Our History

The WMEN conference has been held for the past 20 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, eleven years ago, the venue moved from Cabo San Lucas to the all-inclusive El Presidente Hotel in San Jose del Cabo. This venue has been attractive as the conference facilities are excellent and the staff very attentive. 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, TRSI and UC Berkeley. The spirit of scientific research is enhanced and refreshed in this stunning setting with a stellar list of participants.

SCHEDULE Cabo XX, 2010
World Molecular Engineering Network Twentieth Annual Meeting on Structural Biology

2-5 May 2010, San Jose del Cabo, Baja, Mexico

Sunday Evening, 2 May

17:30 – 17:45 Andrej Sali and Ian Wilson **Introduction and Welcome**

17:45-20:00 ***Self-Introduction***

Dan Santi

Short Presentations (5+1 min.) by TSRI, UCSF, UCB Graduate Students, Postdoctoral Fellows *et al.* (Chair: Ian Wilson)

Daniel Bachovchin	TSRI	Identification and characterization of inhibitors of protein phosphatase methylesterase 1 (PPME1)
Gira Bhaba	TSRI	Divergent evolution of enzyme dynamics in dihydrofolate reductase
Damian Ekiert	TSRI	Broadly neutralizing antibodies against influenza virus hemagglutinin
Robert Kirchdoerfer	TSRI	A crystal structure of VLR4 in complex with the C-terminal domain of BclA
Dmitry Lyumkis	TSRI	New methods for *ab initio* 3-D reconstructions in single-particle electron microscopy applied to the structural characterization of macromolecular complexes
Anke Mulder	TSRI	Visualizing ribosome assembly via time resolved EM
Ashley Pratt	TSRI	Understanding the mechanism of dsRNA transport by Sid-1
Timothy Reichart	TSRI	Analysis of gp41 epitopes in model viral membranes
Cory Rillahan	TSRI	High-throughput synthesis and glycan array screening of high-affinity siglec-inhibitors

	Arne Moeller	TSRI	Carriers for membrane proteins in Cryo-EM
		Break	
	Angela Brooks	UCB	Using RNAi and RNA-Seq to identify alternative exons regulated by individual RNA binding proteins and their associated regulatory motifs
	Debajyoti Datta	UCSF	Allostery and cooperativity in caspases
	Ruchira Datta	UCB	Matchmaker: Improving alignment accuracy through phylogenomics
	Janet Finer-Moore	UCSF	Substrate Recognition by RNA-modifying enzymes
	Christophe Guilbert	UCSF	Flexible Docking with MORDOR
	Jeremy Phillips	UCSF	Integrative structure determination of a heptameric component of the nuclear pore complex
	Elena Sablin	UCSF	Nuclear receptor LRH-1 as a target in pancreatic cancer
20:00–21:00	**Reception**		**Poolside**

Monday Morning, 3 May

Advances in Proteomics (Chair: Ron Milligan)

09:00	Ian Wilson	TSRI	The expanding protein universe
09:20	Stephen Brenner	UCB	RNA regulation and personal genomics
09:40	Andrej Sali	UCSF	Determination of macromoleular structures based on 2D electron microscopy images
10:00	**Break**		
10:30	Kimmen Sjolander	UCB	New methods in protein functional site identification
10:50	Bo Huang	UCSF	STORM: super-resolution microscopy with twinkling molecules
11:10	Graham Johnson	TSRI	Automated visualization at subcellular environments

Monday Afternoon

Immunology and Biomedicine (Chair: Jim Wells)

16:30	Jacob Glanville/Arvind Rajpul	Rinat/ Pfizer	Precise determination of the diversity of an antibody library and insights into the human immunoglobulin repertoire
16:50	Jim Paulson	TSRI	Targeting B cells with glycan ligands of CD22
17:10	Shuvo Roy	UCSF	Engineered microdevices for advancing biomedicine
17:30	**Break**		

Chemical Biology (Chair: David Webb)

18:00	Floyd Romesberg	TSRI	The rise and fall of a class of natural product antibiotics
18:20	Dennis Wolan	UCSF	Small-molecule activators of a proenzyme
18:40	James Wells	UCSF	Engineering cells to death

Tuesday Morning, 4 May

SPONSORS I – (Chair: Dan Santi)

09:00	Matt Benning	Bruker	The pursuit of the trouble-free photon: a low maintenance, high brilliance x-ray source for the home lab
09:20	Angela Criswell	Rigaku	Recent advances in the home lab
09:40	Karyn O'Neill	Johnson & Johnson	Engineering alternative scaffold proteins
10:00	**Break**		
10:30	David R. Webb	Celgene	Understanding ImiD® Mechanism of action at the molecular level: a progress report
10:50	Marcos Milla	Johnson & Johnson	Small molecule antagonists targeting TNF receptor 1: where do we start?

11:10	Hans Parge	PRD West Coast Proteros	Notes from a scientific journey in Academia and Industry
11:30	**Panel Discussion**	Moderator: Dan Santi	**Current state and future prospects of Biotech:** Funding, recent changes in industry, how is translational research at universities coupled with biotech, role of NIH.
Tuesday Afternoon			**Nucleic Acids, Binding Proteins & Enzymes (Chair: Robert Stroud)**
16:30	David Millar	TSRI	DNA polymerase activity at the single-molecule level
16:50	Robert Fletterick	UCSF	Interaction of LRH-1 with beta catenin
17:10	Ron Milligan	TSRI	Microtubule binding proteins involved in cell division
17:30	**Break**		
			Membrane Proteins, etc. (Chair: Andrej Sali)
18:00	Chris Koth	Genentech	Evolving strategies for studying the structures of membrane proteins
18:20	Robert Stroud	UCSF	Insertion, folding and assembly of membrane proteins
18:40	Larissa Podust	UCSF	Targeting CYP51 for new drugs to treat Chagas Disease
Wednesday Morning, 5 May			**Assemblies, Computation, and Drug Design (Chair: Kimmen Sjolander)**
09:00	Mark Yeager	TSRI	Structure of the HIV-1 Capsid: A molecule jigsaw puzzle
09:20	Thomas James	UCSF	What can we do about HIV-1 genome dimerization/packaging?
09:40	Todd Yeates	UCLA	New structures of protein-based bacterial organelles: The ethanolamine utilization microcompartment in *E. coli*
10:00	**Break**		

10:30	Jeff Blaney	Genentech	Unexpected structure-based design failures and successes from fragment hits
10:50	James McKerrow	UCSF	Targeting parasite proteases for new drugs to treat neglected tropical diseases
11:10	Art Olson	TSRI	Recent progress in computational drug design
11:30	Ian Wilson and Andrej Sali		**Closing Remarks**

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

WMEN Conference
San Jose del Cabo
El Presidente Hotel

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Presentation: My research is focused on the discovery and characterization of selective inhibitors of uncharacterized or poorly characterized enzymes. Specifically, I have introduced a substrate-free screening platform (fluopol-ABPP) for HTS that monitors the reaction of broad-spectrum, activity-based probes with enzymes using fluorescence polarization. In collaboration with the Molecular Libraries Screening Center Network (MLSCN), I have applied fluopol-ABPP to screen a dozen previously HTS-inaccessible enzymes against a large (300,000+) compound library, successfully identifying lead candidates for nearly all of these targets. Most notably, I have discovered a remarkably potent and selective inhibitor of protein methylesterase-1 (PME-1), a serine hydrolase that removes the reversible post-translational C-terminal methylesterification of PP2A.

Impressions: I thought the meeting was great. I am not a structural biologist, so this conference exposed me to a wide variety of science that I don't normally have the chance to see.

Name: Gira Bhabha
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Presentation: Different dynamics in structurally conserved E. coli and human dihydrofolate reductases.

Impressions: -great science
-most talks really good, style and content
-personally would have preferred shorter conference with higher density of talks and less downtime

Name: Jeff Blaney
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Overview: My group provides cheminformatics and computer-assisted drug discovery support for small molecule discovery projects. This includes structure-based design (e.g. docking, 3D-shape and pharmacophore searching, interactive design, conformational analysis), fragment-based discovery, calculation of physicochemical properties (e.g. LogP, pKa, TPSA, etc.), machine-learning models for in vitro DMPK properties (e.g. clearance), collection and dissemination of all experimental (e.g. biochemical, physicochemical,analytical, cell biology, in vivo) and calculated data through a chemical/biological database and query system.

Presentation: I summarized the current state of the art and issues in Fragment-Based Lead Discovery, focusing on lessons from unexpected successes and failures on HCV Polymerase. Part of this story was published in Antonysamy et al. Fragment-based discovery of hepatitis C virus NS5b RNA polymerase inhibitors. Bioorg. Med. Chem. Lett. (2008) 18, 2990. Success resulted from an unexpected apparent Pi-Pi stacking interaction between the plane of a tertiary carboxamide and the sidechains of a His-Ser pair on the surface of the enzyme. An intensive structure-based design

effort to place aromatic rings into a groove on the enzyme failed to improve potency. The enzyme proved to be too rigid; cocrystal structures proved we achieved the intended structural result, but with no gains in potency.

Impressions: Excellent venue, great opportunities for informal discussion outside of talks, along with good Q&A during talks. Terrific program covering many different areas, including outstanding talks in areas I normally don't come across. Great depth and breadth of different science.

Name: Steven E. Brenner
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Overview: My laboratory uses computational genomics approaches to understand RNA regulation, protein function prediction, and personal genome interpretation.

Presentation: I presented work demonstrating the extreme evolutionary history of a Byznatine mode of gene regulation. Nonsense-mediated mRNA decay (NMD) is a cellular RNA surveillance system that recognizes transcripts with premature termination codons and degrades them. We discovered large numbers of natural alternative splice forms that appear to be targets for NMD. This coupling of alternative splicing and RNA surveillance can be used as a means of gene regulation. We found that all conserved members of the human SR family of splice regulators have an unproductive alternative mRNA isoform targeted for NMD. Preliminary data suggest that this is used for creating a network of auto- and cross-regulation of splice factors. Strikingly, the splice pattern for each SR protein is shared with mouse, and each alternative splice is associated with an ultraconserved or highly-conserved region of ~100 or more

nucleotides of perfect identity between human and mouse. We have recently dissected the evolutionary history of members of this family, discovering that while the unproductive splicing dates back to the pre-Cambrian, nearly every human SR gene has its own distinctive sequences for unproductive splicing. As a result, this elaborate mode of gene regulation has ancient origins and can involve exceptionally conserved sequences, yet after gene duplication it evolves swiftly and often.

Impressions: This meeting is one I look forward to attending on a routine basis because of the outstanding quality of the research, the small size and integrated location that facilitates extensive interaction amongst participants, and the geographic connections amongst the presenters that support future joint efforts arising from the meeting. The rapid-pace format allows covering many topics, of which most germane ones for each attendee are discussed in detail during the breaks. In terms of new-ideas-per-minute, this meeting led off being one of the best in the past year.

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Presentation: Our group studies alternative splicing regulation in D. melanogaster. The aim of our project is to identify alternatively spliced exons that are regulated by 60 RNA binding proteins by first individually depleting the proteins in the S2 cell line and assaying changes in mRNA splicing using ultra high-throughput sequencing of the transcriptome. Thorough analysis of exons regulated by one splicing regulator, Pasilla, showed that the protein both activates and represses splicing and that the mechanism of

its splicing regulation may be conserved from mammals to fly.

Impressions: I felt both the short student/post-doc talks and the long PI talks were clear and well presented. The location was excellent. My only suggestion would be to have an additional reception or dinner that involves everyone in order to facilitate more interaction with the entire group.

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Presentation: Allostery and cooperativity in caspases.

Impressions: I thought it was a great meeting that provided the opportunity to see various fields of work and also meet people from other institutions. I think the conference would be valuable to more UCSF graduate students if they are able to attend.

Name: Ruchira S. Datta
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Presentation: Motivation: Alignment of distantly related pairs of proteins is a first step for predicting protein structure and comparative (homology) model construction. The

accuracy of the pairwise alignment between a target of unknown structure and a solved structure template is known to be the most critical aspect of a homology modeling pipeline. MatchMaker uses a phylogenomic approach to systematically explore candidate stepping stones in sequence space to bridge the gap between distantly related proteins.
Results: We present a comparison of MatchMaker, COMPASS, and HHalign. On a dataset of 37 structurally aligned pairs from the SABmark benchmark, MatchMaker produces significantly superior pairwise alignments than each of these methods. Remaining challenges and potential solutions in producing a system for large-scale deployment are discussed.

Impressions: I enjoyed the superb line-up of structural biology talks and the size of the conference, intimate enough that I could start getting to know the interesting new people I met.

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Presentation: Pre-existing immunity to H1N1 swine flu

Impressions: Excellent scientific content, very stimulating sessions. But the density was too low (better to have 1.5-2 full days and be done with it, rather than stretch it out over 4 days).

Name: Janet Finer-Moore
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Presentation: Pseudouridine synthases catalyze the most common modification of noncoding RNA, isomerization of uridine to pseudouridine. Pseudouridine synthases comprise a large family of enzymes with structurally conserved catalytic cores and nonconserved accessory domains that determine substrate selectivity. We have used X-ray crystallography, mutagenesis, and biochemical assays to determine why some pseudouridine synthases are relatively promiscuous, modifying several sites within an RNA substrate, while other pseudouridine synthases are specific for a single site. TruA modifies the anticodon stem loops of most tRNAs at any one of three positions. The basis for this regional specificity is a flexible stem loop, which can adopt at least three distinct conformations after tRNA is docked to the enzyme; each conformation orients one of the target uridines for catalysis. RluF, on the other hand, specifically modifies only one of two adjacent uridines on stem loop in E. coli ribosomal RNA. Binding of the substrate stem loop to RluF triggers conformational changes in the enzyme and concomitant base pair rearrangement in the stem loop. These rearrangements uniquely position the target uridine so that it can flip into the active site.

Impressions: There was an interesting mix of speakers and the quality of the talks was very high. It was impressive that most people attended the whole meeting and there were thoughtful questions after most talks. Company representatives were very engaged and contributed a lot to the scientific discussion. The format of talks in the morning and evening with afternoons free was enjoyable.

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Overview: The meeting was fabulous. After the talks there were many, many questions and answers and good discussions at the presentations and at free time.

Presentation: I spoke about the nuclear receptor LRH-1. This protein controls cell differentiation and relates to determination of embryonic stem cells. I showed the structure for the hormone binding domain of this protein in a two protein complex with the oncogene beta-catenin. This was the first structure for this oncogene with a protein. The structure revealed how the LRH-1 receptor acts as a scaffolding protein to attract coactivators, repressors and beta catenin to build machines that control transcription. There may be important biological consequences of these interactions with LRH-1 since it is the only protein shown by SNP analysis to be associated with pancreatic cancers.

Impressions: The venue was very hospitable. The hotel staff were helpful and attentive and the meeting room, grounds and rooms were very comfortable. The meeting and talks were appropriate in length.
This was the most interactive meeting that I have been to in several years.
My single suggestion for improving the meeting would be to turn the air conditioning down in the meeting room.

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Presentation: Flexible Docking with MORDOR

Impressions: It is very clear that this meeting is a must.
I was very impressed by the quality of the talks.
People from the industry were meeting those working in academia. I think that the location and organization did really favor interactions between both worlds!

Name: Bo Huang
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Overview: Our current research program mainly focuses on the development of super-resolution light microscopy techniques and their applications in structural biology and neuron cell biology. Specifically, for the application in structural biology, we are developing an optical approach to resolve the architecture of macromolecular complexes, which includes a suite of new methods in instrumentation, specific protein labeling, and data analysis. The yeast nuclear pore complex (NPC) and the centrosome are the two structures of major interest to us. In the other direction, we are interested in understanding the spatial organization and dynamics of protein machinery in neuronal synapses, especially those involved in synaptogenesis, neurotransmitter release and synaptic vesicle recycling.

Presentation: The ability of fluorescence microscopy to perform noninvasive imaging of live samples with molecular specificity has made it one of the most powerful imaging techniques to study cellular processes. However, the diffraction of light limits the spatial resolution of conventional fluorescence microscopy, leaving many biological structures too small to be observed in detail. To overcome this limit, we have developed the Stochastic Optical Reconstruction Microscopy (STORM) technique. It utilizes the photoswitching of fluorophores to isolate their spatially overlapped images, and single-molecule localization to reconstruct the sample structure with the position of labeled fluorescent probes. We have achieved a 20-30 nm lateral resolution in cellular samples, which is an improvement by more than an order of magnitude over conventional fluorescence microscopy. The incorporation of three-dimensional (3D) single molecule localization further enables 3D STORM of a whole cell with 50-60 nm axial resolution. We have also created photoswitchable fluorophores for multicolor imaging by combinatorial pairing of various activator dyes and reporter dyes. We have demonstrated the ability of STORM to visualize structures unresolvable by conventional fluorescence microscopy, including in vitro reconstituted clathrin-mediated endocytic machinery.

Impressions: The size, location and the length of the meeting were perfect and the science was great. This is my very first trip to the Cabo meeting and it was fantastic!

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Overview: Major goals of our research are (a) to investigate

selected biological processes that have RNA as an essential component at the molecular level, which typically entails studies of molecular interactions as well as biomolecular structure and dynamics often using NMR, and (b) to use three-dimensional nucleic acid structures with computational search algorithms and subsequent NMR screening to discover novel ligands. The subjects for study are chosen to be targets for subsequent drug design.

Presentation: What can we do about HIV-1 genome dimerization/packaging? With growing resistance of HIV-1 to current drugs based significantly on the proclivity of HIV-1 to mutate, there is need for research on other HIV-1 targets. Although it may not be possible to devise a drug to which resistance will never emerge, some molecular targets are constrained by structure and function, and therefore may be more difficult for the virus to alter in order to acquire resistance. Also due to cross-resistance, it is also mandatory to find new molecular targets. We are exploring a crucial feature in viral replication entailing the HIV-1 RNA genome. Each retroviral particle contains two copies of HIV-1 RNA as a noncovalent dimer with strands aligned parallel and in register, contacting each other most stably at a highly conserved region called the dimer linkage site (DLS) within the 5'UTR. We use NMR and other techniques to examine the intermolecular interaction and refolding of the RNA, including structure determination. Our lab also has a program to identify new small-molecule ligands, entailing three-dimensional RNA structure-based virtual screening and NMR, with the aim of modifying the genomic refolding such that the production of mature infectious virions can be inhibited. We have developed a computational screening algorithm, MORDOR, which is most suitable for screening a large database of compounds for binding to RNA, as MORDOR permits docking of a flexible small molecule with a flexible target, and RNA is generally a more flexible target than is a protein. Using NMR, we have identified ligands that bind to the genomic moiety involved with initial steps in HIV-1 genome dimerization.

Impressions: Location: Excellent
Number of participants: Just right
Length: Just right

The presentations and quality of science presented were first-rate. The size of the meeting, focus of interests, location in an isolated setting conducive to strong interactions among participants, and quality of the science presented made this one of the best meetings I have attended. Although I had some notion of the research areas of my colleagues, it was good to have those updated as well as learn much more about the exciting research at Scripps, at UC Berkeley, and at the industrial labs represented.

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Presentation: Automated Visualization of Subcellular Environments

Impressions: Good depth and breadth within the discipline of structure and exciting diversity at the fringe. The mix of social to seminar time works well to aid networking. I've made several project connections at this meeting over the years.

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Presentation: All vertebrate species posses an adaptive immune system. However the adaptive immune system of jawless fish like lamprey and hagfish, evolved independently of the immunoglobulin-based immune systems of other vertebrates. Jawless fish instead solved the problems of antigen recognition by shuffling together leucine-rich-repeats into variable lymphocyte receptors (VLR). We have determined the crystal structure of VLR4 in complex with its antigen, BclA. This structure revealed that VLR4 binds BclA on its concave surface and makes extensive use of the LRRCT loop to bind a groove on the surface of the antigen. These findings are similar to those reported in other VLR-antigen complexes and reveal the conformational diversity of the VLR to bind diverse antigens.

Impressions: The meeting was great. I liked the format of the talks and the diversity of the audience. I believe that the participants from industry really added to the dynamic. I think the meeting could be improved by better encouraging faculty-student interactions as well as a better format for the panel discussion. It would be good to see a round-table discussion about a current topic rather than a panel of descriptions from different walks of life.

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Overview: We study the structure and function of proteins of therapeutic interest and their interactions with ligands. We currently support several small- and large-molecule targets in various therapeutic areas, including Parkinson's disease and diabetes. Whenever possible, we attempt to develop

and implement automated high-throughput (HTP) methods that build our capacity to screen, purify and perform structural studies of therapeutic targets.

Presentation: Among the many therapeutic targets we study, some are membrane proteins. We are developing various approaches for enabling structural studies of these challenging targets, including a high-throughput screening assay that permits rapid expression, solubilization and stability scouting of many constructs. The application of this approach to Class B G protein-coupled receptors and voltage-gated ion channels is currently being pursued.

Impressions: Location: Fantastic
Number of participants: Perfect
Length of meeting: Just right

The size of this meeting promotes considerable scientific discussion and fosters future collaborations. It is just right. Without exception, the presentations were of very high quality. The 5-minute student presentations in the first session were particularly impressive. Many speakers discussed highly innovative approaches they had developed to solve basic biological problems. There was a healthy mix of research from multiple disciplines.

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Presentation: Over the last several years, our lab has been developing a software package called Appion, which enables

routine, streamlined image processing for many separate operations within single-particle electron microscopy. Their combinatorial use is becoming increasingly necessary in order to reconstruct a good 3D map. In building this "pipeline" for image processing in EM, our goal is to make the procedures integrated with one another, and most importantly, transparent. At the conference, I have presented an overview of the Appion package. I also talked about the expansion of Appion and the incorporation of a comprehensive "toolbox" for ab initio 3D reconstructions of biological samples using several different strategies. The combinatorial use of the techniques within this toolbox facilitates overcoming the fundamental challenge of establishing a reliable 3D map using only 2D projection images. I finished by presenting data on the optimization of a distinct type of reconstruction procedure entitled angular reconstitution. The aberrant nature of the algorithm as it is generally employed can be addressed with a highly automated and iterative approach, which attempts to recover the individual reconstructions that are most consistent with the input data.

Impressions: This meeting had exceeded my expectations. By incorporating talks from both academic and industry environments, the conference successfully presented several sides to the current state of molecular engineering. With respect to the former, I very much enjoyed listening to some of the hybrid approaches to structural biology, which were prevalent at this conference and allowed me to make some useful connections. I was also very pleased to hear the candid stories from the discussion panel from industry representatives. To me, the broad nature of the conference was very successful, and I was quite pleased to get a chance to speak rather than present a poster.

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Overview: Excellent focus and the right number of participants

Presentation: The Challenges of Drug Discovery/Development Targeting Neglected Parasitic Diseases

Impressions: A great opportunity for interaction, networking and building new collaborations. Bo Huang and I got together this week to follow up on some ideas. I would just suggest more biotech/VC participation next time.

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Overview: My group employs approaches from molecular pharmacology and biochemistry to support efforts aimed at the identification and optimization of small molecules targeting receptors and enzymes relevant to inflammatory diseases. As part of these activities, we are studying selected cytokine receptors as targets for the discovery of small molecule antagonists, by exploiting exo-site/allosteric mechanisms.

Presentation: Signaling events triggered by the pro-inflammatory cytokine tumor necrosis factor-alpha (TNF) play a major role in the development of several autoimmune diseases including rheumatoid arthritis, inflammatory bowel disease and psoriasis. In fact, several biodrugs acting as TNF scavengers have demonstrated efficacy in the clinic for the treatment of these diseases. Surprisingly, little is know

about how TNF receptor family members become active in response to cytokine binding. Our studies with osteoprotegerin, a naturally soluble TNF receptor family member, demonstrate that receptor oligomerization occurs prior to cytokine binding, and is actually critical for the high affinity of that interaction. Pre-ligand receptor oligomerization and ligand-dependent conformational transitions offer novel points of entry for the discovery of small molecules that modulate such events.

Impressions: Location: excellent
Number of participants: perfect
Length of meeting: just right
I truly enjoyed the highly interactive yet relaxed environment, and especially the effort that the organizers placed in recruiting industry participants. Having everyone presenting really adds a lot to the dynamic of the conference. This is a great format and with a bit more regional diversity (invited speakers from UC-Berkeley, UCSD, Stanford, the Salk and Sanford-Burnham Institutes) it could further establish the WMEN as one of the premier meetings in structural biology.

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Overview: My lab is involved in the development and application of single-molecule fluorescence methods. We have three main areas of interest: (1) Ribonucleoprotein assembly during nuclear export of HIV-1 mRNA, (2) Structural dynamics of DNA replication enzymes, and (3) Dynamics of integral membrane proteins.

Presentation: This year I described our most recent studies of DNA polymerase dynamics. DNA polymerases are essential components of the cellular machinery in all

organisms, responsible for the accurate replication and repair of genetic material. To achieve high fidelity replication of DNA, polymerases must select the correct incoming nucleotide substrate during each cycle of incorporation, and reject incorrect nucleotides. While X-ray crystal structures have provided static snapshots of the polymerase at some points in the reaction cycle, the actual sequence of events occurring during nucleotide incorporation has not been observed directly. We have developed a single-molecule FRET system to monitor dynamic conformational changes of a DNA polymerase (Klenow fragment) during nucleotide selection and incorporation. In this system, a donor dye was attached to a specific base within the DNA primer/template, immobilized on a quartz surface, and an acceptor was attached at various positions on the polymerase, using a range of engineered single cysteine mutants. FRET trajectories of individual polymerase-DNA complexes were recorded using TIRF microscopy. In the absence of any nucleotide substrates, the polymerase-DNA complex continually fluctuates between three distinct FRET states. Following initial docking with the DNA primer/template, the polymerase partitions between “open” and “closed” conformations, while also dissociating frequently from the DNA. However, when the correct incoming nucleotide is present, the polymerase preferentially populates the closed conformation and remains stably bound to the DNA, presumably in readiness for the ensuing phosphoryl transfer reaction. In contrast, the presence of incorrect nucleotide substrates drives the polymerase-DNA complex into a unique conformation, previously unknown, in which the DNA primer terminus is remote from the polymerase active site. Moreover, this complex is kinetically unstable, undergoing rapid dissociation. This state may act as a roadblock to prevent nucleotide misincorporation.

Impressions: This was another successful and highly enjoyable meeting. The WMEN meeting is one of the most informative meetings that I typically attend and has become a highlight of the scientific year for me. The breadth of topics and the quality of the science presented are always

outstanding. This meeting provides a unique opportunity to learn about exciting new areas of research at both Scripps and UCSF, while mixing with both groups of colleagues in a friendly, relaxed atmosphere. The number of participants is just right and there is a good mix of faculty, postdocs and graduate students. The duration of the meeting is also perfect. The El Presidente is getting a bit dated, but it continues to provide a convenient venue for the meeting.

Name: Ron Milligan
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Overview: My lab uses molecular electron microscopy to study the structure and mechanism of action of a number of cellular machines. One focus of the lab is molecular motors - myosin, kinesin, dynein - and microtubule associated proteins involved in cell division. A second focus is membrane proteins such as drug transporters and toxins. Our overall goal is to visualize the conformational changes these machines undergo during their functional cycles.

Presentation: I presented recent work on botulinum toxin associating with lipid membranes at different pHs. Our data suggest that at low pH, the toxin becomes more intimately associated with the membrane and appears to disrupt the underlying leaflet of the bilayer. Under the condition so our study, there is no channel traversing the membrane.

Impressions: This was an outstanding meeting. The size and duration is ideal for promoting interactions and fostering new collaborations between the participants. I will definitely go again.

Name: Arne Moeller

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Presentation: Carriers for Membrane Proteins in Cryo-EM

Impressions: It was a great meeting. It was very well organized and interesting.
It really helped me, being new to San Diego and TSRI, to get into contact with the other groups and start exciting collaborations. I really liked the mixture of presentations from industry and academy.

Name: Anke Mulder
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Presentation: 30S Ribosome Assembly

Impressions: Enjoyed the TSRI student talks. UCSF 5-minute talks were too long and not of the same caliber. Faculty and sponsor presentations were great. Wonderful conference for networking.

Name: Arthur Olson
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Overview: My laboratory focuses on computational molecular biology developing and applying software to analyze, predict and visualize biomolecular interactions.

Presentation: This year I presented AutoDock Vina a new docking program developed in the lab. The program uses a simplified scoring function derived by machine learning to co-optimize both structural and energetic correlations with observed complexes. It also uses explicit gradient information to accelerate the search of the energy landscape. In comparison tests, AutoDock Vina outperforms our AutoDock code in both accuracy and speed.

Impressions: As usual, an outstanding meeting, both in terms of the science presented, and the interaction between the participants.

Name: Hans E. Parge PhD
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Overview: Europe's most experienced and largest company focusing on X-ray protein structure analysis. Successful in business since 1998, the company has continuously expanded its client base and collaborates with more than 40 international pharma, biotech and agro companies. Proteros offers expertise and innovative platform technologies to improve productivity of structure-based drug discovery through research services, product sales, and licensing.

Presentation: The presentation detailed some personal notes on a life pursuing macromolecular structural work in

academia and the pharmaceutical industry. Henry David Thoreau summarizes my experiences very well at the end of his Walden essay with the following observation: *"If one advances confidently in the direction of one dreams, endeavoring to live the life one has imagined, one will meet with uncommon success in normal hours*". I'll add a helpful piece of advice from Vince Lombardi *"get fired up with enthusiasm or you will be fired with enthusiasm".*
As regards my ongoing quest to make safe medicines, I find myself extremely fortunate to be involved with Proteros, a premier SBDD technology focused CRO, leading the way to make this possible.

Impressions: This is always my favorite meeting when I can make it. The location and format is close to perfect with most everybody getting an opportunity to present. The quality is always top notch and the graduate students this year have outdone themselves once again. I can unequivocally recommend this venue to any industrial sponsor.

Name: James C. Paulson
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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 main interests are in the siglec family of glycan binding proteins that are expressed on most white blood cells, and both mediate cell-cell interactions and regulate cell signaling receptors. I am

also the Principle Investigator of the Consortium for Functional Glycomics, a large NIH funded consortium that comprises 500 investigators worldwide

Presentation: This year I described the development of liposomal nanoparticles that are targeted to B cells by virtue of being decorated with glycan ligands of the B cell receptor CD22. The targeted liposomes efficiently target B cells in vivo, and are rapidly endocytosed. We have demonstrated that CD22-targeted liposomes loaded with the chemotherapeutic doxorubicin exhibit strong efficacy in reducing lethality in a murine model of human B cell lymphoma. The liposomes also target and kill human patient B cell leukemia/lymphoma cells in proportion to the amount of CD22 expressed on them. Since other siglecs are expressed on other types of white blood cells, the results suggest the potential for a broad platform for cell specific targeting by conjugating the respective glycan ligand of the siglec(s) expressed on that cell.

Impressions: Although there was hiatus of one year due to the economy in 2009, the World Engineering Conference resumed with the extraordinary high quality that has made it a an annual pilgrimage for many attendees. As always, the presentations mix of students, faculty, technology companies and sponsors give this meeting a unique blend of perspectives. While the sessions were all terrific, the morning covering innovations in EM and light microscopy and graphical representations of cell biology was just transporting. I found myself talking about it in numerous conversations in the weeks to follow. I expect that word of mouth from this year will further increase enthusiasm and interest to attend next years meeting. It goes without saying that the superb science is enhanced by the venue and ambiance of CABO.

Name: Jeremy Phillips
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Presentation: The nuclear pore complex (NPC) is a multiprotein assembly that serves as the sole mediator of exchange of macromolecules between the nucleoplasm and the cytoplasm in eukaryotic cells. We have applied a highly integrative approach to determine the overall structure of the Nup84 complex, one of the essential subcomplexes forming the scaffold of the NPC. Using predicted solvent accessible disordered segments as truncations points, we isolated different tagged versions of various Nup84 complex nucleoporin domains and analyzed their interactions by high performance immunoprecipitation and mass spectrometry. We also generated 2D negative stain electron microscopy images of the complex. We translated these data into spatial restraints and applied the restraints to crystal structures and homology models of individual proteins and domains, determining a pseudo-atomic model of the Nup84 complex. This work demonstrates the utility of using an integrative structure determination approach that incorporates all available information about a macromolecular assembly.

Impressions: I enjoyed the meeting and thought it was very well run. I think the size of the group was near-optimal, as it allowed for more interactions between students/postdocs and faculty in small groups than would not otherwise be possible. The location was great and less expensive than the vast majority of conferences I've previously attended. I'd suggest a further skew in the direction of industry speakers over academics (if possible), as the participation of industry is something that makes this meeting very unique. The meeting length and talk lengths were all fine - the short talks allow for the most broad overview of research topics from the attendees, which was appropriate for this meeting

Name: Larissa M. Podust
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Overview: My research focuses on structure-aided design of inhibitors targeting sterol 14a-demethylase (CYP51), a validated drug target in pathogenic fungi and protozoa. We are developing and applying high-throughput screening, medicinal chemistry, and x-ray crystallography methods to identify, validate and optimize promising inhibitors of CYP 51 in the multi-disciplinary environment of the Sandler Center at UCSF.

Presentation: We have structurally characterized CYP51 targets in the parasites *Trypanosoma cruzi* and *Trypanosoma brucei,* and identified and validated a potent inhibitor of *T. cruzi* in a mouse model of Chagas Disease. In parallel efforts, we probe the structural space of the *T. cruzi* CYP51 active site with a library of small-molecule compounds to identify novel scaffolds. Upon validation, these drug design frameworks will be tested for binding to CYP51 targets in different pathogenic and host species. Over the course of the coming year we will explore this approach with a view to selection of scaffolds with reduced host-pathogen cross-reactivity. We will present our results at the next Cabo meeting.

Impressions of the meeting:
Location: Excellent
Number of participants: Excellent
Length of meeting: Just right.

The size of the meeting this year was perfect. The small size provided an excellent basis for interaction amongst all participants. The presentations were of very high quality throughout. The meeting is an excellent forum for discussion and fostering of new ideas and collaborations.

Suggestion for next year: group together presentations from the same lab (PI and postdocs). A backgrounder by the PI at the beginning would set the stage for the group's 5-min individual presentations.

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Presentation: My research aims to understand the mechanism of the Sid-1 RNA transporter. Sid-1 is a transmembrane protein involved in cellular import of silencing dsRNA in the worm *C. elegans*, and possibly in higher organisms as well. We are pursuing an x-ray crystal structure of the protein, first focusing on its large, ectodomain, which appears to form a pore-shaped oligomer. Using functional assays to study substrate preferences of the full-length transporter, we have determined that Sid-1 exhibits some flexibility in recognition of RNA for transport. We hope to couple both structural and functional data to clarify how this natural transporter of gene silencing information functions.

Impressions: I really enjoyed the meeting, and found the location, group size and length to be ideal. The talks were excellent, and I took home a lot of interesting ideas to think about. As for the sponsors, I expected mostly product informational pitches, and was pleasantly surprised to hear mostly research and applicable findings. My only suggestion might be a second organized dinner or lunch, where people had another chance to speak with each other, as not everyone was around during the breaks or up late at night.

Name: Arvind Rajpal
Department: Rinat

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Overview: I found the conference to be very informative and the environment to be relaxed and intimate, which facilitated several fruitful and interesting conversations.

Presentation: Some of the presentations were very illumination (i.e. the talk on Sid1 an its role in dsRNA entry, allostery in caspases, and the talks on membrane proteins). I found the short format of 5 minutes to be very interesting and surprisingly effective way of rapid dissemination of results and ideas.

Impressions: This was my first time and I had a wonderful time. I hope to return in the future. Sun, sand, sangria, and science...what else could you ask for. :)

Name: Timothy Reichart
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Presentation: My works focuses on incorporating synthetic transmembrane peptides into a soluble membrane mimetic called Nanodiscs. The synthetic peptides are based off of the membrane proximal external region (MPER) of the HIV protein gp41, and have a variety of modification in order to probe the binding characteristics of HIV-1 neutralizing antibodies.

Impressions: The meeting was fantastic. I particularly liked the unique format where every participant presented their research. Short talks are difficult to prepare for, but when done well they are extremely informative to the whole

audience, and many result in much longer discussions of science after the presentation.

Name: Cory Rillahan
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Presentation: My presentation was on high-throughput inhibitor screening of sialyltransferases. In collaboration with the Scripps Molecular Screening Center I have developed a fluorescence-polarization based assay to screen for inhibitors of mammalian sialyltransferases. I have screened ~16,000 compounds against three sialyltransferases and have identified both pan- and selective- inhibitors using this method. These initial hits are currently being tested for in vitro efficacy, and larger libraries are being screened simultaneously to identify even more potent and selective molecules.

Impressions: Overall the meeting was great. The talks from both the PI's and sponsors alike were of very high caliber. I would also note that the size of the meeting is really nice and encourages discussion amongst all attendees (especially since everyone presents).

Name: Floyd Romesberg
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Overview: As always, this meeting was great.

Presentation: The rise and fall of a class of natural product antibiotics

Impressions: The combination of the science and the environment is really fantastic. I really don't have any major suggestions to improve it. Perhaps the only minor suggestion would be to mix the student talks in with the PI talks. So many short talks in a row are difficult to follow, and if mixed in with the PI talks, a short talk would be refreshing. Also, it might allow us to give a little more time to the student talks (sometimes they seem like they would be amongst the best presentations if only they had a little more time). It would probably only reduce the afternoon break by 20 min.

Name: Shuvo Roy
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Overview: The general topic of the meeting is outside my research area, which is the development and application of bioengineering for medical applications. However, I was intrigued by the possibility of learning more about molecular engineering and the range of tools available. I also hoped that I could excite my colleagues about the possibilities of my work, and possibly develop collaboration across the widely disparate fields.

Presentation: I felt that the meeting was very well organized and the sessions were organized around cogent themes. While most of the material was beyond the scope of my research, I thought that most presentations conveyed the knowledge and state-of-the-research very well. To get outsiders (like myself) more calibrated to the latest research and significance, it might be worthwhile to consider a "big

picture" session perhaps during a lunch or dinner. Another suggestion would be to host the presentations on a website for review after the meeting.

Impressions: The facilities and location of the meeting were fantastic. I thought that having a mixture of postdocs and faculty was particularly exciting, and with the overall small number of attendees, this made for intimate interactions that might not normally happen within the regular lab or conference environments. Finally, while the topic of the meeting was far from my research field, I am appreciative of the opportunity to learn more about structural biology and the impressive work that has been done by pioneers in this field.

Name: Elena Sablin
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Presentation: My current research is focused on mechanisms of regulation of the nuclear receptor LRH-1 and its role in development and progression of pancreatic cancer. Preliminary data show that LRH-1 is significantly up-regulated in both human pancreatic cancer cells and pancreatic ductal adenocarcinoma tumors. Selective blocking of LRH-1 by receptor specific siRNA leads to inhibition of pancreatic cancer cell proliferation. These data suggest that LRH-1 could be a marker of pancreatic oncogenesis and a plausible therapeutic target for treatment of pancreatic cancer.

Impressions: I enjoyed the meeting very much. The short talks by students and postdocs were very impressive, addressing numerous questions critical for modern molecular and structural biology. The PI's presentations

were informative and stimulating. I was very fortunate to have the opportunity to talk to many outstanding young and established scientists, including the sponsors whose talks were very thoughtful and multifaceted. The current format and location for this meeting are superb, and I would recommend no changes for the future meetings.

Investigator: 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: To determine a macromolecular assembly structure by single particle electron microscopy (EM), a large number of two-dimensional (2D) particle images need to be collected, aligned, averaged, clustered and finally assembled via reconstruction into a three-dimensional (3D) density map. This process is limited by the number and quality of the particle images, the accuracy of the initial model and compositional and conformational heterogeneities. We developed a computational method that bypasses single particle reconstruction by translating 2D images into spatial restraints, adding other spatial restraints (e.g., molecular

docking, cross-linking, proteomics derived protein interactions), and modeling against all restraints as implemented in our Integrative Modeling Platform (IMP) package (http://salilab.org/imp). The method was described, benchmarked, and illustrated by its application to a 7-member Nup84 complex, part of the Nuclear Pore Complex.

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

There was plenty of time to be engaged in free format discussions with other participants. A large fraction of presentations were inspiring and informative.

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Overview: Interesting meeting as usual.

Presentation: In my talk, I described new methods for predicting enzyme active sites.

Impressions: Well-organized with good talks.

Name: Robert M. Stroud
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Overview: The project I described was titled 'Insertion Folding and Assembly of Membrane Proteins'. The work from my laboratory discussed the mechanisms that determine correct targeting of membrane proteins and receptors, highlighted by the structural determinations of membrane protein structures at high resolution by X-ray crystallography. Particularly I discussed the signal recognition system and the structure of the translocon through which membrane proteins get inserted into their membrane.

Presentation: The mechanism of signal-dependent targeting was described in reference to a high resolution structure of the SRP in complex with its receptor SR that directs targeting to the translocon pore in the target membrane. The structure of the translocon, a three-protein complex was presented and revealed a partially opened pore that enables lateral movement of membrane proteins into the membrane during folding. The C-terminus was shown to be a key trigger to the interaction with the ribosome. .Alongside, two human membrane proteins, expressed heterologously, were defined for the first human Rh factor, and for an Aquaporin from human brain that is a target for drugs against the damage in the brain following stroke. These Protein crystal structure reveal key roles in the understanding of an essential process in cell biology.

Impressions: Location: Excellent.
Number of participants: Good size
Length of meeting: Just right

Convenient for access from California, and sufficiently remote to concentrate people's time and attention. Cabo San Lucas is excellent after refinement of location over the years.
Number of participants: A comfortable size for the meeting is about 40 people, with 20 speakers. Attendees and presenters were excellently chosen from the superb groups

in structural biology at Scripps and at UCSF.
Length of meeting: The meeting of 3 days length is quite adequate and more would probably be too much.

The science presented was absolutely first rate with many important new breakthroughs in the fields of immunology, drug design, chemical basis for inhibition, chemical basis for understanding enzyme mechanisms and cell surface receptor interactions.

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Overview: Celgene is a biotechnology company dedicated to delivering novel therapies for life threatening diseases with a focus in oncology and inflammatory and autoimmune diseases. Its main products are used for the treatment of hematological malignancies including multiple myeloma, lymphomas, and leukemias. A number of new products are currently in clinical development for hematological

Presentation: We are currently engaged in a significant effort to understand the molecular details of how our immunomodulatory drugs known as IMiDs, such as lenolidimide exert their biological effects. The data gathered so far show that the mode of action involves elements of the cytoskeleton, small molecular weight G-proteins such as Rho, and the Wnt pathway. Studies by us and others are drilling down to understand exactly what are the key molecular targets of these drugs.

Impressions: The meeting is an excellent opportunity to see what is going on at the cutting edge of protein engineering and structural biology. The size is perfect and the insistence

that everyone speak is a key element of the quality of the meeting. I would definitely attend again and will continue to support the meeting.

Name: Jim Wells
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Overview: Great colleagues and fun meeting. I thought would be good to get the attendance up, and provide mixers for interacting more with students (maybe posters in addition to the Blitz presentations). Good to have industrial folks there.

Presentation: Generally good.

Impressions: The venue is fine, but a hassle to get to and feel a bit trapped there. I think good to consider some California locations. There are some desert locales that I think would be interesting to check out and less expensive too.

Name: Ian A. Wilson
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Overview: My lab works on structural immunology and structural virology, and we focus on recognition of microbial pathogens by the immune system. We have a large effort in HIV-1 and influenza (1918 and H5N1) their recognition and neutralization by broadly neutralizing antibodies.

Presentation: In the Joint Center for Structural Genomics (JCSG), we are exploring the expanding protein universe. The genome sequencing projects have opened up a veritable flood of novel sequences, many of which have unknown functions, from a broad range of organisms. The diversity of proteins is much greater than we anticipated, and the JCSG as part of the NIH NIGMS Protein Structure Initiative (http://www.nigms.nih.gov/Initiatives/PSI/Centers/) is investigating novel families, and metagenomes (such as the human gut microbiome). We are mapping the evolution of large families as they accumulate new functions. The JCSG has developed a high throughput platform that can produce over 200 novel structures per year. We are now starting to gain many valuable insights into the evolution of these families, as well as the entire proteome of *T. maritima*.

Impressions: The 20th meeting this year was absolutely outstanding with excellent diversity of speakers from TSRI, UCSF and from industry and biotech. The interaction among the participants was particularly good this year and many exciting new possibilities for collaborations were enhanced and developed. The brief student and postdoc talks were action packed and generated a lot of excitement and enthusiasm among the participants.

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Presentation: Small Molecule Activators of a Proenzyme

Apoptosis is a primary mechanism of chemotherapy-induced cell death, and is regulated by complex intracellular signaling

cascades known as the intrinsic and extrinsic pathways. Both signaling pathways ultimately converge to proteolytically activate dormant executioner procaspases into active caspase enzymes. Once activated, executioner caspases specifically target and proteolyze a variety of vital cellular proteins, thus resulting in programmed cell death. We have developed small molecules that directly activate executioner procaspases, thereby bypassing the regulatory upstream signaling pathways. These compounds can induce apoptotic death in cell lines of multiple cancers including, but not limited to; leukemia, multiple myeloma, and lymphoma. Importantly, these compounds potentially represent a completely novel class of anti-cancer drugs.

Impressions: This is my eight time to the conference and was certainly one of the best. The presentations by both students/postdocs and faculty clearly illustrated the cutting-edge research being performed at TSRI, UCSF and UCB. Similarly, talks by the sponsors were very informative and encouraged collaborative efforts between academia and industry. The roundtable discussion was extremely useful, particularly for students and postdocs, and provided insight into transitioning ideas and concepts from an academic setting into industrial endeavors.

Name: Mark Yeager, M.D., Ph.D.
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Overview: Macromolecular Assemblies Visualized by Electron Cryo-microscopy and X-ray crystallography
In our laboratory, we use electron cryo-microscopy (cryo-EM) and X-ray crystallography to examine the structures of multicomponent, supramolecular complexes. For cryoEM, biological specimens are quick frozen to preserve their

native structure and functional properties. A special advantage of this method is that we can capture dynamic states of functioning macromolecular assemblies, such as open and closed conformations of membrane channels and viruses actively transcribing RNA. Three-dimensional density maps are obtained by digital image processing of the high-resolution electron micrographs. Maps at low resolution (~20 Å) reveal the overall shape and symmetry of the protein capsid layers, as well as the location, shape, dimensions, quaternary arrangement and stoichiometry of the component proteins. In some instances the specimens are sufficiently well-ordered so that maps at intermediate resolution (~6 Å) display elements of secondary structure. By the use of X-ray crystallography, we can determine atomic resolution structures (<3 Å) of individual domains within larger complexes. We can then computationally dock the domains within the cryoEM maps to determine high-resolution models. The cryoEM-based maps reveal the structural organization of complex biological systems that can be related to the functional properties of such assemblies.

Presentation: Mechanisms of HIV-1 Capsid Assembly
The mature capsids of human immunodeficiency virus type 1 (HIV-1) and other retroviruses are variably curved, closed fullerene shells composed of ~250 hexamers and exactly 12 pentamers of the viral CA protein. The capsid encloses the viral genome, facilitates its delivery into new host cells, and promotes reverse transcription. Guided by a cryoEM-based model, we engineered disulfides that enabled isolation and crystallization of soluble HIV-1 CA hexamers and pentamers. The inter-subunit quaternary bonding interactions are remarkably similar between the quasi-equivalent hexamers and pentamers. The oligomers are comprised of a central symmetric ring of N-terminal domains surrounded by a mobile "belt" of C-terminal domains. An electrostatic switch at the center of the oligomers appears to be a key regulator of assembly. This study completes the gallery of sub-structures describing the components of the HIV-1 capsid, and enables atomic modeling of the complete capsid. Two rigid-body motions about flexible interfaces are

sufficient to generate the continuous variable lattice curvature in the fullerene cone.

Impressions: I have been fortunate to have attended more than a dozen of the total of 20 meetings, and this continues to be one of my favorite meetings! The size and informal workshop format is similar to a Gordon conference with the advantages of a broad scientific scope and resort location. The quality of the science presented at this meeting is outstanding, and it is not uncommon for scientific collaborations to be launched at this meeting. I also appreciate the participation of scientists in industry in order to gain insight into translational research and the potential for commercial applications of basic research.

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Overview: My group is interested in computational and structural biology, with special interests in protein assembly, symmetry, design, and topology.

Presentation: I presented our most recent work on bacterial microcompartments, which are protein-based organelles that resemble virus capsids and enclose sequentially acting enzymes in diverse bacteria. They typically function to prevent the escape of a volatile or toxic metabolite into the cytosol by enclosing together the enzyme that produces the metabolite in one step and the enzyme that consumes it in the subsequent step. Enteric bacteria, including Salmonella and E. coli, can produce a bacterial microcompartment (known as the Eut microcompartment) for metabolizing ethanolamine without releasing the acetaldehyde intermediate into the cytosol. I reported the crystal

structures of most of the proteins from the *E. coli* Eut microcompartment shell. The structures reveal mechanisms for gated molecular transport through pores in the protein shell, as well as additional clues regarding the function of these poorly studied cellular structures.

Impressions: The meeting remains one of my favorites owing to the high level of the science (including presentations by students and postdocs) and to the meeting atmosphere.