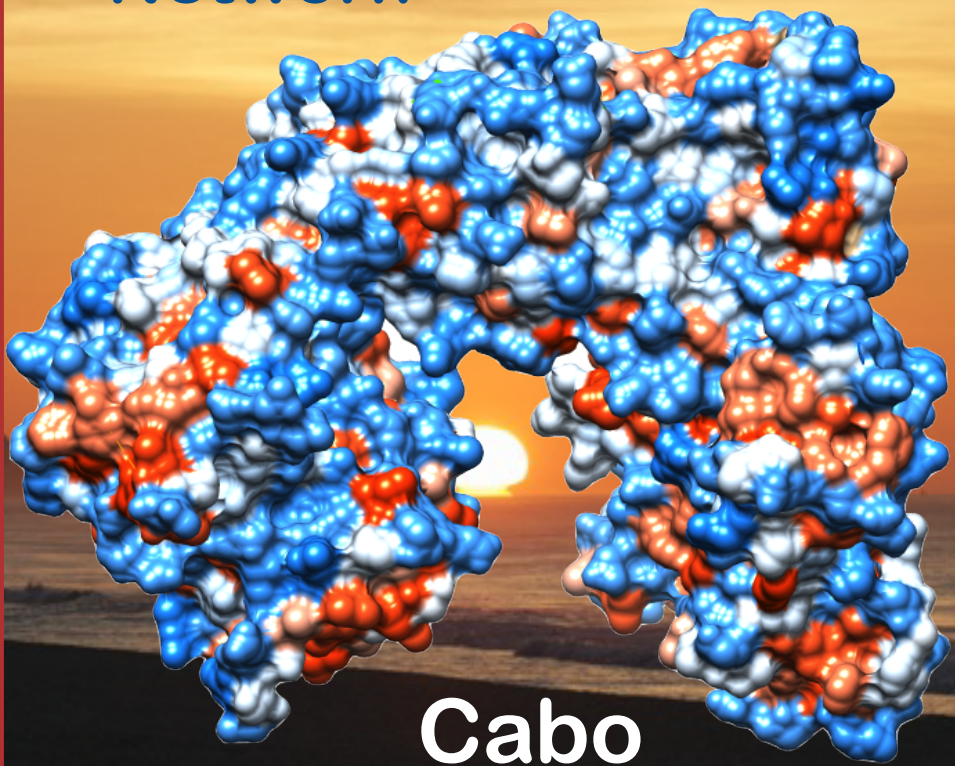
World Molecular Engineering Network



Cabo 2013

The Scripps Research Institute

University of California San Francisco
UCSF
School of Pharmacy

Our History

The WMEN conference has been held for the past 23 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 2013 meeting was again held at the 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 XXIII Program
World Molecular Engineering Network Twenty-Third Annual Meeting on Structural Biology

5-8 May 2013, San Jose del Cabo, Baja, Mexico

Sunday Evening, May 5

17:00	Ian Wilson and Andrej Sali	**Introduction and Welcome**
17:15	Richard Lerner, TSRI	**Keynote Lecture- Autocrine Signaling Based Selection of Combinatorial Antibodies that Regulate Cell Fates**

18:00-18:10 ***Self-Introductions***

Jack Kirsch	UCB
James Kiefer	Genentech
Joseph Guglielmo	UCSF
Al Stewart	Pfizer

18:10-20:00 **Short Presentations (5+1 min.) by TSRI and UCSF Graduate Students, Postdocs and Researchers(Chair: Dennis Wolan)**

Devin Sok	TSRI	Role of somatic hypermutation in HIV-1 bNabs
Joseph Jardine	TSRI	Rational HIV design to target specific germline B cell receptors
Peter Lee	TSRI	Head-hunting: Episode II – attack of the antibody clone
Melody Campbell	TSRI	Structural studies of soluble guanylate cyclase
Dmitry Lyumkis	TSRI	An unusual mechanism of enzyme activation provides structural and evolutionary insight into phage-host competition
David Marciano	TSRI	Modulating the PPARG paradigm
Joseph Nagano	TSRI	Selective inhibitors and tailored activity probes for Lp-PLA2
	Break	
Peter Cimermancic	UCSF	Analysis and prediction of cryptic binding sites

	Jonathan Sockolosky	UCSF	Engineering FcRn-mediated recycling and transcytosis in recombinant proteins by short terminal peptide extensions
	Felix Findeisen	UCSF	Lessons from a bacterial sodium channel structure for the function of mammalian calcium channels
	Elena Sablin	UCSF	Nuclear receptor LRH-1 in cancer: Search for receptor specific modulators
	Thomas Tomasiak	UCSF	Pushing the size limits of membrane protein structural biology: A crystal structure of a single TM cytochrome p450 and a subnanometer EM structure of an ABC transporter
	Daniel Suveges	UCSF	Isolation and characterization of full length HER receptors
	Min Zhuang	UCSF	Substrates of IAP ubiquitin ligases identified with a designed orthogonal E3 ligase, the NEDDylator

20:15–21:45 **Reception** **Poolside**

Monday May 6

Structural and Computational Biology (Chair: Robert Stroud)

09:00	Andrej Sali	UCSF	Macromolecular structures by chemical cross-linking
09:20	John Tainer	TSRI	Hybrid methods with X-ray scattering for accurate structures
09:40	Ashok Deniz	TSRI	Single molecule biophysics of protein disorder
10:00	Robert Fletterick	UCSF	SfTuRnUcCtTiUoRnE of nuclear receptor LRH-1 for developmental and cancer biology
10:20	Break		

HIV-1 (Chair: Ian Wilson)

10:40	Graham Johnson	UCSF	Contest-catalyzed community science HIV visualization challenge
11:00	Andrew Ward	TSRI	Structural and biophysical studies of HIV-1 envelope glycoproteins
11:20	Bill Schief	TSRI	Epitope-focused vaccine design
11:40	Art Olson	TSRI	HIV interactions and the evolution of drug resistance

Immunology and Vaccinology (Chair: Bill Schief)

16:30	Jim Wells	UCSF	Challenging targets for antibody engineering
16:50	Jim Paulson	TSRI	Induction of B cell tolerances to antigens
17:10	Ian Wilson	TSRI	Broadly neutralizing antibodies to Influenza Virus: Implications for vaccines and therapy
17:30	Phil Dawson	TSRI	Structure-based design of HCV mimics
17:50	Break		

Chemical Biology (Chair: Jack Kirsch)

18:10	Dan Santi	UCSF/Pro Lynx	A chemical approach to half-life extension of therapeutics
18:30	Phil Baran	TSRI	Studies in natural product synthesis
18:50	Dennis Wolan	TSRI	Direct and specific regulation and detection of human caspases

Tuesday , May 7

SPONSORS (Chair: Dan Santi)

09:00	Ye Jin	Bayer	Global substrate profiling of proteases in Neutrophil Extracellular Traps reveals consensus motif predominantly contributed by Elastase
09:20	Neel Anand	Nektar	The design of novel and improved oncolytics utilizing Nektar's advanced polymer conjugation technology
09:40	Magdalena Dorywalska	Rinat	Location matters: Site of conjugation modulates stability and pharmacokinetics of antibody drug conjugates
10:00	Nicholas Skelton	Genentech	Adventures with AKT: small molecule inhibition and mechanism of activation
10:20	Break		
10:40	Craig Muir	Third Rock	An update on TRV interests in antibody and protein engineering

		Ventures	
11:00	Johanna (Hanneke) Jansen	TDTi	Computational chemistry workflows to support education and drug discovery for neglected diseases
11:20	Glen Spraggon	GNF	One residue makes all the difference: The structural basis for lack of toxicity of CRM197

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

16:30	Carlos Barbas	TSRI	Gene-free gene therapy and other advances with novel enzymes that act on DNA
16:50	Jamie Williamson	TSRI	Dynamics of ribosome assembly in cells
17:10	Joel Gottesfeld	TSRI	Epigenic therapy for neurological diseases
17:30	Break		

Membrane Proteins (Chair: Andrew Ward)

17:50	Robert Stroud	UCSF	Wiggle Wiggle not a Trickle
18:10	Dan Minor	UCSF	Structural and functional studies of cation channels
18:30	Mark Yeagar	TSRI/UVA	X-ray structures of the human Cx26 gap junction channel suggest a novel electrostatic mechanism for calcium-mediated gating
18:50	David Millar	TSRI	Single molecule studies of GPCR's

Wednesday, May 8

Assemblies, Design and Drug Discovery (Chair: Jim Wells)

08:30	Vijay Pande	Stanford	Simulating the functional dynamics of proteins: intermediates and transition states of conformational change in GPCRs and kinases
08:50	Frank Szoka	UCSF	Hyaluronan- a ligand and a target in cancer biology
09:10	Jim McKerrow	UCSF	Discovery and validation of a repurposed drug for amebiasis

09:30	Larissa Podust	UCSF	Structural analysis of thioredoxin reductase, the target of auranofin
09:50	Break		
10:20	Ron Zuckerman	UCB/LBL	Adapting protein design rules to the assembly of peptoid polymers
10:40	Natalia Jura	UCSF	Insights into activation of HER receptors by hetero-oligomerization
11:00	Floyd Romesberg	TSRI	Efforts toward the in vivo expansion of the genetic code
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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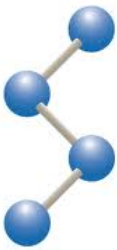

The Scripps Research Institute

University of California
San Francisco

School of Pharmacy

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

WMEN Conference
San Jose del Cabo
Barcelo Los Cabos
Palace Hotel

For more information, contact:

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Name: Neel K. Anand
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Overview: At Nektar Therapeutics, our goal is to deliver efficacious and safe medicines for patients by producing differentiated new chemical entities utilizing our advanced polymer conjugation technology.

Presentation: Nektar's advanced polymer conjugation technology has been applied to design and develop novel and improved oncolytics using large molecular weight PEGs conjugated to cytotoxic scaffolds via releasable linkers. The application of our technology in this manner increases half-life and tumor-targeting of the cytotoxic agent to improve efficacy, while reducing Cmax and volume of distribution to minimize toxicity. Two case studies were presented to illustrate the benefits of the technology; a late stage program: NKTR-102 (etirinotecan pegol) and an early stage program: NKT-TSI-4a.

Impressions:
Location: Excellent
Number of participants: Perfect
Length of meeting: Ideal

The presentations were of an excellent quality and, because everyone presented, the meeting provided an opportunity to learn about a broad range of cutting edge structural biology, and set the stage for excellent scientific discourse. The small size of the meeting is very conducive to discussion of science and spawning of new collaborations.

Overall, a fantastic meeting!

Name: Phil Baran
Affiliation: TSRI Department of Chemistry
Mailing address: 10550 North Torrey Pines Road, BCC-436, La Jolla, CA 92037
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Phone number: 858 784 7373

Presentation: Studies in natural product synthesis

Impressions: This was an incredibly exciting meeting for me and I was exposed to a fantastic cross section of science that I had not been exposed to before (some from my beloved colleagues and some from those in other institutions). This conference is like a GRC meeting but better because the 15-minute presentations keep it very exciting and give a "heart-cut" of the research topic. Awesome venue, awesome talks, and a great experience. I hope to come back.

Name: Carlos Barbas
Affiliation: TSRI Depts. of Chemistry and Cell and Molecular Biology
Mailing address: 10550 North Torrey Pines Road, La Jolla, CA 92037
Email address: carlos@scripps.edu
Phone number: 858 784 9098

Overview: Zinc-finger nucleases (ZFNs) are powerful reagents that have redefined genome engineering; however, current ZFN delivery systems may limit clinical applications of this technology. We demonstrate the intrinsic cell-penetrating capabilities of the established ZFN architectures and show that direct application of ZFN proteins leads to efficient endogenous gene disruption in a variety of mammalian cell types. This method represents an effective alternative to existing ZFN delivery systems with the potential to increase the safety of therapeutic human gene editing. Advances in zinc finger recombinases and TALE

recombinases will also be presented

Presentation: Gene-free Gene Therapy and other advances with designed enzymes that act on DNA

Impressions: Tremendous intersection of science. Multidisciplinary with many real world applications. Always gives me new ideas and facilitates new collaborative studies.

Name: Ashok Deniz
Affiliation: TSRI Dept. of Integrative Structural and Computational Biology
Mailing address: 10550 North Torrey Pines Rd., MB-19 La Jolla, CA 92037
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Overview: My research interests are in the area of single-molecule biophysics. This research area has emerged during the past decade or so, leveraging new state-of-the-art developments in detection methods to truly revolutionize several fields of science, including biology, physics and chemistry. This outstanding meeting provides a strong emphasis on the broad context of structural biology. In this regard, my group's research provides a fundamental perspective on the detailed structural distributions and dynamics of proteins and other biological systems, and how these relate to fundamental biology. The breadth and high quality of this meeting provides a great opportunity for connecting the concepts from our work with a range of complementary basic and applied biology.

Presentation: I presented a couple of recent sets of exciting results in the area of single-molecule biophysics. Our research is uncovering novel insight into the dynamic features of a class of proteins often termed as intrinsically disordered. In contrast with many proteins that have been studied most often thus far, intrinsically disordered proteins

comprise long stretches of sequence that are relatively devoid of structure. The special properties of these proteins make them important and prevalent in many functional contexts in the cell. While important, these dynamic species are hard to study via traditional structural methods. We have used state-of-the-art single-molecule methods in this context, revealing new insight into the dynamic structural features of these molecules, including rapid fluctuations and complex folding linked to binding to partners, both of which have functional relevance.

Impressions: Top-notch scientific sessions and speakers and meticulous organization combined with an excellent venue and interactions between participants to result in an outstanding meeting. Sessions consisted of a number of exciting presentations, with plenty of detailed and motivated discussion at the end of talks. Topics were wide-ranging within the context of the meeting, making it intellectually stimulating and informative about the latest results in a range of both basic and applied structural biology research. Furthermore, the format of the meeting highly encouraged close interactions and potential collaborations among attendees during multiple breaks during and between sessions. The size of the meeting was optimal, balancing very well a critical number of attendees with a smaller format for close scientific and social interactions. I have attended a number of larger and smaller meetings and conferences over the years, and would give this meeting my very highest rating due to the reasons that I discuss above.

Name: Magdalena Dorywalska
Affiliation: Rinat / Pfizer
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Phone number: 650 615 7502

Overview: Our research focuses on antibody-drug

conjugates which offer increased antitumor potency and reduced toxicity compared to traditional nontargeted chemotherapy. We are developing novel methods for site-specific conjugation of toxic payloads to antibodies to increase product homogeneity as compared to conventional methods.

Presentation: We have developed an enzymatic method for site-specific conjugation allowing us to attach diverse payloads at multiple positions on antibodies. We show that conjugation site has a significant impact on the stability and pharmacokinetics of antibody-drug conjugates. With this approach, we can generate homogenous conjugates and tune their properties to achieve a better therapeutic outcome.

Impressions: I greatly enjoyed the scientific presentations and discussions during the meeting. It provided a nice perspective of important ongoing research, and a chance for informal chats with top research scientists and enthusiastic students. It was a great pleasure to participate, and very well organized.

Name: Felix Findeisen
Supervisor: Dan Minor
Affiliation: CVRI
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Phone number: 415 359 8503

Presentation: I presented data on my work on the regulation of voltage-gated calcium channels by the calcium sensors calmodulin and CaBP1. I characterized the binding of the calcium sensors to an element in the channel C-terminus using isothermal calorimetry. I used these results to make prediction on the competition of these two calcium sensors to predict the interaction on the full-length calcium channel in functional assay using electrophysiological

recordings in Xenopus oocytes. The predictions turned out to be accurate, suggesting that the in vitro elements studied is sufficient to explain competition between calmodulin and CaBP1.

Impressions: Location and size of the meeting was excellent. The meeting allowed ample time for networking and it was a wonderful opportunity to get an overview of research at The Scripps Research Institute. I also thought the session of speakers from industry was well presented and engaging. Participating in the conference was an entirely positive and enriching experience.

Name: Robert Fletterick
Affiliation: UCSF Dept. of Biochemistry
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Overview: The meeting was exciting, interactive and a great place to learn and form collaborations. The venue was perfect.

Presentation: My presentation described finding compounds that bind to nuclear receptor LRH-1, active in stem cells. The hormone is unknown for this transcription factor and the receptor is active without it.

To search for inhibitors, we generated a computer model of a partly denatured protein, and screened the Zinc database to find about 30 compounds for further testing. Binding was discerned by affecting the melting temperature of the receptor.

The compounds bind to the hormone binding site: Those compounds with promise, lowering the melting temperature, were tested for function as allosteric inhibitors in binding

coactivator peptides using a biosensor.

An additional biosensor test showed that the compounds bound to wild type receptor but not to mutant receptor with a Trp residue replacing an Ala in the hormone binding pocket.

The Trp mutant showed normal activity and was more stable than wild type receptor. Cell proliferation assays showed that the compounds were effective in most human cancer cells from pancreas, and some from colon and breast. The compounds had no effect in pancreatic cancer cells that did not depend on LRH-1 for growth.

Impressions: The talks were exceptional. The speakers kept to time, mostly, and their presentations were clear. I liked the discussions outside the meeting hall and had several ideas about new collaborations.

The hotel was super. The food was better than very good. The staff were engaging and helpful.

Name: Matthew Jacobson
Affiliation: UCSF Department of Pharmaceutical Chemistry
Mailing address: UCSF MC 2540, 1700 4th St., Byers Hall, Room 408E, San Francisco, CA 94158-2330
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Phone number: 415 514 9811

Overview: My group has a broad interest in computer-aided drug design and protein structure-function relationships. In the area of drug design, we have developed and applied new methods for modeling protein-ligand interactions, membrane permeability, the blood-brain barrier, and macrocycle drugs. We also have a broad interest in mechanisms of protein regulation by post-translational modifications, pH, and allostery broadly.

Presentation: I presented our most recent work on inferring

enzyme function from sequence and structure, using a combination of computational and experimental approaches in a large collaboration involving Patsy Babbitt, John Gerlt, John Cronan, Steve Almo and many co-workers. In published work from my lab and others, docking methods (more commonly used for structure-based drug design) have been successfully used to predict what metabolites could be substrates of an enzyme. In recent work, we have expanded this concept to multiple enzymes in a pathway, discovering a novel enzymatic activity and novel pathway for degrading osmolytes including hydroxyproline betaine. The predictions were verified by an extensive series of structural, enzymatic, and microbiology experiments.

Impressions: Terrific, as always. My main motivation for attending is to hear about the fantastic work from Scripps. It might be possible to increase interactions between the Scripps/UCSF/industry contingents, e.g. by organizing in advance some groups to have dinner together, based on shared scientific interests.

Name: Joe Jardine
Supervisor: Bill Schief
Affiliation: TSRI Dept. of Immunology
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Presentation: Rational HIV Immunogen Design to Target Specific Germline B Cell Receptors

Impressions: The meeting was very good. I liked the blend of academic and industry. This was my first real experience talking to people who had careers in industry and it was interesting to see the differences. The only thing that I would have changed was to make it less chemistry focused. I got lost during a lot of the chemistry talks.

Name: Ye Jin
Affiliation: Bayer Healthcare Pharmaceuticals
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Phone number: 415 437 5813

Overview: My research focuses on protease activities and their potential pathogenic role in inflammations. On the technology side, we have been collaborating with Dr. Charlie Craik's lab at UCSF and using their proprietary peptide substrate libraries to profiling protease activities in immunological functions.

Presentation: Representing our collaborating team from Bayer and Dr. Craik's lab at UCSF, I presented "Global substrate profiling of proteases in Neutrophil Extracellular Traps (NETs)". I got many positive and insightful comments and suggestions.

Impressions: The quality and content of the meeting was very impressive. The PI's researches are cutting edge. Not being a structural biologist, I learned a lot from this meeting, and am following up with a few PI's on potential collaborative opportunities. I wish the postdoc and graduate's talks could be a little longer. The small size of the meeting also means there is ample opportunity to network. I was able to mingle with and talk to several professors, graduate students and postdocs.

The site is relaxing and beautiful.

Name: Graham Johnson
Affiliation: BTS / qb3@UCSF
Mailing address: Room N476A Genentech Hall, 600 16th Street, San Francisco, CA 94158-2517
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Phone number: 415 476 5379

Overview: The Mesoscope lab focuses primarily on developing algorithms to enable scientists to generate, simulate, and visualize molecular models of cells, namely developing a software called autoPACK/cellPACK. We also develop outreach software that enables scientists and illustrators to interoperate the computational tools of science and art and work closely on these fronts with ties to industry and through both formal and informal outreach mechanisms.

Presentation: Contest Catalyzed Community Science: HIV Visualization Challenge

We initiated a new approach to stimulate user feedback and development efforts for our large-scale open-source software project autoPACK. With this inaugural effort, we applied industry funding to host and finance prizes for a contest to visualize models generated by our software. The contest bridged a gap between Hollywood caliber production value for outreach education and researchers interested in visualizing comprehensive models structural systems biology, in this first case, HIV in Blood Plasma. The contest provided feedback needed to polish our software from an early alpha to a stable beta release, garnered ~2,400 new users, and generated a collection of top quality visualizations of HIV suited for both general and scientific audiences.

Impressions: I'm sold on the new location. Last year, the transition to the larger and more opulent setting proved distracting, but this year everything came together nicely. The new attendees from all campuses mixed and networked more effectively than I'd seen in years. Excellent size and format.

Name: Natalia Jura
Affiliation: CVRI/UCSF, Department of Cellular and Molecular Pharmacology

Mailing address: MC:3122, 555 Mission Bay Blvd South, Rm 452W ,San Francisco, CA 94158-9001
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Overview: My group at UCSF studies molecular basis for signal transduction by receptor tyrosine kinases. We apply a combination of structural biology, imaging and biochemical approaches to ask basic questions about the structure and function of full length receptors.

Presentation: "Single molecule studies on HER receptor heterodimerization". The presentation described a chemical labeling and imaging method developed in my group to investigate spatiotemporal parameters of interactions between the members of the human epidermal growth factors receptors.

Impressions: The meeting was terrific. A beautiful and relaxing location, which facilitated discussions and interactions. An inspiring mix of scientists that inspired thinking about basic science and future therapeutics. I especially appreciated candid discussions with scientists from the industry. One thing I would like to recommend for future improvement is the organization of evening activities or rather lack of thereof. It was a bit hard to interact with conference participants in the evening due to lack of an organized common event (such as dinner, or drinks). The resort was so big that it took a while to find others.

Name: Jim Kiefer
Affiliation: Genentech, Department of Structural Biology
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Phone number: 650 467 8216

Overview: My research interests revolve around structure

based drug discovery in oncology and inflammation. I have worked on a variety of targets, including membrane proteins, proteases, kinases, and DNA replication and repair enzymes. My current projects include epigenetics targets and nuclear receptors.

Impressions: The talks were rich with new data and creative application of technologies to attack some of the most difficult and interesting problems. The breadth of topics covered was outstanding.

Name: Jack Kirsch
Affiliation: UC Berkeley, QB3 Institute
Mailing address: QB3 Institute, Univ. of CA. Berkeley, CA 94720-3220
Email address: jfkrisch@berkeley.edu
Phone number: 510 642 6368

Impressions: This is ca. my 15th attendance. I am now retired, but continue to benefit from the high quality presentations. This is the only meeting that I still attend regularly, and it is because I learn so much for the time committed.

For what it is worth, I do note that there has been an increasing emphasis on drug discovery as opposed to basic science over the years. I do understand the motivation, but feel that the continuation of this trend may ultimately slow the pace of truly innovative scientific discovery.

Name: David Marciano
Supervisor: Patrick Griffin
Affiliation: TSRI, Dept. of Molecular Therapeutics
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Phone number: 631 891 5860

Presentation: The nuclear receptor peroxisome proliferator-activated receptor gamma (PPARG) is the pharmacological target of the antidiabetic thiazolidinedione (TZD) class of drugs. Full agonist TZDs are extremely effective as insulin-sensitizers but concerns over adverse effects have limited their utility and created a need for next generation therapeutics. Recently, it was demonstrated that the insulin sensitization of TZDs correlate with their ability to block the obesity-induced phosphorylation of PPARG at S273 (S273-p), while the associated adverse effects are a result of receptor activation. Based on this discovery we developed SR1664, an active antagonist ('non-agonist') that is efficacious at insulin sensitization and demonstrates negligible TZD-associated adverse effects in vivo. Efforts to develop SAR around this novel class of ligands led to the rational design of SR2595, the first PPARG inverse agonist to be reported. These findings hold significant promise for the development of next generation insulin sensitizers and may provide useful strategies for pharmacologically targeting other nuclear receptors.

Impressions: As a first time attendee I was very impressed with the conference. The small size and requirement that all participants present created a great dynamic between students, faculty, and guests. The conference was well organized as far as scheduling/facilities but also in terms of the content of presentations being cohesive while avoiding redundancy. From a personal perspective, because the conference was attended by many accomplished faculty from TSRI and UCSF, it provided a great opportunity to scout potential post docs and collaborators. I also thought that as the first TSRI-Florida attendee (and hopefully not last) it provided a great opportunity to further bridge the gap between campuses. Overall, an excellent meeting that I hope to attend again in the future.

Name: Jim McKerrow
Affiliation: UCSF

Mailing address: UCSF Byers Hall MC 2500, 1700 4th Street, San Francisco, CA 94158-2330
Email address: james.mckerrow@ucsf.edu
Phone number: 415 476 2940

Overview: A wonderful meeting at a wonderful site. Good science coupled with chance for collaborations.

Impressions: Continues to be a highlight. Good breadth of science but small enough to foster discussion and collaboration.

Name: David Millar
Affiliation: TSRI Dept. of Integrative Structural & Computational Biology
Mailing address: 10550 North Torrey Pines Road, La Jolla, CA 92037
Email address: millar@scripps.edu
Phone number: 619 618 5352

Overview: My lab develops single-molecule fluorescence methods to study protein-nucleic acid interactions. We have two main current areas of interest. (1) Assembly of the HIV-1 Rev protein on the Rev Response Element (RRE). We are studying the role of cellular cofactors on Rev-RRE assembly. (2) Fidelity mechanisms of DNA polymerases. We are studying how DNA polymerases discriminate between cognate and non-cognate nucleotides during nucleotide incorporation. In addition, we have developed novel methods to visualize polymerases switching among their different modes of activity (nucleotide incorporation, proofreading or 5' nuclease cleavage).

Presentation: This year I described a new project that arose out of conversations at the Cabo meeting three years ago. During that conversation, my colleague Ray Stevens described the need for new methods that could characterize the conformational dynamics of G protein coupled receptors

that underlie their signaling activity. Rising to the challenge, we have developed a single-molecule fluorescence method to monitor conformational changes of the beta 2 adrenergic receptor. Using a cysteine-light version of the receptor, we have attached a Cy3 fluorophore to the tip of various transmembrane helices and incorporated the labeled receptors into lipid nanodiscs, which are subsequently immobilized on a quartz slide of a TIRF microscope. We have visualized individual receptor molecules over time by means of fluorescence measurements, revealing that receptors spontaneously interconvert between three distinct conformations (active, inactive and intermediate). The single-molecule measurements have been performed on the apo receptor and in the presence of various ligands (agonists, partial agonists and inverse agonists). We have been able to quantify the rate constants for exchange among the different conformational states, which are relatively slow (in the second range). These promising initial studies suggest that single-molecule fluorescence methods will be useful for analyzing the fluctuating structure of other GPCR's in model membrane environments.

Impressions: The scientific content of this year's meeting was at an extremely high standard, confirming that the meeting remains vital and continues to attract leading investigators from TSRI, UCSF and other institutions. After 23 years, the meeting is stronger than ever. Who would have predicted such success? The Barcelo hotel is a significant improvement over the previous venue. The meeting continues to provide a friendly and relaxing environment to exchange ideas with colleagues from academia and the biotech and pharmaceutical industries.

Name: Daniel Minor
Affiliation: Cardiovascular Research Institute/ UCSF
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Phone number: 415 514 2551

Overview: The WMEN meeting continues to be an exceptionally exciting meeting. The mixture of academic and industrial scientists in such an open setting in which there is plenty of time and space for informal discussions is unmatched by any other meeting I attend. The presentations by scientists from UCSF, Scripps, Stanford, and others were all excellent and showed the cutting edge of biomolecular science.

Presentation: I presented new work from my laboratory on the three dimensional structure of sodium channels and on our efforts to develop and implement systems for screening small molecules against ion channel targets in order to expand the available pharmacologies.

Impressions: This was an excellent meeting. The presentations were stimulating. The size of the conference is ideal for encouraging active discussions among the participants. It is a fantastic format for strengthening existing connections and for forging new relationships with both academic and industrial scientists

a) the optimal size of the group - Ideal as is. There is enough critical mass to generate lively discussion but not too many participants that would dilute the effects.

(b) location of the meeting - Fantastic

(c) attendees and presenters - Engaged, interesting, and all high quality

(d) length of the meeting - Ideal.

Name: Arthur Olson
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Email address: olson@scripps.edu
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Overview: Great meeting, excellent talks, lots of opportunity for conversation and developing new collaborations. Great venue.

Presentation: My talk was entitled: "HIV Interactions and the Evolution of Drug Resistance." In it I gave an overview of our new NIH funded HIVE Center whose goal is to characterize at the atomic level the structural and dynamic relationships between interacting macromolecules in the HIV life cycle in order to understand the basis of drug resistance. I then focused on the work in my lab to discover new allosteric sites using molecular docking and other computational approaches to find new small molecule hits and elaborate them to leads for new inhibitors to the current drug targets.

Impressions: Another excellent meeting. Impressive work that covered the range of structural techniques as well as computational and synthetic methods. Good interaction both in the sessions and in the free time. The new venue was very good. The rooms and the food were much improved over Presidente.

Name: Vijay Pande
Affiliation: Stanford University, Chemistry Dept.
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Overview: The central theme of our research is to develop and apply novel theoretical methods to understand the physical properties of biological molecules, such as proteins, nucleic acids, and lipid membranes, and to apply this understanding to design novel synthetic systems, including small molecule therapeutics. In particular, we are interested in the self-assembly properties of biomolecules: for example,

how do protein and RNA molecules fold? How do proteins misfold and aggregate and how can we use our understanding of this process to tackle misfolding related diseases, such as Alzheimer's or Huntington's Disease? How can we design or discover novel small molecules to inhibit this process?

Presentation: A key challenge in molecular simulation is reaching experimentally relevant timescales with models that are sufficiently detailed to quantitatively predict experiment. Indeed, most atomistic simulations typically only reach the nanosecond to microsecond timescale, whereas experimentally relevant timescales for many phenomena are on the millisecond to second timescale.

We describe a new approach for simulating long timescale dynamics using Markov State Models (MSMs). MSMs are a systematic sampling scheme to both get to long timescales as well as to gain insight from the results. Indeed, this approach allows a cluster of GPUs to simulate a millisecond of aggregate dynamics and to use that data to quantitatively predict experiment, indicate the degree of robustness of results, and yield novel insights.

Finally, I will demonstrate this method with applications to all-atom molecular simulations on the millisecond timescale and beyond, with applications to protein folding, protein misfolding in Alzheimer's Disease, and protein conformational change in disease-relevant drug targets of GPCRs and kinases.

Impressions: Location: Excellent
Number of participants: Excellent
Length of meeting: Excellent

This was my first time at the WMEN meeting. I was extremely impressed. It is a very unique style of meeting where everyone gives some presentation and the group is

very tightly knit, but yet with a broad set of interests.

Name: James Paulson
Affiliation: TSRI Dept. of Cell and Molecular Biology
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Overview: Our group investigates the roles of carbohydrate binding proteins that mediate cellular processes central to immune regulation and human disease. Our primary focus is a sub-group of the immunoglobulin superfamily called siglec that binds sialic acid containing carbohydrates as ligands, and regulate trans-membrane signaling of receptor complexes. We want to understand how binding to carbohydrate ligands modulates the regulatory functions of the Siglecs.

Presentation: This year I described our work suggesting that B cell siglecs help enforce B cell tolerance to self-membrane antigens. When a B cell contacts an antigen on a cell that contain siglec ligands, the siglecs are recruited to the site of the immunological synapse, resulting in suppression of B cell signaling. Moreover, the impact of the siglec is to suppress the Akt mediated survival pathway, resulting in apoptosis of the antigen reactive cell. We have also found that this natural regulatory mechanism can be exploited to induce tolerance to any desired antigen. To this end, we have developed liposomal nanoparticles bearing a multivalent display of an antigen and high avidity siglec ligands that can target antigen reactive cells in vivo. Remarkably, injection of the antigenic liposomes into mice results in induction of apoptosis in reactive B cells, and the mice are then incapable of mounting an antibody response to that antigen in a subsequent challenge. Since development of inhibitory antibodies to FVIII is a serious problem in treatment of hemophilia A patients, we

investigated the potential of this approach for inducing tolerance to FVIII in a hemophilia mouse model. Our tolerizing liposomes prevented formation of inhibitory FVIII antibodies, allowing for effective administration of FVIII to hemophilia mice to prevent bleeding. Thus, we suggest that a major function of the B cell siglecs is to recognize sialic acid as self, and to induce apoptosis in autoreactive B cells for maintenance of peripheral tolerance. Exploiting this mechanism has therapeutic potential in the areas of autoimmunity, allergies, and biotherapeutics

Impressions: As in past years the meeting is an amazing mix of fantastic science, and a relaxed atmosphere conducive to socialization and networking. Everyone feels welcome as a participant, whether a regular over the last 20 years or a first-time attendee. I get more ideas at this meeting than any other meeting I attend, and always come away feeling enriched, and look forward to the next year.

Name: Larissa Podust
Affiliation: UCSF
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Overview: The meeting was well organized and location was wisely chosen. The presentation schedule was intense and at the same time allowed enough time for informative discussions and sightseeing.

Presentation: The meeting covered a great variety of the state-of-the-art and thought-provoking topics presented by the leading scientists in the academia and industry. Equally exciting were presentations from the post-docs and students. Particularly important that new and unpublished data were presented during the meeting.

Impressions: Community integrating meeting. Good environment to establish new collaborations to test new ideas.

Name: Floyd Romesberg
Affiliation: TSRI Dept. of Chemistry
Mailing address: 10550 North Torrey Pines Rd., CV262R, La Jolla, CA 92037
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Phone number: 858 784 7290

Overview: In addition to just getting to see what my colleagues are up to this meeting gives me a chance to present our work to colleagues from both TSRI and UCSF. Every year I get a lot of great feedback.

Presentation: I presented my groups progress toward the expansion of the genetic alphabet. Specifically I presented an overview of our now completed in vitro efforts that have culminated in a fully functional third base pair that is for example suitable for PCR. I also presented our initial efforts to establish replication in vivo.

Impressions: My overview of the meeting was that it was great as usual! The 15 min talks are great because it allows so much science to be presented. This is the only place I get to hear what many of my colleagues are working on.

Investigator: Andrej Sali
Dept./Institution: UCSF Dept. of Biopharmaceutical Sciences
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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: Daniel Santi
Affiliation: UCSF/ProLynx
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Overview: presented an overview of ProLynx, start-up company I recently co-founded. The company develops technology for half-life extension of drugs, in particular peptides and proteins.

Presentation: Conjugation to macromolecular carriers is a proven strategy for improving the pharmacokinetics of drugs, with many stable polyethylene glycol conjugates having reached the market. Stable conjugates suffer several limitations: loss of drug potency due to conjugation, confining the drug to the extracellular space, and the requirement for a circulating conjugate. Current research is directed toward overcoming such limitations through releasable conjugates in which the drug is covalently linked to the carrier through a cleavable linker. We have developed conjugation linkers on the basis of a nonenzymatic beta-elimination reaction with pre-programmed, highly tunable cleavage rates. A set of modular linkers is described that bears a succinimidyl carbonate group for attachment to an amine-containing drug or prodrug, an azido group for conjugation to the carrier, and a tunable modulator that controls the rate of beta-eliminative cleavage. The linkers provide predictable, tunable release rates of ligands from macromolecular conjugates both in vitro and in vivo, with half-lives spanning from a range of hours to >1 y at physiological pH. Using slow- cleaving

linkers, we developed a hydrogel format provides a generic approach for once-a-month dosage forms of potent drugs. The hydrogel format has been developed to contain slow-cleaving beta-eliminative linkers to control drug release, and very slow-cleaving beta-eliminative linkers to allow subsequent controllable degradation rates. The releasable linkers provide additional benefits that include lowering Cmax and pharmacokinetic coordination of drug combinations.

Impressions: The meeting was, as always, terrific. The talks were crisp, and the science was terrific. There was plenty of time to interact, and the hotel and food very good. The attendees and talks from our keynote speaker, Richard Lerner, and Industry participants were particularly impressive.

Name: Jonathan Sockolosky
Supervisor: Frank Szoka
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Presentation: My research focuses on the design of more convenient protein therapeutics by enabling non-invasive administration and increasing their duration of activity through prolonged circulation. We developed a method termed "FcBP fusion" to engineer proteins to interact with the human neonatal Fc receptor (hFcRn) through genetic fusion of short hFcRn binding peptides (FcBP) to the N- and C-termini of model proteins. FcBP fusion enables transport of proteins across epithelial barriers and protection from intracellular degradation in cell monolayers that express hFcRn. Initial attempts at demonstrating enhanced circulation of FcBP fusion proteins in a human FcRn transgenic mouse model have been unsuccessful; however, our results provide insight on the importance of beta-2

microglobulin (B2m) in the function of FcRn in vivo. We are now developing new mouse models to evaluate the importance of species specific B2m and FcRn expression on the serum half-life of FcBP fusion proteins, IgG, and albumin.

Impressions: This was one of the best meetings I have attended as a graduate student even compared to some Gordon and Keystone meetings. Although the conference focus is narrow and the institutions represented are limited I believe this provided a great forum for students, post-docs, and faculty to exchange ideas and build close relationships. The 5 minute student / post-doc presentations were somewhat hard to follow given the speed; however, they provided a general idea of others research and made it very easy to talk further throughout the meeting. The PI talks were very good and an appropriate length. Most of the sponsor talks were equally good, and some were excellent, but I would encourage others to focus less on pipeline or development decisions and more on the science / biological mechanisms behind their technology.

Name: Glen Spraggon
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Overview: As part of the Novartis Institute of Biomedical Research (NIBR), the Genomics Institute of the Novartis Research Foundation (GNF) focuses on the discovery of new molecules and technologies to address unmet medical needs.

My group is focused on the design of novel protein based biotherapeutics and small molecules using structure and computation to guide the innovation. The collaboratory projects that take place within the group range from the

optimization of protein properties guided by structure, via protein engineering, to the development of bioactive organic molecules by structure-aided drug design. These activities are closely coupled with the adoption and development of new technologies to further enable these endeavors.

Presentation: CRM197 is an enzymatically inactive and nontoxic form of diphtheria toxin that contains a single amino acid substitution (G52E). Being naturally nontoxic, CRM197 is an ideal carrier protein for conjugate vaccines against encapsulated bacteria and is currently used to vaccinate children globally against *Haemophilus influenzae*, pneumococcus, and meningococcus. To understand the molecular basis for lack of toxicity in CRM197, we determined the crystal structures of the full-length nucleotide-free CRM197 and of CRM197 in complex with the NAD hydrolysis product nicotinamide (NCA), both at 2.0-Å resolution. The structures show for the first time that the overall fold of CRM197 and DT are nearly identical and that the striking functional difference between the two proteins can be explained by a flexible active-site loop that covers the NAD binding pocket. We present the molecular basis for the increased flexibility of the active-site loop in CRM197 as unveiled by molecular dynamics simulations. These structural insights, combined with surface plasmon resonance, NAD hydrolysis, and differential scanning fluorimetry data, contribute to a comprehensive characterization of the vaccine carrier protein, CRM197.

Impressions: The WMEN conference was a wide mixture of novel techniques and molecular engineering topics, covering everywhere from small molecule chemistry and drug discovery to the development of novel biotherapeutics and vaccines.

The format and location of the meeting was pleasant, sociable and provided an outstanding setting for education, collaboration and active discussion with the many scientific

leaders at the conference.

Name: John Tainer
Affiliation: TSRI
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Overview: Besides hypothesis-driven research, my laboratory works on advanced technology development to bridge the gaps from molecular structure to quantitative, predictive cell biology. I have authored over 200 scientific publications and deposited 300 structures in the Protein Data Bank for researchers worldwide. However, I strive for high quality results and cross-disciplinary papers that make substantial contributions to advance and broadly impact knowledge. I am committed to collaborative research, to bringing together researchers to successfully tackle challenging problems, and to training the next generation of collaborative scientists. I am a Senior Scientist at the Lawrence Berkeley National Lab, Professor at the Scripps Research Institute, and Member of the Skaggs Institute of Chemical Biology. At the Advanced Light Source synchrotron at LBNL, I designed and direct the Structurally Integrated BiologY for Life Sciences (SIBYLS) beamline that combines macromolecular x-ray crystallography (MX) and small angle X-ray scattering (SAXS) technologies to determine high-resolution structures plus protein assembly and conformation in solution.

Presentation: I presented new metrics for accurate assessment of solution conformation and assembly by x-ray scattering. These results have implications for drug discovery and target selection as well as defining structures in solution under near physiological conditions. The metrics allow quantitative objective and high-throughput analyses. I also presented a novel method to directly compare structural

similarities without modeling from the SAXS data.

Impressions: This meeting pushed boundaries for structure-function relationships with key biological implications ranging from drug discovery to control of epigenetics. The mix of industry and academic research creates energetic discussions and useful ideas. The number of people made for many productive informal discussions and the initiation of collaborative research.

Name: Andrew Ward
Department: TSRI Dept. of Integrative Structural and Computational Biology
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Email address: abward@scripps.edu
Phone number: 858 784 7320

Overview: The second year at the new venue was great. Solid science as usual and stimulating discussions.

Presentation: I presented the use of electron microscopy to map the epitopes of broadly neutralizing antibodies on the surface of viral antigens, particularly HIV envelope (Env). Using our negative stain EM pipeline we can rapidly characterize novel Env antigens that are being developed for use in vaccine trials, providing important insights into the structure and behavior of these molecules. By coupling our observations with other biophysical assays we were able to carefully characterize these antigens and use this information to design better antigens in an iterative manner. We also showed the importance of full processing of gp160 into gp41 subunits via furin cleavage, paving the way for the next generation of Env immunogens.

Impressions: Left with new collaborations and excitement about science**.**

Name: Jim Wells
Affiliation: UCSF PC
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Phone number: 415 514 4498

Overview: Great program and meeting

Name: Jamie Williamson
Affiliation: TSRI Dept. of Integrative Structural and Computational Biology
Mailing address: 10550 North Torrey Pines Road, MB-33, La Jolla, CA 92037
Email address: jrwill@scripps.edu
Phone number: 858 784 8740

Overview: The scientific program this year was particularly excellent. The students and postdocs gave particularly interesting discussions, and even the keynote speaker hit a good note. The accommodations and venue for the meeting were excellent.

Presentation: We should work a bit more to mix the groups together...take a UCSF professor for lunch!

Impressions: This is a great mix of biomedical science. It is good to have industry sponsors present talks that I usually don't get to hear. There is plenty of time for interaction and the overall quality of the science presentations and discussion is spectacular.

Name: Ian Wilson
Affiliation: TSRI Dept. of Integrative Structural and Computational Biology
Mailing address: 10550 North Torrey Pines Road, BCC-206, La Jolla, CA 92037
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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 150) and are using many of these for structure-assisted vaccine design for flu, HIV-1 and HCV. I also direct one of the NIH PSI high-throughput structural biology centers that develops methods and technologies that are advancing structure determination by X-ray and NMR. We have great collaborations in PSI:Biology with the Fletterick group at UCSF on stem cells, the Williamson/ Salomon group at TSRI on T cells, and Kendall Nettles at Scripps Florida on nuclear receptors.

Presentation: The major surface antigen, the hemagglutinin (HA), of influenza virus is the main target of neutralizing antibodies. However, most antibodies are strain-specific and protect only against highly related strains within the same subtype. Recently, a number of antibodies are much broader and neutralize across subtypes and groups of influenza A, as well as influenza B, viruses through binding to functionally conserved sites, including the stem and receptor binding site. We have determined several x-ray and EM structures of broadly neutralizing antibodies with the HA and have identified highly conserved sites in the HA fusion (stem) in influenza A and B. We have also structurally characterized a number of antibodies that bind to the conserved receptor binding site and protect against different strains and subtypes. The identification and characterization of these exciting new antibodies provide new opportunities for structure-assisted vaccine design as well as potential therapeutics that afford greater protection against influenza viruses.

Impressions: Another terrific meeting 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. The keynote speaker Richard Lerner was a highlight of the meeting. The venue was also excellent and made for good interactions with all of the attendees. I have not missed a single meeting in 23 years and certainly don't intend to miss one in the future.

Name: Dennis Wolan
Affiliation: TSRI Dept. of Molecular and Exp. Medicine
Mailing address: 10550 North Torrey Pines Rd., MEM L43, La Jolla, CA 92037
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Phone number: 858 784 7936

Overview: Caspases are required for essential biological functions, most notably apoptosis and pyroptosis, but also cytokine production, cell proliferation, and differentiation. One of the most well studied members of this cysteine protease family includes executioner caspase-3, which plays a central role in cell apoptosis and differentiation. Unfortunately, there exists a dearth of chemical tools to selectively monitor caspase-3 activity under complex cellular and in vivo conditions due to its close homology with executioner caspase-7. Commercially available activity-based probes and substrates rely on the canonical DEVD tetrapeptide sequence which both caspases-3 and -7 recognize with similar affinity and thus the individual contributions of caspase-3 and/or -7 toward important cellular processes are irresolvable. Here, we present a variety of permutations of the DEVD peptide sequence in order to discover peptides with biased activity and recognition of caspase-3 versus caspases-6, -7, -8, and -9. Through this study, we identify fluorescent and biotinylated probes capable of selective detection of caspase-3 using key unnatural amino acids. Likewise, we determined the X-ray crystal structures of caspases-3, -7, and -8 in complex with our lead peptide inhibitor to elucidate the binding mechanism

and active site interactions that promote the selective recognition of caspase-3 over other highly homologous caspase family members.

Presentation: Specific Caspase-3 Probes with Unnatural Amino Acids

Impressions: This was my 10th meeting and I continue to be impressed with the quality of the presentations and relevance of each speaker's research. Additional to the structure-based research, I appreciated the inclusion of organic synthesis and other disciplines. I hope to be able to continue attending this high-quality meeting for years to come.

Name: Ronald Zuckermann
Affiliation: Molecular Foundry, Lawrence Berkeley National Lab
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Phone number: 510 486 7091

Overview: I direct the Biological Nanostructures Facility at the Molecular Foundry, as well as the User Program. I study bio-inspired nanomaterials, which draws heavily on advances in structural biology. This conference brings together top investigators in the field, and it is an excellent way for me to stay abreast of current advancements, as well as participate in discussions and establish new collaborations. The atmosphere is informal and it is easy to interact with other people.

Presentation: The presentations were all of exceptionally high quality.

I presented work on peptoid-based nanostructures as a new class of protein-mimetic materials. I described how we aim

to close the gap between polymer science and structural biology. I showed structural and mechanistic details of peptoid nanosheets and how they form, and their potential as a convenient platform for engineering a broad range of structure and function into 2D nanomaterials.

Impressions: The overall quality of the talks and of all the attendees was extremely high. The conference was very stimulating, and I really enjoyed discussing science with the top scientists in the field of structural biology. I really like the format of the meeting, including the 20 minute format and the 5 minute jr. scientist presentations on the first day.

AT THE 2014 CABO MEETING ---

Sunday, May 4th to Wednesday, May 7th, 2014

Barceló Los Cabos Palace

Herb Boyer, Ph.D., will be our keynote speaker. Herb is a former UCSF faculty member, co-founder of Genentech and currently Director 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.