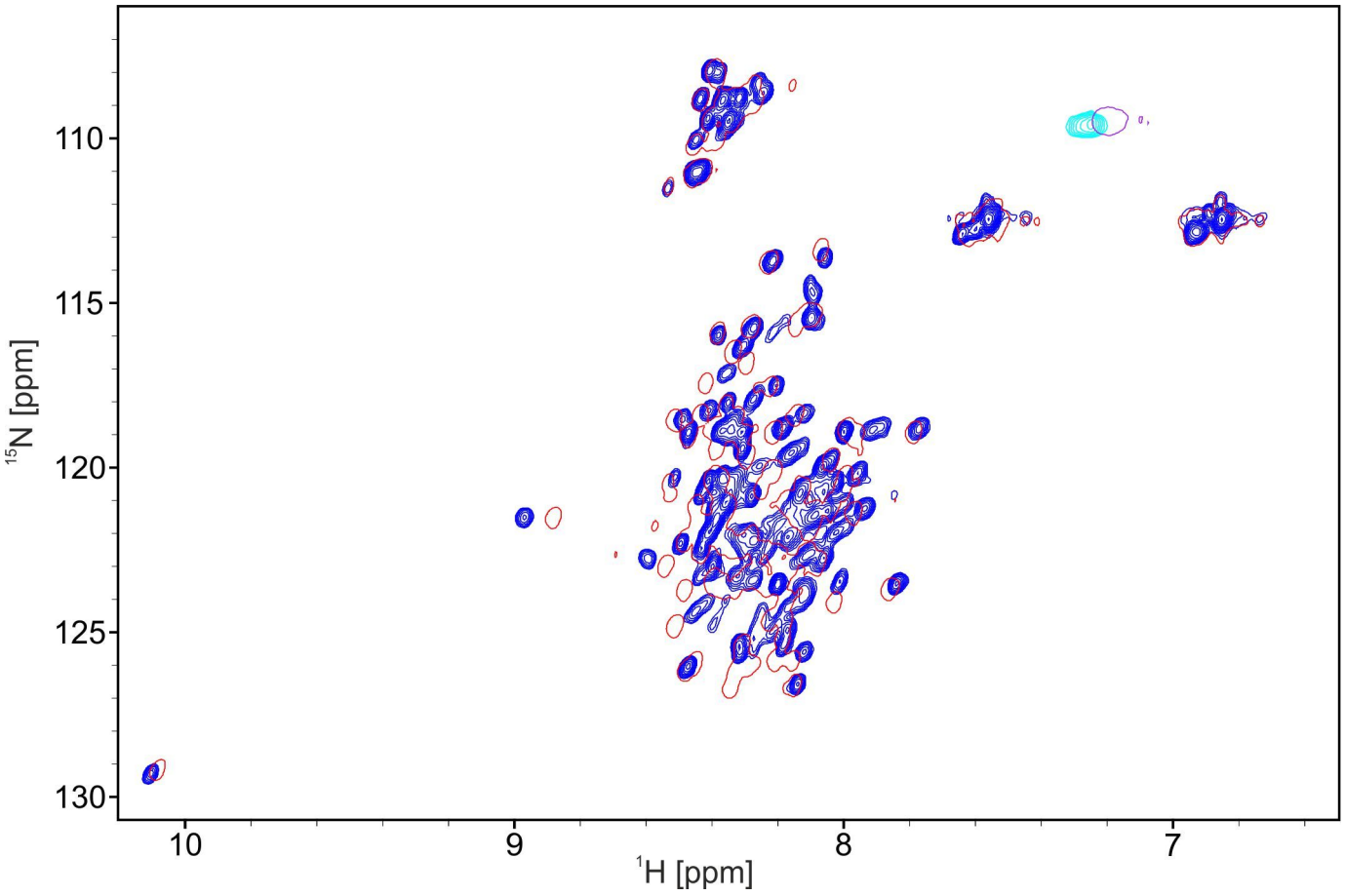

FIGURE S1 Overlay of ^{1}H, ^{15}N-HSQC spectra of A2A-ctL(single red contour) and A2A-ctL in 10 % TFE (blue contours). Peaks drawn in magenta and cyan originate from aliased arginine sidechain N^{ε}-H^{ε} groups.

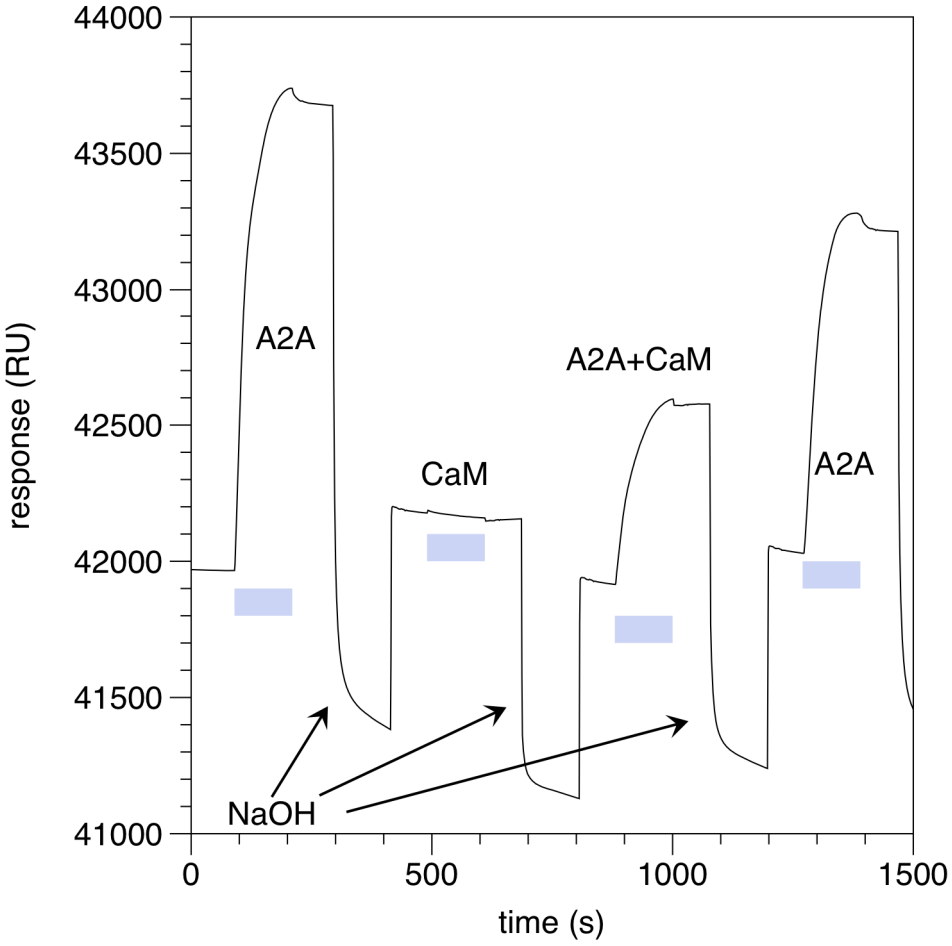

FIGURE S2 Binding of A2A-ctL, CaM and the A2A-ctL-CaM complex to lipid vesicles measured with SPR. The durations of the protein injections are indicated by the shaded light blue areas. Between protein injections, regeneration with NaOH was carried out (arrows). The first and last protein (A2A-ctL) injections were identical, showing a specific effect on the amount of membrane-bound protein by CaM.

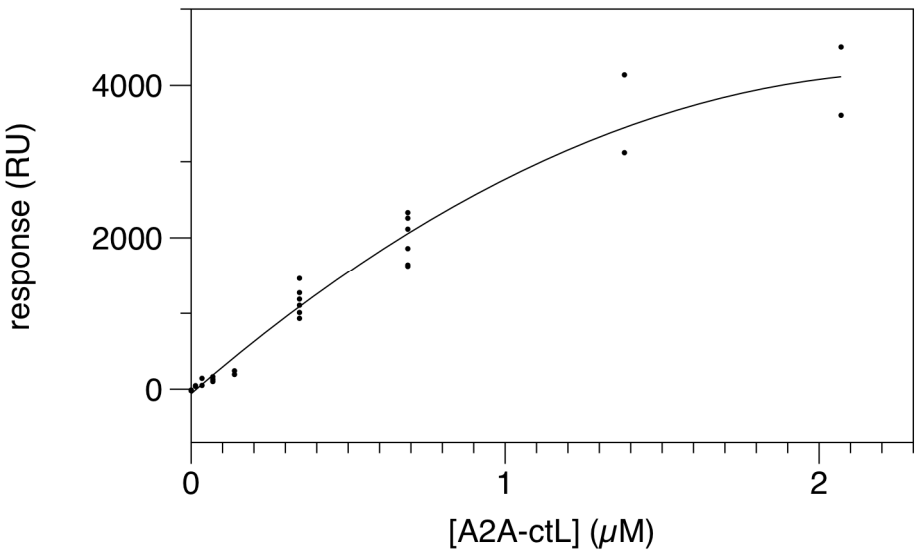

FIGURE S3 Titration of A2A-ctL binding onto immobilized lipid vesicles using SPR. A K_d value of approximately 1 μM can be estimated for the protein-membrane interaction. All individual data points are shown on the graph.

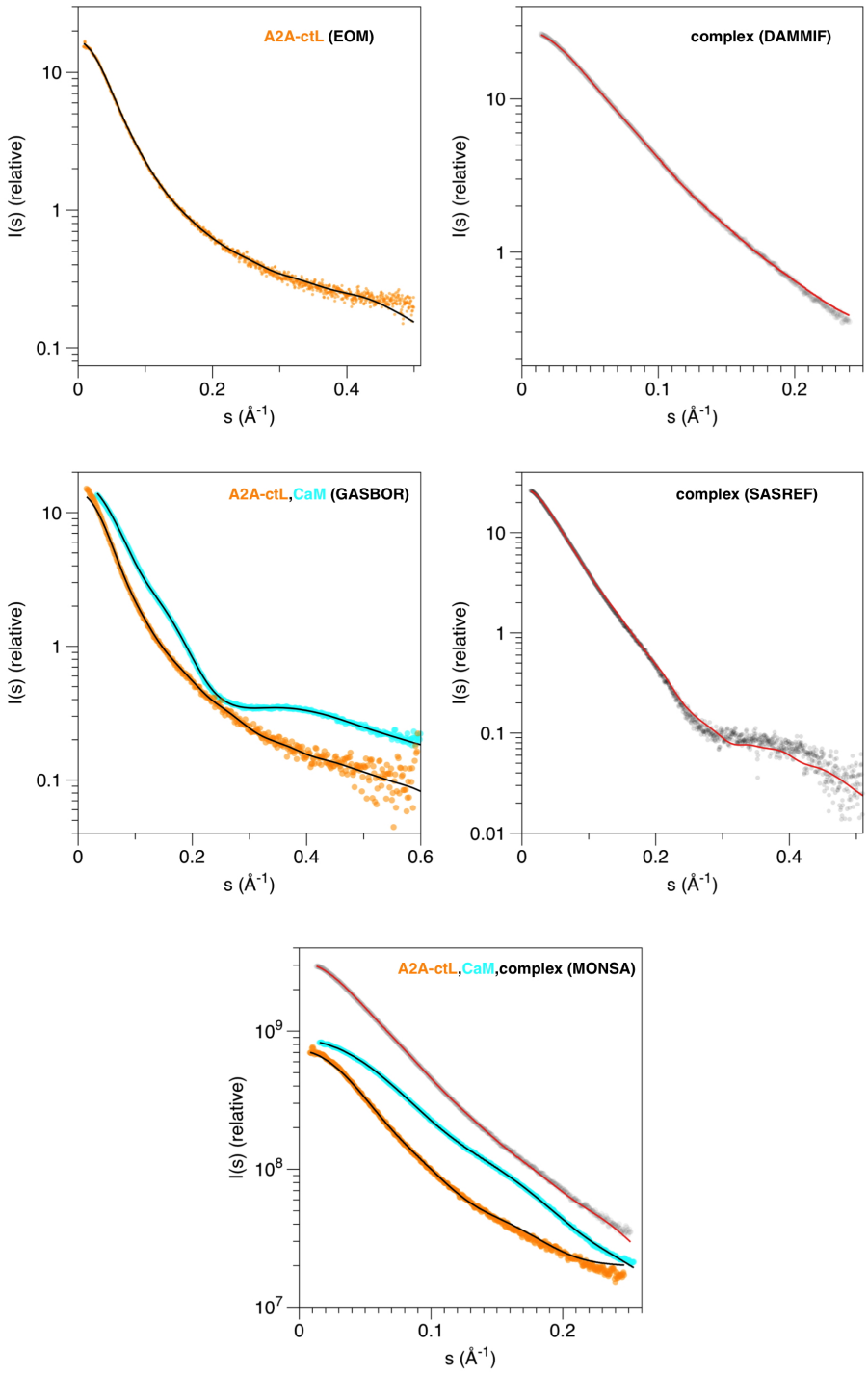

FIGURE S4 Fitting of the different SAXS models to the raw scattering data. The data for A2A-ctL are in orange, for CaM in cyan, and for the complex in gray, and the fitting curve for the latter is in red. The corresponding models are shown within the main text, in Figure 7.

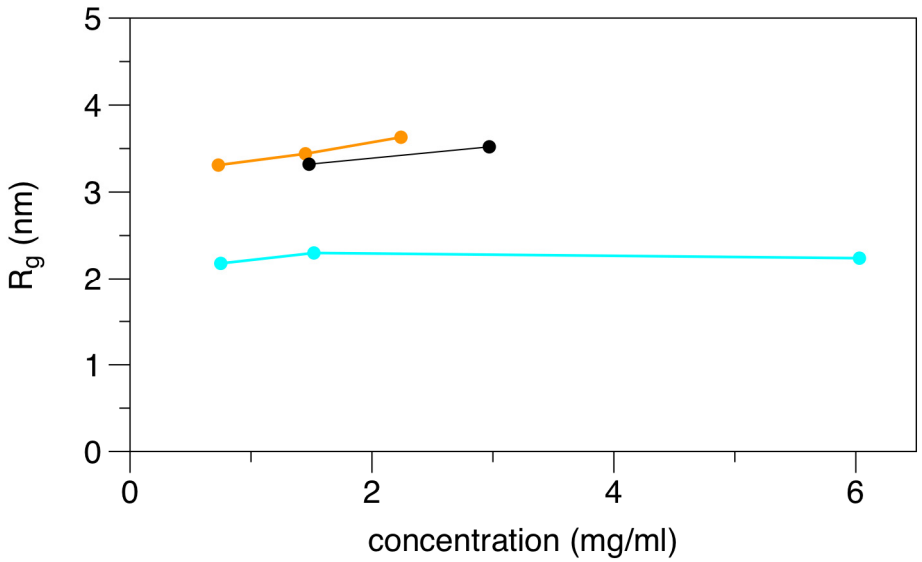

FIGURE S5 Dependence of the radius of gyration on protein concentration. The shown R_g values are obtained from Guinier analysis. CaM, cyan; A2A-ctL, orange; complex, black.

TABLE S1 SAXS modeling Chi-values.

Program	Sample	Chi
EOM	A2A-ctL	0.8
DAMMIF	Complex	1.3
SASREF	Complex (using models of the components built by GASBOR)	1.6
MONSA	A2A-ctL	1.4
	CaM	1.1
	complex	1.1

TABLE S2 GPCR classification based on calmodulin binding predictions.

	Name	UniProtKB ID	Sequence	Contiguous scores of 8 or 9	Score	CT	Other	Site	Ref. (bind.)	S-p Cys	Ref. (S-p Cys)	Class
A)	**GRM5**	**P41594**	**VVRMHVGDGKSSSAASRSSSLVNLWKRR**	**99999999999999999999999999**	**9,00**	**x**		**CT**	(1)			C
	HTR1A	**P08908**	**LVLYGRIFRAARFRIRKTVKKVEKTG**	**99999999999999999999999999**	**8,36**		**x**	**ICL3**	(2)			A
	HTR1A	**P08908**	**EAKRKMALARERKTVKTLGIIMG**	**999999999999999999999**	**7,39**		**x**	**ICL3**	(2)			A
	EDG2	Q92633	QLHTRMSNRRVVVVIVVIWT	99999999999999999999	6,43		x	ICL2		327	similarity	A
	OR10H3	O60404	FLSPIIFSLRNKELKNAINK	99999999999999999999	6,43	x	x	CT				A
	HTR1B	P28222	LEKKKLMAARERKATKTLGI	89999999999999999998	6,36		x	ICL3		388	sequence	A
	MC1R	Q01726	YISIFYALRYHSIVTLPRA	9999999999999999999	6,11		x	ICL2		315	sequence	A
	GPR21	Q99679	IYSLSNSVFQRGLKRLSG	9999999999999999999	5,79	x	x	CT				A
	GPR52	Q9Y2T5	VIYSLSNSVFRLGLRRLS	9999999999999999999	5,79	x	x	CT				A
	MC4R	P32245	IYALRSQELRKTFKEIIC	9999999999999999999	5,79	x	x	CT		318	sequence	A
	CHRM4	P08173	KRQMAARERKVTRTIFAI	8889999999999999998	5,64		x	ICL3				A
	CHRM2	**P08172**	**SREKKVTRTILAILLAF**	**89999999999999998**	**5,39**		**x**	**ICL3**	(3)			A
	OPN1SW	P03999	LNAMVLVATLRYKKLRQ	89999999999999998	5,39		x	ICL1				A
	OPN1MW	P04001	TNGLVLAATMKFKKLRH	89999999999999998	5,39		x	ICL1				A
	DRD5	P21918	ASIKKETKVLKTLSVIM	89999999999999998	5,39		x	ICL3		375	similarity	A
	HTR4	Q13639	WDRQLRKIKTNYFIVS	9999999999999999	5,14		x	ICL1		329	similarity	A
	CNR2	P34972	SYKALLTRGRALVTLG	9999999999999999	5,14		x	ICL2				A
	NPGPR	Q9Y5X5	HVVSRKKQKIIKMLLI	9999999999999999	5,14		x	ICL3				A
	MC3R	P41968	FYALRYHSIMTVRKAL	8999999999999998	5,07		x	ICL2		315	sequence	A
	GALR3	O60755	VYALASRHFRARFRRL	8999999999999998	5,07	x		CT		308	similarity	A
	AVPR2	P30518	GLVLAALARRGRRGHW	8999999999999998	5,07		x	ICL1		341, 342	(4)	A
	NPY2R	P49146	HLESKISKRISFLIIG	8899999999999998	5,04		x	ICL2		342	sequence	A
	FPR1	P21462	GLIATKIHKQGLIKSS	8999999999999988	5,04		x	ICL3				A
	HRH2	P25021	ARDQAKRINHISSWKA	8888999999999998	4,96		x	ICL3		305	similarity	A
	GRM7	**Q14831**	**KRKRSFKAVVTAATM**	**999999999999999**	**4,82**	**x**		**CT**	(5)			C
	OPN1LW	P04000	TNGLVLAATMKFKKL	899999999999998	4,75		x	ICL1				A
	ADORA1	P30542	YAFRIQKFRVTFLKI	899999999999998	4,75	x	x	CT		309	sequence	A
	CCKBR	P32239	ARVWQTRSHAARVIV	899999999999998	4,75		x	ICL2		408	similarity	A
	GPR10	P49683	LRRRISLRLSAYAVLA	8998888888888888	4,64		x	ICL2				A
	NPY2R	P49146	LGIISFSYTRIWSKLK	8888888888888888	4,57		x	ICL3		342	sequence	A
	OPN1MW	P04001	YLQVWLAIRAVAKQQK	8888888888888888	4,57		x	ICL3				A

PTGER4	P35408	SDFRRRRSFRRIAGA	888888999999998	4,57		x	ICL3				A
CRHR1	**P34998**	**YCFLNSEVRSAIRK**	**99999999999999**	**4,50**	**x**	**x**	**CT**			(6)	B
ADRB2	P07550	VFVYSRVFQEAKRQ	89999999999998	4,43		x	ICL3		341	(7-9)	A
DRD3	P35462	VYARIYVVLKQRRR	89999999999998	4,43		x	ICL3				A
ADRB3	P13945	FVVATRQLRLLRGE	89999999999998	4,43		x	ICL3		361	similarity	A
MTLR1	O43193	GRERGHRQTVRVLL	89999999999998	4,43		x	ICL3				A
OR10H2	O60403	SLRNKELKVAMKRT	89999999999998	4,43	x	x	CT				A
GPR10	P49683	IARVRRLHNVTNF	8999999999998	4,11		x	ICL1				A
TACR3	P29371	ILAHKRMRTVTNY	8999999999998	4,11		x	ICL1		374	sequence	A
HCRTR1	O43613	STARRARGSILGI	8999999999998	4,11		x	ICL2				A
DRD4	P21917	TFRGLQRWEVARR	8999999999998	4,11		x	ICL3				A
LGR7	Q9HBX9	NQVKKEMILAKRF	8999999999998	4,11		x	ICL3				A
OR10H1	Q9Y4A9	RNKELKVAMKKTF	8999999999998	4,11	x		CT				A
OPN4	Q9UHM6	RAIRETGRALQTF	8999999999998	4,11		x	ICL3				A
CASR	**P41180**	**AFKVAARATLRRS**	**8999999999998**	**4,11**	**x**		**CT**	(10)			C
ADRA1A	P35348	RVYVVAKRESRGL	8999999999998	4,11		x	ICL3		345	sequence	A
ADORA2A	**P29274**	**YRIREFRQTFRKI**	**8899999999998**	**4,07**	**x**	**x**	**CT**	(11)			A
DRD2	**P14416**	**IKIYIVLRRRRKRV**	**88888888888998**	**4,07**		**x**	**ICL3**	(12)			A
CHRM2	P08172	TVLYWHISRASKSR	88888888888888	4,00		x	ICL3				A
CHRM5	P08912	RVVLVKERKAAQT	8888999999998	4,00		x	ICL3				A
PTGER4	P35408	EKIKCLFCRIGGSR	88888888888888	4,00	x		CT				A
CHRM3	**P20309**	**TKRKRMSLVKEK**	**899999999998**	**3,79**		**x**	**ICL3**	(3)			A
TACR2	P21452	IILAHRRMRTVT	899999999998	3,79		x	ICL1		324	sequence	A
HCRTR1	O43613	LSGKFREQFKAA	899999999998	3,79	x		CT				A
HTR5A	P47898	IYKAAKFRVGSR	899999999998	3,79		x	ICL3				A
GHSR	Q92847	SLIGRKLWRRRR	899999999998	3,79		x	ICL3				A
GPR1	P46091	WFTGFKWKKTVT	899999999998	3,79		x	ICL1				A
OPRM1	P35372	IVRYTKMKTATN	899999999998	3,79		x	ICL1		353	sequence	A
HTR6	P50406	TKHSRKALKASL	899999999988	3,75		x	ICL3				A
GALR1	P47211	RRSSSLRVSRNA	899999999988	3,75		x	ICL2		320	similarity	A
MTLR1	O43193	ISKKYRAAAFKL	888999999998	3,71	x	x	CT				A
NTSR2	O95665	LVRHKDVRRIRS	889999999988	3,71		x	ICL3		377	sequence	A
EDNRB	P24530	DRYRAVASWSRI	899988888888	3,54		x	ICL2		402, 403, 405	(13), sequence	A
GALR2	O43603	KHFRKGFRTIC	89999999998	3,46	x		CT				A

GPR50	Q13585	VTKNKKLRNSG	89999999998	3,46		x	ICL1				A
LTB4R	Q15722	SILKRMQKRSV	89999999998	3,46		x	ICL1				A
ADRA2B	P18089	IFNQDFRRAFRR	888888888888	3,43	x	x	CT		439	sequence	A
DRD4	P21917	RQGGSRRQLLLI	888888888888	3,43		x	ICL2				A
OR10J1	P30954	ASVEGRKKAFA	89999999988	3,43		x	ICL3				A
AVPR1A	P37288	SISRAKIRTVK	88999999998	3,43		x	ICL3		365, 366	similarity	A
CHRM1	**P11229**	**KEKKAARTLSA**	**89999999888**	**3,39**		**x**	**ICL3**	(3)			A
ADRA2A	P08913	AVFTSRALKA	9999999999	3,21		x	ICL1		442	similarity	A
ADRA2C	P18825	AVLTSRALRA	9999999999	3,21		x	ICL1				A
EDG1	P21453	YSLVRTRSRR	8999999998	3,14		x	ICL3		328	similarity	A
HCRTR2	O43614	IKQIRARRKT	8999999998	3,14		x	ICL3				A
HRH1	P35367	AVRSERKLHT	8999999998	3,14		x	ICL1				A
HRH2	P25021	VGLNRRLRNL	8999999998	3,14		x	ICL1		305	similarity	A
MTNR1A	P48039	KEYRRIIVSL	8999999998	3,14	x		CT				A
PTH1R	**Q03431**	**WTLALDFKRK**	**8999999998**	**3,14**	**x**		**CT**	(6)			B
HTR2C	**P28335**	**IYRRAFSNYL**	**8899999998**	**3,11**	**x**		**CT**	(14)			A
DRD5	P21918	IVRSRHLRAN	8999999988	3,11		x	ICL1		375	similarity	A
HTR7	P34969	IFKREQKAAT	8999988888	3,00		x	ICL3		401	sequence	A
HTR2B	P41595	AFGRYITCNY	8899988888	2,96	x		CT		397	sequence	A
VIPR1	**P32241**	**EVQAELRRK**	**999999999**	**2,89**	**x**		**CT**	(6)			B
GLP2R	**O95838**	**VKAELRKYW**	**899999998**	**2,82**	**x**		**CT**	(6)			B
HTR1F	P30939	RAAKTLYHK	899999998	2,82		x	ICL3				A
ADRA2B	P18089	RRAQLTREK	899999998	2,82		x	ICL3		439	sequence	A
ADORA3	P33765	TVRYKRVTT	889999988	2,75		x	ICL2		303	sequence	A
DRD1	P21728	IAQKQIRRI	889999988	2,75		x	ICL3		347, 351	(15)	A
PTGFR	P43088	AYQRFRQKS	889999988	2,75		x	ICL1				A
CALCR	**P30988**	**WNQRWGRR**	**99999999**	**2,57**	**x**		**CT**	(6)			B
OPRM1	**P35372**	**KEKDRNLR**	**89999998**	**2,50**		**x**	**ICL3**	(16)	353	sequence	A
ADRA1A	P35348	LKFSREKK	89999998	2,50		x	ICL3		345	sequence	A
ADRA1B	P35368	FSREKKAA	89999998	2,50		x	ICL3		365	sequence	A
ADRA1D	P25100	LLKFSREK	89999998	2,50		x	ICL3		419	sequence	A
GNRHR	P30968	KKEKGKKL	88899988	2,39		x	ICL1				A
OPRD1	P41143	VRYTKMKT	88888888	2,29		x	ICL1		333	sequence	A
OPRD1	**P41143**	**GSKEKDR**	**8999998**	**2,18**		**x**	**ICL3**	(16)	333	sequence	A

	GPR1	P46091	QARFRSS	8999998	2,18	x		CT				A
	HTR1E	P28566	YARKRTA	8899988	2,11		x	ICL2				A
	HRH1	P35367	RTKTRA	888888	1,71		x	ICL2				A
B)	ADCYAP1R1	P41586				x		CT	(6)			A
	GLP1R	P43220				x		CT	(6)			A
	AVPR2	P30518				x		CT	(17)	341, 342	(4)	A
	HTR2A	P28223					x	ICL2	(18)			A
	HTR2A	P28223				x		CT	(18)			A
	MC1R	Q01726					x	ICL3	(19)	315	sequence	A
	GRM5	P41594				x		CT	(1)			C
C)	GLP1R	P43220	PLRLALLLLGMVGRAGPRPQ	99999999999999999999	6,43		x	signal peptide				A
	TACR1	P25103	LAHKRMRTVTNYFLVNL	99999999999999999	5,46		x	H2		322	sequence	A
	NPY1R	P25929	SGNLALIIIIILKQKEMR	99999999999999999	5,46		x	H1		338	sequence	A
	TRHR	P34981	YKDAIVISCGYKISRNY	89999999999999988	5,36		x	ECL2				A
	MC2R	Q01718	ILENILIILRNMGYLK	9999999999999999	5,14		x	ECL1		293	sequence	A
	CRHR1	P34998	IGKLYYDNEKCWFGK	999999999999999	4,82		x	ECL2				B
	HTR2A	P28223	FNSRTKAFLKIIAVW	899999999999998	4,75		x	H4				A
	NTSR1	P30989	RSRTKKFISAIWLAS	899999999999988	4,71		x	H4		381, 383	(20)	A
	TBXA2R	P21731	RTTEKELLIYLRVA	99999999999999	4,50		x	H7				A
	OXTR	P30559	RRRTDRLAVLATW	8999999999998	4,11		x	H4				A
	FPR1	P21462	ATVRIRELLQGMYK	88888888888888	4,00		x	ECL3				A
	PTGER3	P43115	PLLIMMLKMIFN	999999999999	3,86		x	H6		358, 376	sequence	A

Proteins are divided into three groups based on the prediction results. Group A contains proteins and binding sites for which predictions were considered to be successful (i.e. proteins known to bind CaM by other methods and proteins which were predicted to bind CaM via the intracellular loop or C-terminal domain). Group B contains proteins that are shown to bind CaM by other methods, but for which binding could not be predicted with the Calmodulin Target Database and selected scoring criteria. Group C contains proteins that were predicted to bind to ”nonsensical” sites on a receptor (i.e. N-terminal domain or transmembrane helix). Binding sites are divided to C-terminal “CT” and “other” sites. “Site” describes the binding sites more in detail. Palmitoylation sites “S-p Cys” and their references are shown. “Sequence” and “similarity” refer to the UniProt database description of the corresponding modification. GPRC classes into the receptors belong are shown.

TABLE S3 Distribution of predicted CaM binding sites to palmitoylated and non-palmitoylated GPCRs and intracellular domains.

	ICL1	ICL2	ICL3	CT	Totally	
Palmitoylated	9	8	19	6	42	
	21,4	19,0	45,2	14,3	100,0	%
Non-palmitoylated	11	7	24	25	67	
	16,4	10,4	35,8	37,3	100,0	%

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