polysilsesquioxanes: Controlled Functionalization for Specific Protein Immobilization, *Langmuir*, 25 (2009) 10068-10076.