WORLD MOLECULAR ENGINEERING NETWORK

CABO 2014

UCSF University of California, San Francisco
School of Pharmacy

The Scripps Research Institute®

Our History

The WMEN conference has been held for the past 24 years during the month of May in Los Cabos, Mexico. The meetings originated from a grant from the Rockefeller Foundation supporting research collaborations between scientists at UCSF, MRC Cambridge and The Scripps Research Institute, now called TSRI. Drs. Daniel Santi and Ian Wilson started the meetings and created the unique scientific ambience. The meeting style has remained unchanged but, twelve years ago, the venue moved from Cabo San Lucas to an all-inclusive resort in San Jose del Cabo. The 2014 meeting was held at the Hyatt Ziva (formerly Barcelo Los Cabos Palace), an attractive resort with excellent conference facilities and very attentive staff. Each year, the meeting attracts approximately 60 academic, industrial, and biotech participants, as well as venture capitalists and patent attorneys. The majority of the attendees are professors, laboratory heads or research directors, but we also encourage participation of the next generation of scientists through selecting a number of the top graduate students and postdoctoral fellows from UCSF, TSRI, UC Berkeley and Stanford. The spirit of scientific research is enhanced and refreshed in this stunning setting with a stellar list of participants.

Cabo XXIV Program
World Molecular Engineering Network Twenty-Fourth Annual Meeting on Structural Biology

4-7 May 2014, San Jose del Cabo, Baja, Mexico

Sunday Evening, May 4

16:45	Ian Wilson and Andrej Sali	**Introduction and Welcome**
17:00	**Herb Boyer**	**Keynote Lecture-** **Personal recollections of early biotech and what's next**

17:45-17:50 ***Self-Introductions***

Joseph Guglielmo UCSF

17:50-20:30 **Short Presentations (5+1 min.) by TSRI, UCSF and Stanford Graduate Students, Postdocs and Researchers (Chair: Dennis Wolan)**

Devin Sok	TSRI	A heterologous native-like recombinant HIV envelope trimer selects diverse antibodies specific for the trimer apex glycan-dependent epitope
Peter Lee	TSRI	Recognition of functionally conserved neutralizing epitopes on influenza virus hemagglutinin
Melody Campbell	TSRI	Structural studies of nitric oxide synthase
Rebecca Miller	TSRI	The forgotten opioid receptor: structural characterization of the nociception receptor
David Marciano	TSRI	Structure-guided design of PPARAG inverse agonist: Less fat & more bone
Jessica Bruhn	TSRI	Building a virus: Structural studies of Ebola matrix protein at the membrane
Sandip Chatterjee	TSRI	An informatics method for metaproteomics
Daniel Murin	TSRI	Bivalent binding to a viral glycoprotein by an Ebola monoclonal antibody
JH Lee	TSRI	Describing the novel gp120-gp41 interface epitope of the HIV-1

	John Chen	TSRI	ATF6 activation increases ER quality control and reduces secretion of destabilized variants of an amyloidogenic protein
	Chris Lee	TSRI	smFRET study of AAA+ ATPasep97
	Peter Thuy Boun	TSRI	A survey of sialic acid processing proteins associated with the human gut microbiota
	Matthias Pauthner	TSRI	Molecular characterization of the HIV-1 N332 supersite of vulnerability
	Ana Wang	TSRI	Chemical-based metaproteomics of the human distal gut microbiota
	Break		
	Jessica Thomaston	UCSF	High-resolution crystal structures of the influenza A M2 proton channel: insights into water networks
	Patrick Weinkam	IO Data Center	Allostery and data science
	Samantha Liang	UCSF	DNA-guided assembly of Epidermal Growth Factor Receptor complexes on cells
	Sue Mok	UCSF	Cracking the chaperone code for inhibition of tau aggregation
	Christopher Kimberlin	UCSF	SARAF luminal domain, illuminated
	Daniel Keedy	UCSF	Discovering coupled conformational heterogeneity in proteins by multi-temperature crystallography and computation
	Matthew Child	Stanford	TgDJ-1 integrates multiple signals to regulate vesicle exocytosis
	Nicolas Strauli	UCSF	Coevolution between HIV and the antibody repertoire
	Shujun Yuan	UCSF	Identifying membrane protein interactors
20:30–22:00	**Reception**		**Poolside**

Monday Morning, May 5

Structural and Computational Biology (Chair: Robert Stroud)

09:00	Andrej Sali	UCSF	Expanding the druggable proteome by characterization and prediction of cryptic binding sites
09:20	John Tainer	TSRI	Flexible complexes defined by combined X-ray methods
09:40	James Fraser	UCSF	Mining the dark matter of X-ray

			crystallography
10:00	**Break**		
10:20	Ian Wilson	TSRI	HIV envelope trimer
10:40	Andrew Ward	TSRI	Structural studies of viral envelope glycoproteins
11:00	Jack Johnson	TSRI	CryoEM analysis of a 75mD virus at 4Å resolution
11:20	Erica Ollmann Saphire	TSRI	The molecular toolkit of a viral hemorrhagic fever

Monday Afternoon, May 5

Virology and Vaccinology (Chair: Erica Ollmann Saphire)

16:30	Jiang Zhu	TSRI	Technical advances in rational vaccine design
16:50	Jim Paulson	TSRI	Influenza virus receptor specificity

Membrane Proteins (Chair: Andrew Ward)

17:10	Robert Stroud	UCSF	Redefining transmembrane transport-the textbooks are all wrong-(today)!
17:30	**Break**		
17:50	Dan Minor	UCSF	Bacterial sodium channels: from Mono Lake to your heart
18:10	Bill Degrado	UCSF	Analysis and design of proton transporters
18:30	David Millar	TSRI	Conformational dynamics of the beta-2 adrenergic receptor

Tuesday Morning , May 6

SPONSORS (Chair: Dan Santi)

09:00	Brief Informal Introductions:		
	David Meininger	Merck	
	Gopalan (Raghu) Raguhunathan	Merck	
	Kurt Deshayes	Genentech	
09:20	Kathleen Aertgeerts	Dart NeuroScience	Introduction to Dart NeuroScience
9:35	Dan Santi	UCSF/Prolynx	A chemical approach to half-life extension
9:55	Hans Purkey	Genentech	Structure-based design and optimization of in vivo inhibitors of human Lactate Dehydrogenase A (LDHA) for the treatment of cancer
10:15	Deborah	Nektar	Expanding the possibilities in cancer

	Charych		immunotherapy: Engineering cytokine receptor selectivity through polymer modification
10:40	**Break**		
11:00	Dana Ault-Riche	Reflexion	D-Protein therapeutics
11:20	Jody Berry	BD	V cells: a novel cell lineage of the immune system
11:40	Badry Bursulaya	GNF	Protein-protein interfaces: hot-spots and their utility

Tuesday Afternoon, May 6

Nucleic Acids and Nucleic Acid Binding Proteins and Evolution (Chair: David Millar)

16:30	Ryan Hernandez	UCSF	Evolutionary forces shaping patterns of human genetic variation
16:50	Jamie Williamson	TSRI	Ribonucleoprotein complexes in T-cell activation
17:10	Floyd Romesberg	TSRI	Expansion of the genetic alphabet
17:30	**Break**		

Chemical Biology (Chair : Jason Gestwicki)

17:50	Dennis Wolan	TSRI	Specific caspase probes with unnatural amino acids
18:10	Matt Bogyo	Stanford	A unique cysteine protease domain of a primary virulence factor as a therapeutic target for *Clostridium difficile* infections
18:20	Jack Kirsch	UCB	Why do nudix hydrolases shred the cellular energy currency?
18:30	Zev Gartner	UCSF	The physical rules guiding the self-organization of the human mammary gland

Wednesday Morning, May 7

Assemblies, Drug Discovery and Neurobiology (Chair: James Fraser)

08:50	Jason Gestwicki	UCSF	Chemical inhibitors of multi-chaperone complexes
9:10	Larry Gerace	TSRI	Endoplasmic reticulum proteins that regulate cellular lipid homeostasis
9:30	Joel Gottesfeld	TSRI	Therapeutics for neurogenerative disease
09:50	**Break**		
10:20	Gabe Lander	TSRI	Structural studies of neuronal cargo transport
10:40	Phil Dawson	TSRI	Structure-guided optimization of peptide-based ephrin receptor

			antagonists for neuroprotection
11:00	Michelle Arkin	UCSF	Small-molecule modulators of protein homeostasis in cancer and neurodegeneration
11:30	Ian Wilson and Andrej Sali		**Closing Remarks**

In order to protect individual rights and promote discussion, it is a requirement of the Scripps-UCSF Cabo WMEN Annual Meeting on Structural Biology Conference that no information presented is to be used or disclosed without the specific approval of the disclosing party. Each attendee of the Conference agrees that any information presented, whether in a formal talk or discussion, is a private communication from the individual making the contribution and is presented with the restriction that such information is not for public use. Each member of a Conference acknowledges and agrees to these restrictions as a condition of attending the Conference.

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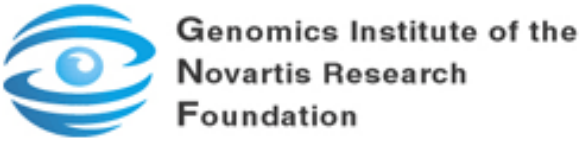

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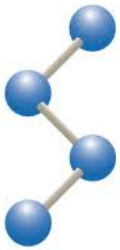

The Scripps Research Institute

University of California
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The following pages are summaries of presentations and comments on the meeting and venue.

WMEN Conference
San Jose del Cabo
Hyatt Ziva Hotel

For more information, contact:

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Ian Wilson
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JoAnne Williams
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Name: Michelle Arkin
Affiliation: UCSF
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Overview: described multiple approaches toward developing small-molecule inhibitors of caspase-6 to investigate its role in neurodegeneration.

Presentation: Caspases are cysteine proteases involved in apoptotic cell death and non-apoptotic cellular processes. Caspase-6 in particular has been implicated in neuronal development and in proteolytic processing of neuronal proteins. For example, caspase-6 cleaves the microtubule-associated protein tau at its C-terminus, which may facilitate tau's precipitation and eventual formation of neurotoxic tangles. Small-molecule inhibitors that selectively bind to caspase-6 have been hard to come by, but would be very useful for exploring the role of tau cleavage in tangle formation. We and our colleagues at Genentech have developed chemical probes that bind to caspase-6 by three different mechanisms. Of these series, the best probe of neurobiology is a set of thiol-reactive compounds discovered by Tethering. Compounds bind to a non-conserved cysteine residue in the enzyme's substrate-binding groove and are therefore selective for caspase-6 over other caspases. Preliminary characterization of the compounds' in vitro- and cell-based activity are promising. Future work will further develop these cysteine-reactive compounds to explore the role of caspase-6 in neurodegeneration.

Impressions: This was my first Cabo meeting, and I understand why it is such a beloved conference. It was fantastic to spend time with my colleagues at Scripps, Berkeley, and Stanford – to see old friends and to meet people I've admired for years but never met. The scientific discussion during the sessions was matched only by the scientific discussions over meals. I was particularly impressed by the way the presentations interwove – multiple biological problems, varied approaches, but a common perspective that united us. I'm already angling for another invitation….

Name: Jody Berry
Affiliation: BD Biosciences
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Presentation: I am engaged in Immunological research in Antibody Technology and Antibody product development. Especially interested in novel scaffolds, repertoire evolution and exploitation of the immune system to improve the lives of humans.

Presentation: We have identified a cell population termed V cells which have phenotypic characteristics of myeloid and lymphocyte cells. V cells have a unique cell surface marker expression profile, a polymorphonuclear morphology and express surface immunoglobulin. This uncharacterized immunoglobulin bearing-cell lacks surface expression of B cell lineage specific markers such as B220, CD19, as well as T cell, NK, NKT, basophil and stem cell specific markers as determined by flow analysis. V cells are characterized as positive for CD24, CD43, CD45, CD49b, CD48, CD79b, IgG and IgE. These cells are also present in multiple strains of mice and also in humans. Remarkably, following immunization with protein antigens, antigen specific V cells are induced very rapidly. Antigen specific V cells have been generated following immunization of at least 6 different protein antigens and appeared as early as 7 to 14 days following a single immunization. They are observed in the spleen, bone marrow, and blood of immunized mice but are not detected in other tissues such as the thymus, lymph nodes and peritoneal exudate cells. Molecular analysis indicates the presence of shared VH genes between the spleen and bone marrow suggests migration of the V cells between the two compartments. RNA transcriptome analysis is underway on the single cell sorted V cells from immunized animals for comparison to the other cellular lineages. While we have observed the presence or absence of these cells in various disease states, in both mice and humans, we can only speculate that V cells are involved in regulating immunity and autoimmunity and their presence certain tissues could be used as a diagnostic and /or prognostic marker of disease. V cells potentially provide a target population for immunological intervention solution in autoimmunity, allergy, and chronic inflammation. The role of this novel cell population in immunity is currently under investigation.

Impressions: The meeting was excellent and enabled me to rekindle old ties with colleague and make brand new connections with experts in Molecular engineering. Truly and engaging venue and I would recommend it to anyone in my field who is looking for talent, new collaboration or simply to see the cutting edge.

Name: Matthew Bogyo
Affiliation: Pathology, Stanford University
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Stanford, CA 94305-5324
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Phone: 650-725-4132

Presentation: A unique cysteine protease domain of a primary virulence factor as a therapeutic target for *Clostridium difficile* infections

Impressions: This was another great meeting. I found the talks to be just the right length and it was great to have the short talks from the postdoc first. That helped to induce interactions among the postdocs and PIs. I think the location was great and the hotel was very nice. The meeting was very well organized by Hilary. Overall, a great meeting for me which has helped to establish a number of interesting collaborations.

Name: Jessica Bruhn
Supervisor: Erica Ollmann Saphire
Affiliation: TSRI, Department of Immunology
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Overview: Structural studies of viral replication and assembly: I use a variety of techniques (X-ray crystallography, electron microscopy, biochemistry and virology) to study the molecular mechanisms behind the highly lethal Nipah and Ebola viruses

Presentation: The matrix protein from Ebola virus undergoes a highly regulated transition from a dimer in the cytosol of a cell to a membrane bound oligomer that is capable of budding virions and

virus like particles. My work centers around characterizing the membrane binding properties of the Ebola matrix protein and visualizing the oligomerization that occurs at the membrane. This is accomplished through a combination of binding studies (ITC and Biacore), X-ray crystallography, 2D electron crystallography and ex vivo budding assays.

Impressions: The meeting in Cabo was an excellent opportunity to have stimulating scientific discussions and hear about some truly exciting and well done research. This was also an excellent networking opportunity for me, a graduate student. I was able to meet with a variety of people from other institutes and companies, in addition to learning about the laboratories at my own institute. Thank you for this wonderful opportunity.

Name: Melody Campbell
Supervisor: Bridget Carragher
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Presentation: Nitric oxide synthases (NOS) are homodimeric multidomain enzymes responsible for producing nitric oxide (NO). In mammals, NO acts as both an intercellular messenger in a variety of signaling reactions as well as a cytotoxin in the innate immune response. Mammals possess three NOS isoforms, iNOS, eNOS, and nNOS, that are composed of an N-terminal oxidase domain and a C-terminal reductase domain. Calmodulin activates NO synthesis by binding to the helical region connecting these two domains. Although crystal structures of isolated domains have been reported, no structure is available for full-length NOS. We used high-throughput single-particle electron microscopy to obtain the structures and higher-order domain organization of all three NOS holoenzymes. The structures of iNOS, eNOS, and nNOS with and without calmodulin bound are similar consisting of a dimerized oxidase domain flanked by two separated reductase domains. NOS isoforms adopt many conformations enabled by three flexible linkers. These conformations represent snapshots of the continuous electron transfer pathway from the reductase

domain to the oxidase domain, which reveal that only a single reductase domain participates in electron transfer at a time and that calmodulin activates NOS by constraining rotational motions and by directly binding to the oxidase domain. Direct visualization of these large conformational changes induced during electron transfer provides significant insight into the molecular underpinnings governing NO formation.

Impressions: I thought the meeting was fantastic. Almost all the talks were absolutely captivating and it was really great to get to speak to the presenters after the talk in a more informal setting. The meeting room was pleasant and it was great to always have coffee and the rooms were amazing.

Name: Deborah Charych
Affiliation: Nektar Therapeutics
Mailing address: 455 Mission Bay Blvd, South
San Francisco CA, 94158
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Phone: 415 482 5558

Overview: Presented an overview of engineering a cytokine using polymer chemistry to alter its receptor selectivity and its tumor exposure. Tumor immunology, tumor PK and efficacy in vivo were presented.

Presentation: Immunotherapy offers the potential for durable responses in a growing list of cancer indications. One approach towards stimulating the immune system is to target the heterotrimeric interleukin2 receptor, IL2R. Binding of ligand to the β subunit leads to expansion of tumor killing memory effector T cells, whereas engagement of the α subunit expands undesirable regulatory T cells, promoting immune suppression in the tumor. NKTR-214 uses polymer technology to engineer IL-2 so that it has reduced affinity for the IL2Rα subunit, diminishing the expansion of regulatory T cells in the tumor, while maintaining affinity for the β subunit expands memory effector T cells. In addition, polymer conjugation increases exposure of the tumor to drug by 500-fold compared to unconjugated IL-2. This leads to significantly improved efficacy as a single agent and in combination with other agents, in aggressive mouse tumor models.

Impressions: This was my first time attending and I was very impressed with the quality of the science and the presentations. The small size and informal setting allowed for many interactions with senior people, as well as postdocs and graduate students. It was nice to also mentor the junior scientists on what life is like in Biotech and they had many questions for the 'industry' speakers. I particularly enjoyed the talk by Herb Boyer the keynote speaker. I made many new connections with both the academic and the industry participants.

Name: Sandip Chatterjee
Supervisor: Dennis Wolan
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Presentation: My research focuses on the development and optimization of computational methods to search and analyze LC-MS/MS data for metaproteomics of the human commensal gut microbiota. Using a fast and efficient peptide database in conjunction with new spectral scoring software, we are able to begin to characterize the amazingly complex commensal microbiota at the proteome level.

Impressions: The meeting was very well organized and a good size to facilitate interactions between students, PIs, and sponsor scientists. Research talks were generally excellent and sufficiently diverse to keep discussion interesting, and the Cabo location was beautiful and a good choice.

Name: Matthew Child
Supervisor: Matthew Bogyo
Affiliation: Pathology
Mailing address: Bogyo Lab, Edwards Building, Room R341, 300 Pasteur Drive, Stanford CA94305
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Phone: 650-725-4573

Presentation: TgDJ-1 integrates multiple signals to regulate vesicle exocytosis

Impressions: Fantastic - great talks, and a great opportunity to meet and network with PIs, post-docs and grad students in a relaxed and collaborative environment.

Name: John Chen
Supervisor: Luke Wiseman
Affiliation: MEM/TSRI
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Phone: 714-443-1910

Presentation: ATF6 activation increases ER quality control and reduces secretion of destabilized variants of an amyloidogenic protein.

Impressions: Conference overall was very organized and I enjoyed the increase in fields presented at this meeting.

Name: Bill DeGrado
Affiliation: UCSF
Mailing address: UCSF
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Overview: Great meeting. I like the spread of talks and the location. My only suggestion would be to consider a format where students can give somewhat longer talks.

Presentation: great

Impressions: see overview

Name: James Fraser
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Overview: Proteins often move between different conformations. X-ray crystallography is traditionally used to define a single, static

macromolecular structure. However, these structures are based on fitting atomic models into electron density maps that portray an ensemble average of the billions and billions of molecules in the crystal. By mining these maps using the electron density sampling program Ringer (developed in the Alber Lab at UC Berkeley), we have shown that ensemble features can reliably detected and that noise levels are much lower than commonly thought. Features at low-levels of electron density can reveal ligand, protein and solvent flexibility that can be exploited in inhibitor optimization. We are testing how ensemble (e.g. phenix.ensemble_refinement developed by the Phenix consortium at LBL) and multi-conformer (e.g. qFit developed by our collaborator Henry van den Bedem at SSRL/SLAC) modeling methods can improve both the statistical fit to experimental data and the ability to generate novel biological hypotheses. The next major challenge is to determine the extent to which distant parts of the protein are conformationally coupled. NMR spectroscopy is well suited to determining the existence of multiple states and the rates of transitions between them. However, the atomic details of these transitions remain difficult to ascertain and interrogate. To address these challenges, we have found that the conformational distributions of proteins in the crystal are remarkably sensitive to temperature perturbations. Finally, although these biophysical techniques generate beautiful images of electron density maps and NMR spectra, we use a variety of assays to test the importance of alternative conformations and protein motions. We study the role of protein motions in enzyme catalysis using directed evolution screens and selections.

Presentation: I covered a recent collaboration with the Tawfik lab that examines the structural basis for epistasis, i.e., non-additive interactions between mutations, in antibiotic resistance. We examined negative-epistasis between two mutations in TEM-1 beta-lactamase that underline two separate adaptive trajectories. Both mutations introduce conformational flexibility. However, whereas G238S samples between discrete conformations, R164S causes local disorder. Their combination induces structural anarchy and excessive conformational freedom that perturbs the enzyme's catalytic pre-organization. Indeed, R164 is a hub in a highly networked active-site residue, whereby mutations lead to an evolutionary cul-de-sac. G238 is weakly connected, permissive to changes, and thereby leads to the adaptive peak. We thus describe a link between epistasis, protein structure, dynamism and evolvability.

Impressions: This is a great meeting! The mix of industry and academic talks is wonderful. It is always fun to catch up with colleagues down the hall at UCSF beside the beach or to renew friendships that formed at this meeting with Scripps/Industrial colleagues.

Name: Zev Gartner
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Overview: I described a general mechanisms for tissue self-organization among multiple cell types that is robust to dynamic and changing cellular behaviors, as well as cellular heterogeneity. The mechanism has striking similarities to general aspects of protein folding, namely the reliance on the properties of the surrounding medium in determining the basic topology of the final structure.

Presentation: Tissues contain dynamic populations of cells that are heterogeneous in time and space. However, it is unclear how heterogeneous populations of cells can coordinate their self-organization into spatially ordered tissues. The human mammary gland is a prototypical heterogeneous and dynamic tissue. Its ducts and acini comprise two concentrically arranged cell types that retain their relative spatial positions despite enormous plasticity associated with estrous cycles, pregnancy, and the onset of malignant disease. To investigate the consequences of cellular heterogeneity and plasticity on cell positioning in the mammary gland, we reconstituted its self-organization from aggregates of primary human cells *in vitro*. We reveal that self-organization is dominated by a self-generated adhesive interaction between just one cell type and the aggregate-ECM boundary, rather than through a hierarchy of homo and heterotypic cell-cell interactions. Using mathematical modeling and cell-type specific knock-down of key adhesion molecules, we show that this strategy of self-organization can guide the positioning of either cell populations, even upon massive perturbation to cell-cell cohesion. We also find that this mechanism of self-organization is conserved in related tissues such as the human prostate. Therefore, our results reveal

a flexible strategy for forming and maintaining tissue structure among heterogeneous and dynamic populations of cells.

Impressions: I love this meeting! The science is first rate across the board, covering diverse topics from the best institutions in California. The location is lots of fun, providing tons of opportunity to meet new colleagues and catch up with old friends.

Name: Larry Gerace
Affiliation: TSRI, CMB
Mailing address: 10550 N Torrey Pines Road, IMM-10, La Jolla, CA 92037
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Phone: 858-784-8514

Overview: We are studying regulation of signaling and metabolism by the endoplasmic reticulum and nuclear envelope.

Presentation: We found that erlins, which are ER-resident integral membrane proteins, restrict activation of cholesterol and lipid biosynthesis by restraining trafficking of sterol regulatory element binding proteins (SREBPs) to the Golgi. Erlins themselves bind cholesterol as well as the ER machinery previously found to control activation of SREBPs. We present a model wherein erlins promote a cholesterol-rich microenvironment for SREBP regulation.

Impressions: This was an outstanding venue for scientific exchange and generation of new ideas. A wide variety of different biological questions and methodologies and were addressed, and ample time was presented, both formally and informally, for discussion of the talks.

Name: Jason Gestwicki
Affiliation: Pharmaceutical Chemistry / UCSF
Mailing address: 675 Nelson Rising Lane
San Francisco, CA 94158
Email address: jason.gestwicki@ucsf.edu
Phone: 512-7121

Overview: Outstanding meeting. Ample time to interact with colleagues, while also hearing about exciting new developments. The industrial representatives were a particularly important part of the discussion.

Presentation: Good format. I liked starting with the short postdoc talks on the first day.

Impressions: Fantastic meeting. Broad enough focus that the topics were fresh throughout. There was also a good mix of updates on established projects and new, speculative works. Setting was excellent.

Name: Daniel Keedy
Supervisor: James Fraser
Affiliation: BTS/UCSF
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Presentation: I presented a new method for identifying secondary, alternative ligand conformations. The method relies on modifying an electron density map by lowering the occupancy of an existing, primary ligand conformation to less than 100%, then using real-space simulated annealing in PHENIX to minimize into features of the resulting difference map that may represent alternative ligand conformations. Multiple ligand conformations identified by approaches like this may be relevant for rerouting allosteric signaling pathways, entropic effects of binding, etc.

Impressions: I've been to a handful of conferences ranging from small and specialized to large and diverse, and this was definitely among my favorites. The fact that there are few enough attendees that everyone speaks, if only for 5 minutes, is a huge pro in my opinion. That combines remarkably well with the pleasant setting and informal atmosphere: people can chat after sessions about each others' projects and have a better chance of brainstorming interesting productive new ideas / future directions. For example, based on conversations with other attendees, I came away with several solid ideas for my research, one of which I've already pursued and the other of which is very high on my to-do list. Overall, top marks!

Name: Christopher Kimberlin
Supervisor: Daniel Minor
Affiliation: CVRI / UCSF
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Presentation: SARAF luminal domain, illuminated. Calcium ions play a critical role in signaling and cellular processes involving a diverse range of activities and the channels that facilitate calcium ion entry are under tight regulation. My research centers on SARAF, a novel regulator of store operated calcium entry (SOCE) that interacts with SOCE components Orai and STIM1 and prevents overfilling of ER calcium stores. SARAF resides in the ER membrane with a C-terminal, cytoplasmic effector domain that interacts with STIM1 to inhibit SOCE currents. The N-terminal luminal regulates SARAF activity in response to changes in the ER environment, though the mechanism remains unknown. Our structural, biochemical and functional studies show that this luminal domain can form domain-swapped dimers and that these dimers are critical to its regulatory function.

Impressions: As usual, this meeting was excellent. I was thoroughly impressed with the caliber of science and in general, the talks were quite good. There was a nice blend of academic and industry perspectives. I was also pleased to see people sharing new work and not just stories that have already been published. There was plenty of time to catch up with old colleagues as well make new acquaintances. The last two times I attended were at the previous hotel and I have to say the new venue is a big improvement both in terms of food and facilities.

Name: Jack Kirsch
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Phone: 510-642-6368

Overview: I retired officially in 2006, but still participate in research via collaborations. My present projects are directed to

improving the accuracy of genomic annotation of protein function, and of predicting the effect of any given mutation on enzyme kinetics.

Presentation: I presented our findings that the experimental evidence for hydrolytic activity of Nudix enzymes against canonical nucleotide triphosphates is largely meaningless, and that the true functions of these enzymes is yet to be discovered.

Impressions: I only go to one-two meetings per year. This has been the most valuable always. I think that this is about my 15th CABO meeting, and I have missed only 2-3 presentations in all those years. Nearly everyone has new and exciting information to communicate, and I value the interactions with colleagues, whom I see only too rarely. It is likely that a collaboration will emerge with Prof. Fraser, who became interested in Nudix enzymes from my talk.

Name: Gabe Lander
Affiliation: TSRI, ISCB
Mailing address: 10550 N Torrey Pines Road, TRY-21, La Jolla, CA 92037
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Phone: 858-784-8793

Overview: My group utilizes cryo-electron microscopy (cryoEM) to characterize the structures of molecular machines in order to decipher their functional relationships with the cellular environment. By determining the molecular architecture of these protein complexes, we gain a more comprehensive understanding of the mechanisms that underlie important biological processes. In recent years, dramatic improvements in instrumentation and computational algorithms have made it possible to resolve molecules to near-atomic resolution using this powerful technique. My group uses the latest cutting-edge cryoEM instrumentation and processing algorithms to determine the molecular bases for a variety of neurodevelopmental and neurodegenerative diseases, focusing primarily on the roles of the proteasome and microtubule motors in maintaining mitochondrial homeostasis. These studies involve the development of novel strategies for specimen preparation,

imaging, and processing that will enable high-resolution structural determination of the critical motor systems involved in neuronal growth, repair, and function. Through our work, we hope to not only provide significant insights into the molecular bases of neuronal development and degeneration, but will establish methodologies for high-resolution imaging of large complex biological systems that could be applied to many other fields of research.

Presentation: The active transport of organelles, membrane vesicles, and proteins microns in distance along the microtubule (MT) cytoskeleton within axons is critical to the function of our nervous system. This ATP-fueled shuttling of vital cytoplasmic components is accomplished by 2 classes of molecular motors that traverse MTs in opposite directions - kinesins and dyneins. Cargo-binding to dynein is mediated by a multiprotein complex named dynactin, which significantly increases dynein processivity. Using electron microscopy, we are elucidating the structure-function relationships that give rise to the loading and transport of intracellular cargo by the dynein-dynactin complex. Additionally, electron tomographic images of intact axons reveal the organization of motors as they transport mitochondria in situ.

Impressions: The meeting provided an intimate and relaxed atmosphere for scientific discourse, which is unlike any other meeting I regularly attend. The WMEN meeting provides an exceptional opportunity to explore the translational aspects of our research, as we have unparalleled access to a variety of experts from industry. The presentations are top notch, the conversations and discussions are refreshingly stimulating, and I always come away from this trip feeling inspired and motivated to take existing projects down new explorative avenues.

Name: Samantha Liang
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Presentation: I am using modular DNA scaffolds to direct the assembly of the Epidermal Growth Factor Receptor (EGFR) on live cells and investigate the effects of nanoscale organization and multimerization on EGFR signaling. I am interested in whether dimerization or higher order organization of EGFR in the absence of ligand is sufficient to activate EGFR and trigger downstream MAPK and PI3K signals. Due to the modular properties of our DNA scaffold, we can control the distance between receptors with low nanometer resolution and also quickly explore different cluster valencies and compositions.

Impressions: I thought that the meeting was an excellent experience and very well organized. I enjoyed all of the talks and thought that the size of the conference was perfect. I am really thankful for the opportunity to meet all the students, postdocs and PIs at the conference and felt that everyone was really engaged in learning about each other's research. I have no changes to recommend to the meeting.

Name: David Meininger
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Phone number: 650-496-6553

Overview: I attended WMEN 2014 as a representative of Merck's Business Development & Licensing organization.

Presentation: N/A

Impressions: The quality of presentation and supporting science was outstanding across the board - absolutely world class work! The venue, food and drink were wonderful, great value. So good, in fact, that I'm considering taking my family there for a personal vacation.

The only change I'd suggest would be with respect to the long series of short post-doctoral presentations made on the opening night. I'd replace these with selected, longer presentations with the remaining topics to be presented in poster format as many of post-

doc talks had to be cut short or went significantly over. There was simply too much material here to be presented and absorbed in 15-minute bites!

Name: David Millar
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Overview: The overall theme of my research falls within the area of single-molecule biophysics, with an emphasis on studies of nucleic acid folding and dynamics, protein-nucleic acid interactions and integral membrane proteins.

Presentation: I described our recent efforts to develop a single-molecule system to monitor the conformational dynamics of G protein-coupled receptors (GPCRs). GPCRs are the integral membrane proteins that sense extracellular ligands and transmit signals to intracellular effectors. While there has been much progress in the structural biology of GPCRs in recent years, with high-resolution structures of both inactive and active functional states now available, much less is known about the dynamic conformational changes that occur during receptor activation. We devised a new experimental system in which the beta-2 adrenergic receptor was labeled with an environmentally-responsive fluorophore and incorporated into phospholipid nanodiscs tethered to a quartz surface. TIRF microscopy was used to visualize individual receptors over long time periods. We found that the receptor spontaneously fluctuated between inactive and active conformations, even in the absence of an agonist or G protein. Moreover, we determined rate constants for conformational exchange, in the apo-receptor and in the presence of a a set of ligands that span the full range of pharmacological efficacy. Full agonists shortened the waiting periods in inactive conformations and prolonged the time spent in active conformations, whereas an inverse agonist increased the lifetime of inactive states. These observations provide insights into the nature of the receptor activation process and the molecular basis for the variable pharmacological efficacies of different beta 2 AR ligands.

Impressions: As always, this was an outstanding meeting, bringing together some of the top researchers in structural biology and drug design. The enthusiastic and full attendance over many years (myself included) speaks to the high value attached to this meeting. The participation and presentations from biotech and pharma sponsors is a key component of the meeting and helps to foster new collaborations. May this wonderful meeting continue to thrive for another two decades!

Name: Rebecca Miller
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Overview: As a member of the Stevens laboratory my work focuses on the delineation of G-protein coupled receptor structure and function using LCP X-ray crystallography and solution NMR. A special emphasis is given to members of the opioid receptor subfamily.

Presentation: The nociceptin/orphanin FQ (N/OFQ) peptide receptor (NOP) is a member of the opioid receptor subfamily of G-Protein Coupled Receptors (GPCRs) that possesses a unique pharmacological profile. Previously, the structure of the human NOP receptor was solved in complex with the peptide-mimicking antagonist Banyu Compound-24 (C-24), revealing key residues involved in ligand binding that help explain the receptor's unique selectivity profile as compared to 'classical' opioid receptors. In order to expand our understanding of the NOP pharmacophore, we solved the crystal structure of NOP in complex with two selective antagonists, SB-612111 and hybrid Compound-35 (C-35), both at 3.0Å resolution. Each co-crystal structure reveals important ligand-receptor interactions within the orthosteric binding site that contribute to the high affinity and selectivity of these antagonists to NOP over other members of the opioid receptor family.

Impressions: The Cabo meeting was fantastic on both scientific

and interpersonal levels. I made connections with multiple industry professionals, some of which were Scripps graduates. The meeting also provided a relaxed setting to discuss with Scripps faculty and to establish inter-departmental collaborations. The postdocs from UCSF were icing on the cake - I even met one that shared my tiny liberal arts alma mater, Rhodes College. I cannot thank you Ian & Pamela enough for their hard work in organizing and executing such a fantastic meeting. If lucky enough to be selected for coming years, I greatly look forward to attending.

Name: Daniel Minor
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Overview: The annual Cabo meeting was a great success. It is a unique venue for assembling people from academics and industry in a relaxed setting that facilitates interactions. It was easy to initiate new relationships as well as learn about the most exciting new developments in the research of the participants.

Presentation: I presented studies from my laboratory on our efforts to understand the mechanisms of sodium channel function using an integrated approach encompassing both functional and crystallographic approaches. I also presented new results regarding the development of selective small molecule modulators for K2P channels that are involved in pain and depression.

Impressions: The meeting was again a great success. The informal nature of the meeting and the overall high quality of the participants makes for an effective and enjoyable scientific gathering.

Name: Sue-Ann Mok
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Presentation: My research is centered on understanding chaperone recognition of the aggregation-susceptible substrate, tau. We have developed an in vitro tau aggregation assay to screen for the ability of over 20 chaperones/co-chaperones to delay tau aggregation. We have also made more than 20 variants of tau that mimic disease-associated post-translational modifications and mutations to determine if the anti-aggregation effects of chaperones are compromised for pathogenic forms of tau.

Impressions: I really enjoyed the broad range of research topics covered at the meeting. I appreciated the quality and enthusiastic delivery of the presentations by the PIs and sponsors. The student/postdoc presentation session was good but quite long and may be benefited by being broken up into two shorter sessions. I thought the size and location of the meeting was optimal.

Name: David Marciano
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Overview: Structure-function studies centered on the nuclear receptor PPARG aimed at developing novel insulin sensitizers and osteogenic agents.

Presentation: The nuclear receptor PPARγ is a critical mediator of adipogenesis and the pharmacological target of the anti-diabetic Thiazolidines (TZDs). PPARγ activation in the bone marrow promotes adipogenesis at the expense of osteoblast formation, contributing to the reduced bone density associated with TZDs. Here we report the structural mechanism by which classical antagonist SR1664 actively antagonizes PPARγ through an Activating Function 2 (AF2) mediated clash. Based on this finding, PPARγ inverse agonist SR2595 was designed to repress transcriptional activity below basal levels. Treatment of bone marrow derived mesenchymal stem cells (MSCs) with SR2595 led to increased osteoblast formation and these effects were conserved in vivo, where SR2595 drove increased plasma

osteocalcin levels. Together these results demonstrate the effect of pharmacological PPARγ repression on pluripotent lineage commitment and suggest therapeutic potential for this class of modulators.

Impressions: The meeting has been a highlight of my graduate school experience at TSRI. In addition to the opportunity to present our research to the faculty of TSRI and UCSF, the meeting also provides a chance to socially interact in a casual setting. It's clear the format of the meeting has been perfected over the many years it has been hosted.

Name: Daniel Murin
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Overview: I utilize single-particle electron microscopy to study the structures Ebola and Marburg GPs in complex with neutralizing and protective antibodies. Further, I am interested in uncovering the mechanism behind protective antibodies through parallel structural and immunological studies.

Presentation: Cocktails of monoclonal antibodies (mAbs) can provide effective post-exposure protection against Ebola virus. In order to produce the most effective antibody cocktail(s), we must understand where potential mAbs bind, which are most effective, and why. A key component of the MB-003 cocktail is mAb 13C6. The epitope of 13C6 is unknown, although it is thought to be conformational and shared between GP and sGP. Here we present images of 13C6 in complex with GP and sGP. We first determined an 18Å resolution reconstruction of the antigen binding fragment (Fab) of 13C6 in complex with mucin-containing EBOV GP by single-particle, negative stain electron microscopy (EM). We find that 13C6 binds to the apex of the GP trimer, to an epitope located within or overlapping the glycan cap. The Fabs bind upright and parallel, like goal posts, suggesting that the complete 13C6 IgG could bind bivalently to a single GP oligomer. Subsequent EM analysis of a 13C6 IgG - EBOV GP complex indeed demonstrates bivalent binding, with very limited inter-

molecular crosslinking-induced aggregation. Further, we find that a single 13C6 IgG can bind a single sGP dimer, possibly occupying both binding sites concurrently. These results suggest that sGP could be parallel or flexible enough that a near-parallel orientation can be adopted upon 13C6 binding. We further note that IgG 13C6 has a 10-fold higher affinity for sGP over GP. Despite its apparent higher affinity for sGP, 13C6 may provide some therapeutic benefit by sequestering sGP, or else the portion of 13C6 that binds GP is sufficient for protection. Bivalent binding by a single IgG to a viral glyco Cocktails of monoclonal antibodies (mAbs) can provide effective post-exposure protection against Ebola virus. In order to produce the most effective antibody cocktail(s), we must understand where potential mAbs bind, which are most effective, and why. A key component of the MB-003 cocktail is mAb 13C6. The epitope of 13C6 is unknown, although it is thought to be conformational and shared between GP and sGP. Here we present images of 13C6 in complex with GP and sGP. We first determined an 18Å resolution reconstruction of the antigen binding fragment (Fab) of 13C6 in complex with mucin-containing EBOV GP by single-particle, negative stain electron microscopy (EM). We find that 13C6 binds to the apex of the GP trimer, to an epitope located within or overlapping the glycan cap. The Fabs bind upright and parallel, like goal posts, suggesting that the complete 13C6 IgG could bind bivalently to a single GP oligomer. Subsequent EM analysis of a 13C6 IgG - EBOV GP complex indeed demonstrates bivalent binding, with very limited inter-molecular crosslinking-induced aggregation. Further, we find that a single 13C6 IgG can bind a single sGP dimer, possibly occupying both binding sites concurrently. These results suggest that sGP could be parallel or flexible enough that a near-parallel orientation can be adopted upon 13C6 binding. We further note that IgG 13C6 has a 10-fold higher affinity for sGP over GP. Despite its apparent higher affinity for sGP, 13C6 may provide some therapeutic benefit by sequestering sGP, or else the portion of 13C6 that binds GP is sufficient for protection. Bivalent binding by a single IgG to a viral glycoprotein spike is extremely rare: 13C6 may offer particular antiviral potency via its unique mode of intra-molecular bivalent binding.

Impressions: I thought it was an overall excellent meeting. Although it was a bit packed (with many presentations), we were given plenty of time to reflect and relax. The 5 minute limit for

graduate students was pretty excellent, actually. I did a great job and I look forward to challenging my time again next year. I appreciate the opportunity to talk with others whom share similar interests with me.

Name: James Paulson
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Overview: Our group investigates the roles of glycan binding proteins that mediate cellular processes central to immune regulation and human disease. Our main interests are in glycan receptors of influenza viruses, and the functions of the siglec family of glycan binding proteins that are expressed on most white blood cells, and both mediate cell-cell interactions and regulation of cell signaling receptors.

Presentation: Avian influenza viruses have been the source of new influenza pandemics for nearly a century, and humans are infected each year by influenza viruses that do not transmit in man, but have the potential to become a new pandemic virus. A major barrier to human transmission is that the receptor specificity of avian viruses differ from that of human viruses, and it is believed that for efficient transmission to occur, an avian virus must adapt to recognize human type receptors. This year I presented recent work defining novel features of human influenza virus receptor specificity that provide insights into the unique properties of receptor recognition needed for avian viruses to acquire to efficiently transmit between humans.

Impressions: Over the years, the meeting has kept its unique format with all participants speaking, including the 5-7 minute presentations of all students and post-docs the first night, that set a high bar for the science, while providing an introduction and stimulating networking discussions. The presentations of the PIs and industry participants were stunning in their breadth and quality. The novel mix of good science, intimate scientific

interchange, and ambiance of CABO continue to make this meeting one of the most enjoyable and productive of the year.

Name: Andrej Sali
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Overview: We are using computation grounded in the laws of physics and evolution to study the structure and function of proteins. We aim to improve and apply methods for: (i) predicting the structures of proteins; (ii) determining the structures of macromolecular assemblies; (iii) annotating the functions of proteins using their structures. This research contributes to structure-based functional annotation of proteins and thus enhances the impact of genome sequencing, structural genomics, and functional genomics on biology and medicine.

Presentation: The structure and dynamics of soluble proteins, membrane proteins and protein complexes can be probed by cysteine cross linking with scanning mutagenesis. The fraction of the complex that is covalently linked can be quantified by several techniques, such as SDSPAGE, and interpreted in terms of distance restraints between residue pairs. However, the noise and sparseness of the data as well as the presence of multiple structural states in a sample have hindered structural modeling based on this data. Here, we describe how to disentangle structural heterogeneity from noise, using a Bayesian approach that computes the posterior probability of the model based on a forward model, a data likelihood, and prior information; the model includes multiple structural states, their population, the level of noise for each individual data point, and several other parameters. The forward model predicts the fraction of the cross-linked complex from multiple structural states. The likelihood function is the probability of observing the measured data, given a model. The prior function is a probability of observing the model, given excluded volume, secondary structure propensity, other physico-chemical and statistical properties, and expected level of noise.

The method was first tested on real data collected for two complexes of a pair of transmembrane helices, each existing in a single known structure. We then used simulated data for 3 pairs of helices to map the accuracy of the method as a function of data noise, data sparseness, and the number of states that generated the data. Furthermore, we show how histidine kinase PhoQ data can be explained by only two structural states in the sample.

Impressions:

Location: Good
Number of participants: Perfect
Length of meeting: Just right

Name: Nicolas Strauli
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Presentation: The antibody repertoire (AbR) is a component of the adaptive immune system that is capable of undergoing real-time coevolution with infectious pathogens. We aim to deep sequence the AbR and HIV population over multiple patients, and across many time-points in order to characterize the evolutionary interaction taking place between these populations. Specifically, we aim to identify the genetic sites that show clear signals of coevolution, and thus elucidate the sites that are physically interacting. In a test dataset, we find that our mutual information based approach of identifying coevolving loci is able to successfully identify the physical interface region between an antibody and the HIV envelope. This approach has the potential to provide a systems level view of all AbR/HIV interacting sites and will illuminate how these interactions change over time. This will enable insight into the rational design of drugs and vaccines, as well as provide novel methodologies that can be used to detect the epitopes being targeted by the AbR in any quickly evolving pathogen

Impressions: The meeting was great! I was COMPLETELY blown away by how nice the location was. This facilitated much

interaction with like minded scientists, and opened up many avenues for potential collaborations; not to mention was just a really good time!

Name: Peter Thuy-Boun
Supervisor: Dennis Wolan
Affiliation: Chemistry/TSRI
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Presentation: Topic: Proteomics of the Human Gut Microbiome

Gut microbes express glycosidases capable of cleaving N-acetylneuraminic acid (Neu5Ac, sialic acid) from human glycans despite their inability to make this carbohydrate residue. The fate of liberated sialic acid is unknown-- however, aside from using this sugar as an energy source, we hypothesize that it may be a key means of evading destruction by the host immune system and perhaps even a marker for commensal strains. This project focuses on the synthesis of novel sialic acid proteomics probes for the LC/MS/MS identification and enrichment of bacterial sialic acid binding and processing proteins.

Impressions: I recently transitioned over to chemical biology from synthetic organic chemistry and this meeting was a great way to meet and greet with other students and faculty and become familiar with their work in an accelerated manner!

Name: Ana Wang
Supervisor: Dennis Wolan
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Overview: A method is being developed in which bacterial proteins present in human fecal samples can be isolated and

analyzed for studying the distal gut microbiota. Activity-based protein probes and tandem mass spectrometry are used to enrich for and identify bacterial proteins of various functions.

Presentation Current methods for studying the human gut microbiota are limited to metagenomic analyses, by which shotgun and 16s rRNA sequencing are used to identify the species present in the fecal samples. I am developing a method that will allow for the characterization of the bacterial proteome of the gut to gain insight into the functions carried out by the bacteria present. In parallel, 16s rRNA sequencing is also being used to identify the bacterial species present. Preliminary results suggest that this proteomic approach provides information that metagenomics alone cannot access.

Impressions: It was great and unique to be able to interact with not only faculty of other research institutions and universities, but also representatives from industry. It is a great opportunity to network and meet with other scientists, as the size of the conference is not overwhelming, but the content of the conference was diverse enough to keep me interested and listening.

Name: Andrew Ward
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Overview: The meeting featured its usual cadre to high impact research talks and was very enjoyable.

Presentation: I presented the use of electron microscopic and biophysical methods to study envelope virus glycoproteins for vaccine and therapeutic antibody applications. My lab has developed pipelines for obtaining low and high resolution reconstructions of glycoproteins in complex with neutralizing antibodies and have successfully implemented these pipelines to study HIV, influenza, Ebola, Marburg, and Hepatitis C.

Impressions: Reliable format that maximized the time for scientific talks and interaction with colleagues. As usual I was impressed by most of the science presented.

Name: Patrick Weinkam
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Presentation: Allostery and Data Science

Impressions: I was overall happy about the meeting and location. The only real complaint was the lack of temperature control in the room. It was either very cold or very hot.

Name: James R. Williamson
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Overview: Again, the venue for the Cabo meeting was excellent. The facilities for the meeting were great.

Presentation: The science presentations were excellent this year, and the inclusion of new blood added to the scientific quality. The industry speakers did really well in particular this year. The student and postdoc talks continue to be a highlight.

Impressions: Great job. Meeting continues improving trend over the past few years. Great opportunity to meet people from industry, and interact with colleagues at UCSF.

Name: Ian Wilson
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Overview: My lab is focused on recognition of microbial pathogens by the immune system, particularly HIV-1 and influenza virus. We have determined many antibody structures and complexes (over 175) and are using many of these for structure-assisted vaccine design for flu and HIV-1. I also direct one of the NIH PSI high throughput structural biology centers that develops methods and technologies that are being used to advance structure determination by X-ray and NMR. We have great collaborations with the Fletterick group at UCSF on stem cells and the Williamson/ Salomon group at TSRI on T cells under PSI:Biology.

Presentation: The discovery and isolation of highly potent, broadly neutralizing antibodies (bnAbs) that recognize a broad diversity of HIV-1 isolates has opened up tremendous opportunities for enhancing our understanding of how HIV-1 can be neutralized. Most of these human monoclonal antibodies are glycan dependent or have to avoid glycans on the Env surface. Structural characterization by X-ray and EM has identified novel epitopes and the full extent of their interactions on the HIV-1 Env trimer. These bnAbs possess unique features that enable them to penetrate the glycan shield, bind epitopes that consist of glycans and protein segments of Env, and promiscuously adapt to variation in the glycans. Using a combination of structural and biophysical studies, we have identified their mode of binding and analyzed the structural evolution of antibodies within a particular lineage of highly potent glycan-dependent antibodies. Elucidation and characterization of these epitopes, especially in the context of our recent structures of the Env trimer, are now providing valuable insights for structure-assisted vaccine design.

Impressions: A terrific overall program with great opportunities to meet and interact with a diverse set of participants from academia

and industry. The students and postdocs excelled in their short presentations.

Name: Dennis Wolan
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Overview: There is an urgent need to improve methods to regulate and measure specific caspases within cells, as currently available caspase peptide inhibitors, substrates, and probes are highly promiscuous. Our goal is to develop highly selective peptide activity-based probes that covalently bind to individual mature caspases. We incorporate unnatural amino acids into peptides and optimize the warhead leaving group to selectively target individual caspases . We have identified a new class of caspase-3 and caspase-8 specific peptide probes and now use these molecules to selectively monitor caspase activity under complex cellular conditions with sub-cellular accuracy and kinetic resolution.

Presentation: Specific Caspase Probes with Unnatural Amino Acids

Impressions: The meeting was fantastic with excellent scientific presentations as always by both students and faculty. Herb Boyer's keynote presentation focusing on the landmark events in molecular biology was exceptional and provided many of the students and young investigators a unique perspective of the early days of biotechnology. The location of the conference, hotel, and staff were all great.

Name: Shujun Yuan
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Presentation: Viral protein U (Vpu) plays a critical role in HIV induced pathogenesis. It counteracts with several host restriction factors through direct interactions, followed by hijacking SCF E3 ligase to degrade them. We identified several possible Vpu-interacting host factors with IP-MS, and used FSEC to validate such interactions.

Impressions: (a) the optimal size of the group: current size is good
(b) location of the meeting: very nice
(c) attendees and presenters: good
(d) length of the meeting: good
(e) any other comments: It was a nice meeting. Thanks for organizing it!

AT THE 2014 CABO MEETING ---

Herb Boyer, Ph.D., was our 2014 keynote speaker. Herb is a former UCSF faculty member and co-founder of Genentech. A biochemist and genetic engineer, Boyer had demonstrated the usefulness of recombinant DNA technology to produce medicines.

Herb Boyer received his doctorate degree with Ellis Engelsberg from the University of Pittsburgh, and did a postdoctoral with Ed Adelberg at Yale. He was a faculty member at the University of California, San Francisco and an investigator with the Howard Hughes Medical Institute. At the time Genentech was formed, Boyer was a professor of biochemistry and biophysics at the University of California, San Francisco and director of the graduate program in genetics.

For their discovery of recombinant DNA technology, Boyer and Dr. Stanley N. Cohen were awarded the Albany Medical Center Prize in Medicine and Biomedical Research, the Shaw Prize in Life Science and Medicine, the Lemelson-MIT Prize, and the Swiss Helmut Horten Research Award. Boyer was elected to the California Inventors Hall of Fame, National Inventors Hall of Fame and the National Academy of Sciences. He received the Albert Lasker Basic Medical Research Award, the Industrial Research Institute Achievement Award and is a Fellow in the American Academy of Arts and Sciences. Boyer served as Director of Allergan, first as Chairman from 1999-2002 and then Vice Chair from 2003-2013.