Structures Solved Using MPEC Technologies (2005-present)

Target Name	Organism	Resolution Å	PDB ID	Data Method	R-Factor	Publication Date	Journal
Aquaporin Aqpm	*E. coli*	1.68	2F2B	X-ray	19.30%	2005	*PNAS*
Aquaporin Aqpm	*E. coli*	2.3	2EVU	X-ray	22.60%	2005	*PNAS*
Lac Permease (acidic)	*E. coli*	3.3	2CFP	X-ray	32.80%	2006	*EMBO*
Lac Permease (neutral)	*E. coli*	2.95	2CFQ	X-ray	29.80%	2006	*EMBO*
Lac Permease (w.type)	*E. coli*	3.6	2V8N	X-ray	33.30%	2007	*PNAS*
Glur2 Complex Cnqx	*R. norvegicus*	2.5	3B7D	X-ray	28.30%	2007	*Science*
Amtb Glnkx complex	*E. coli*	1.96	2NS1	X-ray	19.80%	2007	*PNAS*
Aqpz Mutant T183c	*E. coli*	2.3	2O9D	X-ray	23.80%	2007	*JMB*
AqpZ T183C mercury	*E. coli*	2.2	2O9E	X-ray	24.30%	2007	*JMB*
AqpZ mutant L170C	*E. coli*	2.55	2O9F	X-ray	28.60%	2007	*JMB*
AqpZ L170C Hg	*E. coli*	1.9	2O9G	X-ray	19.50%	2007	*JMB*
Aquaglyceroporin PfAQP)	*P. falciparum*	2.05	3C02	X-ray	30.60%	2008	*Nat. Struct. Mol. Bio.*
Rh-like protein	*N. europaea*	1.99	3BHS	X-ray	23.70%	2009	*PDB*
Aquaporin 4	*H. sapiens*	1.8	3GD8	X-ray	16.50%	2009	*PNAS*
RhCG	*H. sapiens*	2.1	3HD6	X-ray	19.50%	2010	*PNAS*
Sec 61αγ translocon	*P. furiosus*	2.9	3MP7	X-ray	31.70%	2010	*PNAS*
AcrB pump +peptide	*E. coli*	3.3	refining	X-ray	-		
ZneB	*E. coli*	2.8	3LNN	X-ray	31.40%	2010	*PNAS*
Aqp from A. fulgidus	*A. fulgidus*	3.0	3NE2	X-ray	27.40%*		
CcmG thioredoxin	*E. coli*	2.3	3K8N	X-ray	25.54%*		
OmpF porin	*E. coli*	3.79	3K19	X-ray	28.80%	2010	*Protein Science*
OmpF porin	*E. coli*	4.39	3K1B	X-ray	32.90%	2010	*Protein Science*
Cytoplasmic domain HKR QseQ	*E. coli*	2.5	3JZ3	X-ray	26.20%	2010	*Protein Pept. Lett.*
N-terminal domain of GluN1	*R. norvegicus*	3.4	3Q41	X-ray	27.90%	2011	*J. Neuroscience*
Yeast erg11	*S.cerevisiae*	2.1		X-Ray		2011	*In preparation*
ZneA (+ Zn2+) form 1	*C.metallidurans*	3.0		X-ray	32.9%*	2011	*In preparation*
ZneA (+Zn2+) form 2	*C.metallidurans*	3.8		X-ray	33.7%*	2011	*In preparation*
Gramicidin	*B. subtilis*	1.7	2xdc	X-ray	18.10%	2010	*Biophys. J.*

Gramicidin	*B. subtilis*	1.08	2y5m	X-ray	13.20%	2011	*Cryst. Growth Des.*
Gramicidin	*B. subtilis*	1.26	2Y6N	X-ray	14.9%	2011	*Cryst. Growth Des.*
Cytochrome caa3 oxidase	*T. thermophilus*	2.35	2yev	X-ray		2011	*In preparation*
B2-adrenoreceptor	*Human*	3.5	3pds	X-ray	24.10%	2011	*Nature*
B2AR-Gs complex	*Human*	3.2	3sn6	X-ray	22.80%	2011	*Nature*
					*denotes in refinement		

MPEC List of Commercialized Instruments and Chemicals, and Protocols Established (2006-present)

	TECHNOLOGY DEVELOPMENT/ACHIEVEMENT	FINDINGS/USAGE/COMMENTS
	Protein Production	
1	Established inducible, selectable overexpressing human integral membrane proteins in transient, and stably transformed Human Embryonic Kidney 293S cells	Protocols for overexpression of human and eukaryotic membrane proteins in HEK (human) cells engineered to add only core sugars at glycosylation sites for homogeneity. Published.
2	Established efficient expression screening of human membrane proteins in transiently transfected Human Embryonic Kidney 293S cells.	Screening of proteins produced in HEK cells using fusion to fluorescent proteins to assay expression levels. Published.
3	Established a robust expression system in *S.cerevisiae* for membrane proteins.	Useful for expression of eukaryotic membrane proteins using a suite of vectors including those fused to cleavable e oligo-histidine tags, fluorescent proteins, yeast signal sequences, Precision protease sites.
4	Established baculovirus expression system	
5	Established standard protocol for expression, purification, and characterization of stable membrane protein preparation for structural studies.	
6	Established robust expression of human AQP4 for use in therapeutic applications against Neuromyelitis Optica.	Protein production that feed the community of researchers who study this rare but lethal autoimmune disease. Provision for the Guthy-Jackson Foundation (NMO).
7.	Established robot for screening crystallization plates by X-ray diffraction at the ALS	
8.	Established an E. coli-based cell-free expression system for integral membrane protein production and reconstitution into a bicontinuous lipidic mesophase	For use in tandem expression and crystallization of integral membrane proteins
	Stabilization Technologies	
8.	Synthesis and characterization of new facial detergents	In collaboration with Dr S. Gellman produced dimeric facial amphiphiles. Published
9.	Novel lipids synthesized and purified at the gram scale for use in in meso crystallization trials	
10	Protocol: phage display panning to select Fragments antigen binding (Fabs) against membrane proteins	A naïve B cell library, expressed on phage, optimized for membrane proteins successfully used against various membrane proteins (published)
11	Protocol: ELISA based characterization of phage display selected Fabs	Allows rapid and reliable characterization of Fab binding, using ELISA and unpurified Fabs, and thus eliminates false positives or weaker binders before Fab production (published)
	Biophysical Characterization	
12	Protocol for determining membrane protein subunit stoichiometry and homogeneity while also quantifying associated detergent.	Use of light scattering, refractive index plus viscometry and concentration measurements allows determination of the oligomeric state of an integral membrane protein in detergent solution. (Tetra detector)
13	Protocol - fluorescence assisted size exclusion chromatography (FSEC)	Allows for characterization of expression levels of membrane proteins in S.cerevisiae, HEK293 cells, and E.coli

14	Protocol - fluorescence assisted size exclusion chromatography (TD-FSEC)	Allows for characterization of expression levels of membrane proteins in E.coli,
15	Protocol for Mass Spectrometric Analysis of Membrane Proteins	Allows analysis of integral membrane proteins directly in the presence of lipid and detergent.
16	Protocol for assay of thermal stabilization in 96 well format using qPCR Viia 7 from ABI/Invitrogen.	Assay protocols adapted to measure effects on structure detected by melting curves and stabilization induced by lipids, detergents, buffers and ligands. Dyes co-developed to match qPCR detectors for MP stability measure.
17	Validation of Fab-membrane protein interaction by electron microscopy (EM)	In collaboration with Dr. Yifan Cheng, interactions between phage display selected Fabs and membrane proteins are validated by negative stain EM. Distinctive images of Fabs in negative staining allow easy detection of Fab-membrane protein complexes and thus visual confirmation of complex formation.
18	Established a host lipid screen for use in membrane protein crystallization in lipidic mesophases	Used to extend the range of membrane protein types that yield diffraction quality crystals by the in meso crystallization method
19	Established a high-throughput protocol for assaying the enzymatic activity of integral membrane proteins reconstituted into the lipidic cubic mesophase	Useful in evaluating functional activity of membrane proteins in meso as a prelude to crystallization
20	Established X-ray screening in crystallization plates	Robot designed in operation at ALS synchrotron Berkeley.
21	Automated crystal handling tasks at the ALS	http://bl831.als.lbl.gov/~jamesh/beamline/holton_utilities.html
22	Program that informs on feasibility of structure determination	http://bl831.als.lbl.gov/xtalsize.html
Technology Integration		
23	Pipeline for production in *S.cerevisia* MPEC vector suite through solubilzation, purification, characterization, crystallization and structure determination.	Integration of all protocols/technologies into a pipeline for the efficient determination of the structure of membrane proteins.
Technology Validation		
24	Validation of technology	Structure solution of over 25 membrane proteins including mutant and variant species using MPEC technologies.

Outreach and Training (2006-Present)

Name	Affiliation	Dates	Purpose/Training
Chantal Eckende	Univ Brussels	May 2008 –Jan 2010 Spent at UCSF	Expression Purification ZneA/B/C
Guthy-Jackson Foundation for NMO disease	Private Not-for Profit Research Foundation	2009-present	Contracted to supply 150mg/year pure human AQP4, target of the lethal orphan disease Neuromyelitis Optica
Andre Bachmann	University of hawaii	2008	Human 4 crossing Golgi trafficking protein, now in crystal trials
Niek Dekker	Astra Zeneca Sweden	Provided MP expression systems and purification	Ion Channels, GPCRs, TRP channels Expression
Brian Monk	University of Auckland NZ	Jan 2010-Nov 2010 Spent at UCSF	Yeast expression Purify, Crystallize yeast ABC transporters, and cyt oxidases erg11: crystal structure determined
Richard Cannon	University of Auckland NZ	Feb 2009- Oct 2009 Spent at UCSF	Yeast expression Purify fungal ABC drug exporters.
Erwin Lamping		Feb 2009-Sep 2009 Spent at UCSF	Yeast expression Purify fungal ABC drug exporters.
Cedric Govaerts	Universite libre de Bruxelles (belgium)	2009-	LMRP a multi-drug resistant transporter protein
Nicole Tischler	Fundacion Ciencia para la vida Chile	2009-	Andes virus envelope glycoprotein Gc Preparation
Ignaccio Munoz	Fundacion Ciencia para la vida Chile	May 2009- Sept 2010 Spent at UCSF	Andes virus envelope glycoprotein Gc Preparation
Claudia Mergel	Goethe University in Frankfurt	Mar 2010-Nov 2010 Spent at UCSF	Protein purification, crystallization, succeeded
Sebastian Stiller	Goethe University in Frankfurt	June2010-Sep 2010 Spent at UCSF	Protein purification, crystallization, succeeded
Mickie Cheng	UCSF	July 2011-present	Membrane protein purification training
Natalia Jura	UCSF	Dec 2011-present	Membrane protein purification training
Daniel Süveges	UCSF	Dec 2011-present	Membrane protein purification training
Teresa Garrett	Vassar College	Spent at UCSF	
Mickie Cheng	UCSF	July 2011-present	Membrane protein purification training
Natalia Jura	UCSF	Dec 2011-present	Membrane protein purification training
Daniel Süveges	UCSF	Dec 2011-present	Membrane protein purification training
20 students	GPCR workshop, Maui	Dec 2011	In meso crystallization training /MC
20 students	ACMC11, Melbourne, Australia	Dec 2011	In meso crystallization training /MC
20 Students	University of Helsinki, Finland	May 2011	In meso crystallization training /MC
20 Students	University of Granada, Spain	May 2011	In meso crystallization training /MC
V Srinivasan	Free University of Brussels	April 2011	In meso crystallization training /MC

H Bridges	**University of Cambridge**	**April 2011**	**In meso crystallization training /MC**
F Jaenecke	**Halle-Wuttenburg University**	**January 2011**	**In meso crystallization training**

External Collaborations (outside MPEC)

Collaborator	Affiliation	Description of study	Target
Krieger, Monty	**MIT**	Purification & Structure solution	HDL Receptor –now crystallized
Bachmann, Andre	**University of Hawaii**	Protein Production Structure determination	Human 4 crossing Golgi trafficking protein, now in crystal trials; pediatric canceer target
Belogrudov, Gregori	**UCLA**	Structure determination	Mitochondrial factor B; structure determined. Paper in *PNAS* 2008
Nicoll, Roger	**UCSF, Cellular & Molecular Pharm.**	Structure determination of AMPA receptor drug interactions.	Four membrane proteins in the AMPA receptor protein family and accessory TARPs; Paper in *Science* 2007
Farese, Robert	**UCSF, Gladstone Institute**	Towards Structure determination	Yeast protein DGA1 (Diacylglycerol acyltransferase)
Weissman, Jonathan	**UCSF, Cellular & Molecular Pharm**	Towards Structure determination: Now joined MPEC in 2009	Long chain fatty acid synthetase, 4 yeast proteins, in the FEN, SUR class. Now in crystallization trials
Detitta, George	**Hauptmann Woodward Institute, Buffalo, NY**	Our Membrane Proteins, screening in HT mode in Buffalo	Automated, high throughput microbatch under oil crystallization
Ismagilov, Rustem	**University of Chicago**	Protein supplied to develop Microcapillary crystallization	High throughput capillary crystallization
Lebon, Florence	**UC Belgium**	Protein Production Structure determination	Epilepsy target for drug discovery SV class
Giacomini, Kathleen	**Pharmacogenomics Center, UCSF**	Human Transporters to Structures	28 plasma membrane human transporters
Derisi, Joe	**UCSF, Biochemistry Dept**	Protein Production Structure determination	Chloroquin transporter and other MPs from *P.falciparum*
Rosenzweig, Amy	**Northwestern Univ.**	Protein Production Structure determination	Human metal trafficking proteins
Kossiakoff, Tony	**University of Chicago**	Manufacture of single chain, phage optimized antibodies for crystallization;	TRP channels
Rout, Michael	**The Rockefeller University**	Femtosecond structure determination	Expression and crystallization of nuclear pore complexes proteins
Kenis, Paul	**University of Illinois Urbana-Champaign**	Technology transfer and testing of his method for membrane proteins	Microfluidic crystallization
Gellman, Samuel	**University of Wisconsin**	Structure solution of facial amphiphiles	Tripod detergents, published
Dekker, Niek	**Astra Zeneca, Sweden**	Structure solution; Yeast Expression Systems	Ion Channels, GPCRs, TRP channels
Govaerts, Cedric F	**Universite Libre de Bruxelles (belgium)**	Structure solution	LMRP a multi-drug resistant transporter protein
Tischler, Nicole	**Fundacion Ciencia Para la Vida, Chile**	Structure solution	Andes virus envelope glycoprotein Gc
Yu, Edward	**University of Southern California, School of Medicine**	Protein Production Structure determination	Protein production of human Claudins
Kossiakoff, Tony	**University of Chicago**	Protocols for anti-membrane protein antibodies	TRP channels
VandenBussche, Guy	**Universite do Bruxelles Belgium**	July 2007-ongoing	Pipeline and methods transfer
Cannon, Richard	**University of Auckland NZ**	Sabbatical leave 6 mos at MPEC. Protein production purification crystallization.	Transporters in S.cerevisiae
Monk, Brian	**University of Auckland NZ**	Sabbatical leave 9 mos at MPEC. Protein production purification crystallization and structure.	Erg 11, drug complexes structures

Tampe, Robert	**Goethe University in Frankfurt**	Sabbatical leave 9 mos at MPEC. Protein production purification crystallization.	T.t ABC transporter
Fromme, Petra	**University of Arizona**	Crystals for Free Electron Laser Diffraction	
Parsons, Stanley	**UCSB**	Protein Production Structure determination	Vesicular Ach Transporter
Cassida, John	**UCB**	Expression and Structure determination	GABA activated channels
Koth, Christopher	**Genentech**	X-ray crystallography	Class B GPCR
Kurtz, Ira	**UCLA**	X-ray crystallography	AE1 (Band 3)
Immke, David	**Amgen**	X-ray crystallography	Class B GPCRs and phosphate transporter
Vandenbussche, Guy	**Université Libre de Bruxelles**	X-ray crystallography	Heavy metal transporters
Ekende, Chantal	**Université Libre de Bruxelles**	X-ray crystallography	Heavy metal transporters
Sali, Andrej	**UCSF**	In silico drug screening	Glucagon Receptor
Bonomi, Massimilano	**UCSF**	In silico drug screening	Glucagon Receptor
Zur, Arik	**UCSF**	In vivo drug screening	Glucagon Receptor
Raetz, Chris	**Duke University**	Lipid A biosynthetic enzymes	Glycosyl transferase & hydrolase
Sill, Anita	**UCSF**	Fungal pathogenesis	Fungal pathogen factor
Lee, John K.	**University of Minnesota**	Purification of human membrane protein targets	Claudins
Hays, Frank	**University of Oklahoma**	Assay and purification of membrane proteins in yeast.	Nucleoside and sulfate transporter
Garrett, Teresa	**Vassar College**	Assay of target	
Cheng, Yifan	**UCSF**	Validation of Fab-membrane protein interactions by EM	Glutamate transporter homologue and ABC transporter

Publications (2005 – present)

2011 (32 publications)

83. Kim, J., Stroud, R.M. and Craik, C.S. Rapid identification of recombinant Fabs that bind to membrane proteins. Methods Sep 20, 2011 *in press*
82. Schneider, E., Lee, M.S., Baharuddin, A., Goetz, D., Farady, C.J., Ward, M., Wang, C., Craik, C.S**.** A Reverse Binding Motif that Contributes to Specific Protease Inhibition by Antibodies. J. Molecular Biology Nov. 26, 2011 *in press*
81. Chaudhary, S.*****, Pak, J.E.*****, Gruswitz, F., Sharma, V., and Stroud, R.M. Overexpressing human integral membrane proteins in stably transformed Human Embryonic Kidney 293S cells. Nature Protocols, *in press* (2012). (*denotes equal contribution)
80. Chaudhary, S.*****, Pak, J.E.*****, Pedersen, B.P., Bang, L.J., Zhang, L.B., Ngaw, S.M.M., Green, R.G., Sharma V., and Stroud, R.M. Efficient expression screening of human membrane proteins in transiently transfected Human Embryonic Kidney 293S cells. Methods, *in press* (2012). (*denotes equal contribution)
79. Yang, D., Cwynar, V.A., Hart, D.J., Madanmohan, J., Lee, J., Lyons, J., Caffrey, M. Preparation of 1-Monoacylglycerols via the Suzuki-Miyaura Reaction: 2,3-Dihydroxypropyl (Z)-tetradec-7-enoate. *Org. Synth*. 89*: in press* (2012)
78. Wu, S.*, Avila-Sakar, A.*, Kim, J.*, Booth, D., Greenberg, C., Rossi, A., Liao, M., Alian, A., Griner, S., Juge, N., Mergel, C., Chaparro-Riggers, J., Strap, P., Tampé, R., Edwards, R.H., Stroud, R.M., Craik, C.S. and Cheng, Y. (2011). Fabs enable single particle cryoEM studies of small proteins *Structure submitted.* (*denotes equal contribution)
77. Welch, M., Villalobos, A., Gustafsson, C., Minshull , J. (2011). Designing Genes for Successful Protein Expression. *Methods Enzymology*. **498,** 43-66. (PMID: 21601673)
76. Chaudhary, S., Pak, J.E., Gruswitz, F., Sharma, V., Stroud, R.M. (2011). Overexpressing Human Membrane Proteins in Stably Transfected and Clonal Human Embryonic Kidney 293S Cells. *Nature Protocols*
75. Stroud, R.M. (2011). New tools in membrane protein determination. *F1000 Biol Rep*. 3:8. (PMID: 21655333 / PMCID: 3100781)
74. Stroud, R.M, Schertler, G.F. (2011). Membranes. *Curr Opin Struct Biol.* **21,** 495-6. (PMID: 21875531)
73. Stepanov, S., Hilgart, M., Yoder, D. W., Makarov, O., Becker, M., Sanishvili, R., Ogata, C. M., Venugopalan, N., Aragão, D., Caffrey, M., Smith, J. L., Fischetti, R. F. (2011). Fast fluorescence techniques for crystallography beamlines. J. Appl. Cryst. 44, 772-778. [doi:10.1107/S0021889811016748] (PMID: 21808424 / PMCID: PMC3140417) (Available at URL: http://journals.iucr.org/j/issues/2011/04/00/dz5227/dz5227.pdf)
72. Spence, J. C. H., Kirian, R. A., Wang, X., Weierstall, U., Schmidt, K. E., White, T., Barty, A., Chapman, H. N., Marchesini, S. & Holton, J. (2011). Phasing of coherent femtosecond X-ray diffraction from size-varying nanocrystals. *Opt. Express* 19, 2866-2873. (PMID: 21369108)
71. Smirnova, I., Kasho, V., Sugihara, J., Kaback, H.R. (2011). Opening the periplasmic cavity in lactose permease is the limiting step for sugar binding. PNAS. **108,** 15147-15151. (PMID: 21896727 / PMCID: PMC3174601)
70. Smirnova, I., Kasho, V., Kaback, H.R. (2011). LacY and the alternating access mechanism. *Biochemistry*. **45,** 9684-93 (PMID: 2199533 / PMCID: PMC3140417)
69. Shaya, D., Kreir, M., Robbins, R.A., Wong, S., Hammon, J., Bruggemann, A., and Minor, D.L. Jr. (2011). Voltage-gated sodium channel (NaV) protein dissection creates a set of functional 'pore-only' proteins. *Proc Natl Acad Sci. USA.* **108,** 12313-8. (PMCID: PMC3145705)
68. Rosenbaum, D.M., Zhang, C., Lyons, J.A., Holl, R., Aragao, D., Arlow, D.H., Rasmussen, S.G., Choi, H.J.,

DeVree, B.T., et al. (2011). Structure and function of an irreversible agonist-b2 adrenoceptor complex. *Nature.* **469,** 236-240. (PMCID: PMC3074335)

67. Rasmussen, S.G.F., DeVree, B.T., Zou, Y., Kruse, A.C., Chung, K.Y., Kobilka, T.S., Thian, F.S., Chae, P.S., Pardon, E., Calinski, D., Mathiesen, J.M., Shah, S.T.A., Lyons, J.A., Caffrey, M., Gellman, S.H., Steyaert, J., Skiniotis, G., Weis, W.I., Sunahara, R.K., Kobilka, B.K. (2011). Crystal structure of the β2 adrenergic receptor–Gs protein complex. Nature. **477,** 549-555. (PMCID: PMC3184188)
66. Pye, V. E., Aragao, D., Lyons, J. A., Caffrey, M. **(**2011). Overview of International Conference on the Crystallization of Biological Macromolecules. *Cryst. Growth Des.* In press. (URL available when published) DOI: 10.1021/cg101379p
65. Li, D., Caffrey, M. (2011). The Lipidic Cubic Phase as a Membrane Mimetic for Integral Membrane Protein Enzymes. *PNAS.* **108,** 8639-44. (PMCID: PMC3102357)
64. Li, D., Lee, J., Caffrey, M. (2011). Crystallizing Membrane Proteins in Lipidic Mesophases. A Host Lipid Screen. *Cryst. Growth Des.* **11,** 530-537. (PMCID: PMC3131202)
63. Kirian, R. A., White, T. A., Holton, J. M., Chapman, H. N., Fromme, P., Barty, A., Lomb, L., Aquila, A., Maia, F. R. N. C., Martin, A. V., Fromme, R., Wang, X., Hunter, M. S., Schmidt, K. E. & Spence, J. C. H. (2011). Structure-factor analysis of femtosecond microdiffraction patterns from protein nanocrystals. Acta Cryst. A **67,** 131-140. (PMCID: PMC3066792)
62. Kim, J., Stroud, R.M. and Craik, C.S. (2011). Rapid identification of recombinant Fabs that bind to membrane proteins. *Methods.* (PMID: 21958987)
61. Kaback, H.R., Smirnova, I., Kasho, V., Nie, Y., Zhou, Y. (2011). The alternating access transport mechanism in LacY. *J Membr Biol*. **239,** 85-93. (PMCID: PMC3030946)
60. Jiang, X., Nie, Y., Kaback, H.R. (2011). Site-directed alkylation studies with LacY provide evidence for the alternating access model of transport. *Biochemistry*, **50,** 1634-40. (PMID: 21254783 / PMCID: PMC3057939 [Available on 2012/3/15])
59. Hofer, N., Aragao, D., J.A., Lyons, Caffrey, M. (2011). Membrane Protein Crystallization in Lipidic Mesophases. Hosting lipid affects on the crystallization and structure of a transmembrane peptide. *Cryst. Growth Des.* **11,** 1182-1192. (Available at URL http://pubs.acs.org/doi/abs/10.1021/cg101384p)
58. Hoefer, N., Aragao, D., Caffrey, M. (2011). The Lipidic Cubic Phase as a Membrane Mimetic. Biophys. J. **100,** 2075.
57. Fraser, J. S., Van den Bedem, H., Samelson, A. J., Lang, P. T., Holton, J. M., Echols, N. & Alber, T. (2011). Accessing protein conformational ensembles using room-temperature X-ray crystallography. PNAS USA **108,** 16247-16252. (PMCID: PMC3182744)
56. Duriseti, S., Goetz, D.H., Hostetter, D.R., LeBeau, A.M., Wei, Y**.,** Craik, C.S. (2010). Antagonistic anti-urokinase plasminogen activator receptor (uPAR) antibodies significantly inhibit uPAR-mediated cellular signaling and migration. *J Biol Chem.* **285,** 26878-88. (PMCID: PMC2930687)
55. Chou, S., Krasileva, K. V., Holton, J. M., Steinbrenner, A. D., Alber, T. & Staskawicz, B. J. (2011). Hyaloperonospora arabidopsidis ATR1 effector is a repeat protein with distributed recognition surfaces. PNAS USA 108, 13323-13328. (PMCID: PMC3156156)
54. Chaudary, S., Pak, J., Pedersen, B., Bang, L., Zhang, L., Ngaw, S., Sharma, V., and Stroud, R.M. (2011). Efficient expression screening of human membrane proteins in transiently transfected Human Embryonic Kidney 293S cells. *Methods*. (PMID: 21925269)

53. Chaptal, V., Kwon, S., Sawaya, M.R., Guan, L., Kaback, H.R., Abramson, J. (2011). Crystal Structure of lactose permease in complex with an affinity inactivator yields new insight into sugar recognition. *Proc Natl Acad Sci. USA.* **108,** 9361-6. (PMID: 21593407 / PMCID: PMC3111295)

52. Caffrey, M. **(**2011). Crystallizing Membrane Proteins for Structure-Function Studies Using Lipidic Mesophases. *Biochem. Soc. Trans.* **39,** 725-32. (PMID: 21599641 / PMC in process)

51. Chapman, H. N., Fromme, P., Barty, A., White, T. A., Kirian, R. A., Aquila, A., Hunter, M. S., Schulz, J., DePonte, D. P., Weierstall, U., Doak, R. B., Maia, F. R. N. C., Martin, A. V., Schlichting, I., Lomb, L., Coppola, N., Shoeman, R. L., Epp, S. W., Hartmann, R., Rolles, D., Rudenko, A., Foucar, L., Kimmel, N., Weidenspointner, G., Holl, P., Liang, M., Barthelmess, M., Caleman, C., Boutet, S., Bogan, M. J., Krzywinski, J., Bostedt, C., Bajt, S., Gumprecht, L., Rudek, B., Erk, B., Schmidt, C., Homke, A., Reich, C., Pietschner, D., Struder, L., Hauser, G., Gorke, H., Ullrich, J., Herrmann, S., Schaller, G., Schopper, F., Soltau, H., Kuhnel, K.-U., Messerschmidt, M., Bozek, J. D., Hau-Riege, S. P., Frank, M., Hampton, C. Y., Sierra, R. G., Starodub, D., Williams, G. J., Hajdu, J., Timneanu, N., Seibert, M. M., Andreasson, J., Rocker, A., Jonsson, O., Svenda, M., Stern, S., Nass, K., Andritschke, R., Schroter, C.-D., Krasniqi, F., Bott, M., Schmidt, K. E., Wang, X., Grotjohann, I., Holton, J. M., Barends, T. R. M., Neutze, R., Marchesini, S., Fromme, R., Schorb, S., Rupp, D., Adolph, M., Gorkhover, T., Andersson, I., Hirsemann, H., Potdevin, G., Graafsma, H., Nilsson, B. & Spence, J. C. H. (2011). Femtosecond X-ray protein nanocrystallography. *Nature* **470**, 73-77. (PMID: 21293373)

50. Schlessinger, A., Matsson, P., Shima, J.E., Pieper, U., Yee, S.w., Kelly L, Stroud, R.M., Ferrin TTE, Giacomini KM, Sali A. (2010). Comparison of human solute carriers. *Protein Sci.* **19,** 412-28. (PMID: 20052679 / PMCID: PMC2866268)

2010 (18 publications)

49. Nie, Y., Kaback, H.R. (2010). Sugar binding induces the same global conformational change in purified LacY as in the native bacterial membrane. Proc Natl Acad Sci. 107, 9903-8. (PMCID: PMC2906848)

48. Luan, B., Carr, R., Caffrey, M., Aksimentiev, A. (2010). The effect of calcium on the conformation of cobalamin transporter BtuB. *Proteins.* **78,** 1153-1162. (PMID: 19927326 / PMCID: PMC2903617)

47. Liu, Z., Madej, M.G., Kaback, H.R. (2010). Helix dynamics in LacY: helices II and IV. J Mol Biol. **396,** 617-26. (PMID: 20043916 / PMCID: PMC3043081)

46. Lee, J.K., Stroud, R.M. (2010). Unlocking the eukaryotic membrane protein structural proteome. *Curr Opin Struct Biol*. **4,** 464-70. (PMID: 20739007/NIHMS: 214999)

45. Lang, P. T., Ng, H.L., Fraser, J. S., Corn, J. E., Echols, N., Sales, M., Holton, J. M. & Alber, T. (2010). Automated electron-density sampling reveals widespread conformational polymorphism in proteins. Protein Sci. **19,** 1420-1431. (PMC2974833)

44. Kirian, R. A., Wang, X., Weierstall, U., Schmidt, K. E., Spence, J. C. H., Hunter, M., Fromme, P., White, T., Chapman, H. N., Holton, J. (2010). Femtosecond protein nanocrystallography: data analysis methods. *Opt. Express.* **18,** 5713-5723. (PMID: 20389587 / NIHMSID 213857)

43. Holton, J. M., Frankel, K. A. (2010). The minimum crystal size needed for a complete diffraction data set. *Acta Cryst. D Biol Crystallogr***. 66,** 393-408. (PMCID: PMC2852304)

42. Hoefer, N., Aragao, D., Caffrey, M. (2010). Crystallizing Transmembrane Peptides in Lipidic Mesophases. *Biophys. J.* **99,** L23-5. (PMCID: PMC2913208)

41. Hays, F., Roe-Zurz, Z., Stroud R. M. (2010). Overexpression and Purification of Integral Membrane Proteins in Yeast. *Methods Enzymology.* **470,** 695-707. (PMID: 20946832)

40. Gruswitz, F., Chaudhary, S., Ho, J.D., Schlessinger, A., Pezeshki, B., Ho, C-M, Sali, A., Westhoff, C.M., Stroud, R.M. (2010). Function of human Rh based on structure of RhCG at 2.1Å. Proc Natl Acad Sci USA. 107, 9638-43. (PMCID: PMC2906887)
39. Gros, Y., Schuldiner S. (2010). Directed evolution reveals hidden properties of VMAT, a neurotransmitter transporter. J Biol Chem. 285, 5076-84. (PMCID: PMC2836110)
38. Garcia-Celma, J.J., Ploch, J., Smirnova, I., Kaback, H.R., Fendler, K. (2010). Delineating electrogenic reactions during lactose/H+ symport. *Biochemistry*. **49,** 6115-21. (PMCID: PMC2907097)
37. Elbaz, Y., Danieli, T., Kanner, B.I.,Schuldiner, S. (2010). Expression of Neurotransmitter Transporters for Structural and Biochemical Studies. Protein Expres Purif. 73, 152-60. (PMCID: PMC2913170)
36. Egea, P.F., Stroud, R.M. (2010). Lateral opening of a translocon upon entry of protein suggests the mechanism of insertion into membranes. *Proc Natl Acad Sci USA*. **107,** 17182-7. (PMCID: PMC2951439)
35. Duriseti, K.S., Goetz, D.H., Hostetter, D.R., Wei, Y., Craik, C.S. (2010). Antagonstic antiupar antibodies significantly inhibit uPAR-mediated cellular signaling and migration. *J Biol Chem.* **285,** 26878-88. (PMID: 20501655 / PMCID: PMC2930687)
34. Classen, S., Rodic, I., Holton, J., Hura, G. L., Hammel, M. & Tainer, J. A. (2010). Software for the high-throughput collection of SAXS data using an enhanced Blu-Ice/DCS control system. J. Sync. Rad. **17,** 774-781. (PMID: 20975223 / PMCID: PMC2964114)
33. Chae, P. S., Gotfryd, K., Pacyna, J., Miercke, L. J., Rasmussen, S. G., Robbins, R. A., Rana, R. R., Loland, C.J., Kobilka, B., Stroud, R.M., Byrne, B., Gether, U., Gellman, S. H. (2010). Tandem facial amphiphiles for membrane protein stabilization. J Am Chem Soc. **132,** 16750-2. (PMCID: PMC3050673)
32. Breslow, D.K., Collins, S.R., Bodenmiller, B., Aebersold, R., Simons, K., Shevchenko, A., Ejsing, C.S., Weissman, J.S. (2010). Orm family proteins mediate sphingolipid homeostasis. *Nature.* **463,** 1048-53. (PMCID: PMC2877384)

2009 (13 publications)

31. Welch, M., Villalobos, A., Gustafsson, C., Minshull, J. (2009). You're one in a googol: optimizing genes for protein expression. *J Royal Society*. **4,** S467-76. (PMID:19324676 / PMCID: PMC2843954)
30. Welch, M., Govindarajan S., Ness, J.E., Villalobos A., Gurney A., Jeremy Minshull, J., Gustafsson C. (2009). Design Parameters to Control Synthetic Gene Expression in Escherichia coli. PLoS ONE. **4,** e7002 (PMID: 19759823)
29. Zhou, Y., Nie, Y., Kaback, H.R. (2009). Residues Gating the Periplasmic Pathway of LacY. J Mol Biol. 394, 219-25. (PMID: 19781551 / PMCID: PMC2784193)
28. Smirnova, I., Kasho, V., Sugihara, J., Kaback, H.R. (2009). Probing of the rates of alternating access in LacY with Trp fluorescence. *Proc Natl Acad Sci USA* **106,** 21561-6. (PMID: 19959662 / PMCID: PMC2799877)
27. Smirnova, I., Kasho, V., Sugihara, J., Choe, J.-Y., Kaback, H.R. (2009). Residues in the H+ translocation site define the pKa for sugar binding to LacY. Biochemistry. 48, 8852-8860. (PMID: 19689129 / PMCID: PMC2769999)
26. Newby, Z.E.R., O'Connell III, J.D., Gruswitz, F., Hays, F.A., Harries, W.C., Harwood, I.M., Ho, J.D., Lee, J.K., Miercke, L.J.W., Savage, D.F., Stroud, R.M. (2009). A general protocol for the crystallization of membrane proteins for X-Ray structural investigation. *Nature Protocols.* **4,** 619-37. (PMID: 19360018 / NIHMS: 151516)

25. Li, M., Hays, F. A., Roe-Zurz, Z., Vuong, L., Kelly, L., Ho, C. M., Robbins, R. M., Pieper, U., O'Connell, J. D., 3rd, Miercke, L. J., Giacomini, K.M., Sali, A., Stroud, R.M. (2009). Selecting optimum eukaryotic integral membrane proteins for structure determination by rapid expression and solubilization screening. *J Mol Biol.* **385,** 820-30. (PMCID: PMC2659619 / NIHMS93258)
24. Ho, J.D., Yeh, R., Sandstrom, A., Chorny, I., Harries, W.E.C., Robbins, R.A., Miercke, L. J.W., Stroud, R.M. (2009). Crystal Structure of Human Aquaporin 4 at 1.8Å and its mechanism of conductance. *PNAS.* **106,** 7437-42. (PMID: 19383790 / PMCID: PMC2678640)
23. Hays, F.A., Roe-Zurz, Z., Li, M., Kelly, L., Gruswitz, F., Sali, A., Stroud, R.M. (2009). Ratiocinative Screen of Eukaryotic Integral Membrane Protein Expression and Solubilization for Structure Determination. J Struct Func Genomics. 10, 9-16. (PMID: 19031011 / PMCID: PMC2756966)
22. Hammon, J., Palanivelu, D.V., Chen, J., Patel, C., Minor, D.L., Jr., (2009). A green fluorescent protein screen for identification of well-expressed membrane proteins from a cohort of extremophilic organisms. *Protein Sci.* **18,** 121-33. (PMID: 19177357 / PMCID: PMC2708023)
21. Guan, L., Kaback, H.R. (2009). Properties of a LacY efflux mutant. *Biochemistry.* **48,** 9250-9255. (PMCID: PMC2754601)
20. Garcia-Celma, J.-J., Smirnova, I.N., Kaback, H.R., Fendler, K. (2009). Electrophysiological characterization of LacY. *Proc Natl Acad Sci USA.* **106,** 7373-8. (PMID: 19383792 / PMC2671326)
19. Bassik, M.C., Lebbink, R.J., Churchman, L.S., Ingolia, N.T., Patena, W., LeProust, E.M., Schuldiner, M., Weissman, J.S., McManus, M.T. (2009). Rapid creation and quantitative monitoring of high coverage shRNA libraries. Nature Methods. **6,** 443-5. (PMCID: PMC2783737)

2008 (8 publications)

18. Zhou, Y., Guan, L., Freites, J.A., Kaback, H.R. (2008). Opening and closing of the periplasmic gate in lactose permease. *Proc Natl Acad Sci U S A*. **105,** 3774-8. (PMID: 18319336 / PMCID: PMC2268789).
17. Smirnova, I., Kasho, V., Kaback, H. R. (2008). Protonation and sugar binding to LacY. *PNAS.* **105,** 8896-901. (PMID: 18567672 / PMCID: PMC3021437)
16. Nie, Y., Sabetfard, F.E., Kaback, H.R. (2008). The Cys154→Gly mutation in LacY causes constitutive opening of the hydrophilic periplasmic pathway. *J Mol Biol*. **379,** 695-703. (PMID: 18485365 / PMCID: PMC2769995)
15. Newby, Z., O'Connell III, J., Robles-Colmenares, Y., Khademi, S., Miercke, L.J.W., Stroud, R.M. (2008). Crystal structure of the aquaglyceroporin PfAQP form the malarial parasite P.falciparum. Nature Structural Biology. 15, 619-25. (PMID: 18500352 / PMCID: PMC2568999).
14. Li, M., Hays, F.A., Roe-Zurz, Z., Vuong, L., Kelly, L., Robbins, R., Ho, C., Pieper, U., O'Connell III, J., Miercke, L.J.W., Giacomini, K.M., Sali, A., Stroud, R.M. (2008). Eukaryotic Integral Membrane Protein Production For Structural Genomics. *J. Mol Biol.* **385,** 820-30.
13. Lee, J.K., Belogrudov, G.I., Stroud, R.M. (2008). Crystal structure of bovine mitochondrial factor B at 0.96-Å resolution. PNAS **105,** 13381-13384. (PMID: 18768789 /PMCID: PMC2528870)
12. Kelly, L., Pieper, U., Eswar, N., Hays, F., Li, M., Roe-Zurz. Z., Kroetz, D., Giacomini, K., Stroud, R.M., Sali, A. (2008). A taxonomic profile of the membrane protein universe. *Submitted to: Genome Biology*
11. Adam, Y., Edwards, R.H., Schuldiner, S. (2008). Expression and function of the rat vesicular monoamine transporter 2. *Am J Physiol Cell Physiol*. **294,** C1004-11. (PMID: 18287335).

2007 (9 publications)

10. Stroud, R.M., Nicoll, R.A., Hays, F.A. (2007). TARP auxiliary subunits switch AMPA receptor antagonists into partial agonists. *Science* **318**, 815-7 (PMID: 17975069)

9. Smirnova, I., Kasho, V., Kaback, H.R. (2007). Protonation and sugar binding to LacY. *Proc Natl Acad Sci USA.* **105,** 8896-8901. (PMID: 18567672 / PMCID: PMC3021437)

8. Smirnova, I., Kasho, V., Choe, J.Y., Altenbach, C., Hubbell, W.L., Kaback, H.R. (2007). Sugar binding induces an outward facing conformation of LacY. *Proc Natl Acad Sci U S A.* **104,** 16504-9. (PMID: 17925435 / PMCID: PMC2034228).

7. Schuldiner, S. (2007). When biochemistry meets structural biology: the cautionary tale of EmrE. *TIBS.* **32,** 252-8. (PMID: 17452106)

6. Savage, D. F., Anderson, C.L., Robles-Colmenares, Y., Newby, Z., Stroud, R.M. (2007). Cell-free complements *in vivo* expression of the *E. coli* membrane proteome. *Protein Science.* **16,** 966-76. (PMID: 17456747 / PMCID: PMC2206641)

5. Nie, Y., Ermolova, N., Kaback, H.R. (2007). Site-directed alkylation of LacY: effect of the proton electrochemical gradient. *J Mol Biol*. **374,** 356-64. (PMID: 17920075 / PMCID: PMC2224895).

4. Minor, D.L., Jr., (2007). The neurobiologist's guide to structural biology: A Primer on why macromolecular structure matters and how to evaluate macromolecular structural data. *Neuron* **54,** 511-533. (PMID: 17521566 / PMCID: PMC3011226)

3. Menuz, K., Stroud, R.M., Nicoll, R.A., Hays, F.A. (2007). TARP auxiliary subunits switch AMPA receptor antagonists into partial agonists. *Science*. **318**, 815-7. (PMID:17975069)

2. Guan, L., Mirza, O., Verner, G., Iwata, S., Kaback, H.R. (2007). Structural determination of wild-type lactose permease. *Proc Natl Acad Sci U S A*. **104,** 15294-8. (PMID: 17881559 / PMCID: PMC2000551).

2005 (1 publication)

1. Vardy, E., Steiner-Mordoch, S., Schuldiner, S. (2005). Characterization of bacterial drug antiporters homologous to mammalian neurotransmitter transporters. *J Bacteriol*, **187**, 7518-7525. (PMID: 16237035 / PMCID: PMC1272986)