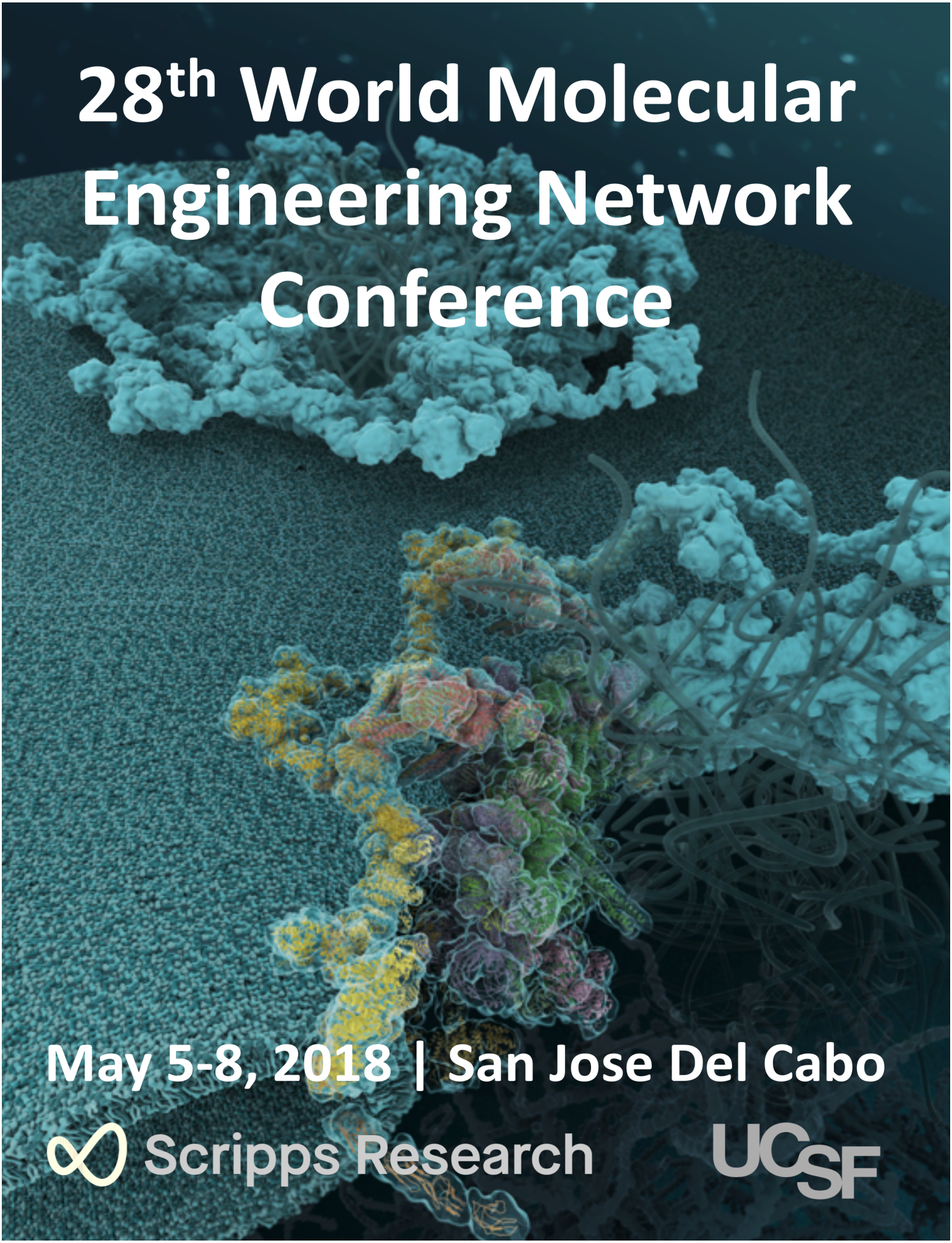
28th World Molecular Engineering Network Conference
May 5-8, 2018 | San Jose Del Cabo
Scripps Research
UCSF

Our History

The WMEN conference has been held for the past 28 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 (TSRI). Drs. Daniel Santi and Ian Wilson started the meetings and created the unique scientific ambience. The meeting style has remained unchanged but, sixteen years ago, the venue moved from Cabo San Lucas to all-inclusive resorts in San Jose del Cabo. The 2016 meeting returned to the Hyatt Ziva (formerly Barceló Los Cabos Palace) that was completely renovated after Hurricane Odile in 2014.

Each year, the meeting attracts approximately 60 academic, industrial, and biotech participants, as well as venture capitalists and patent attorneys. The attendees are composed of Professors, laboratory heads or research directors, but we also encourage participation of the next generation of scientists through selecting around 20-25 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 in Los Cabos with an always stellar and fun group of participants. We are also extremely grateful to our sponsors whose generous support makes this meeting possible every year.

World Molecular Engineering Network (WMEN) CABO XXVIII, May 5 - 8, 2018

San Francisco / San Ignacio Rooms

Saturday Evening, May 5, 2018			
17:00 – 17:15	**Introduction and Welcome**		
	Ian Wilson and Andrej Sali		
17:15 – 18:15	**Keynote Lecture**		
	Peter Schultz	TSRI	Playing with the molecules of life
18:30 – 18:35	**Self-Introductions**		
	Emine Kaya	Global Blood Therapeutics	
	Jack Kirsch	UC Berkeley	
18:35 – 20:30	**Short Presentations (5 + 1 min.) by TSRI , UCSF, UCB and LBNL Graduate Students and Postdocs (Chair: Gabriel Lander)**		
	Cristina Puchades	TSRI	Making mitochondria great again: Protein quality control in the inner membrane
	Christopher Cottrell	TSRI	Structure-based vaccine design
	Ke Yang	TSRI	Structure, cooperativity and dynamics of a hematopoietic transcription factor:coactivator complex
	Angelo Solania	TSRI	Caspase 3 selective inhibitors for biological studies
	Qinheng Zheng	TSRI	Sulfur fluoride exchange: chemistry and applications
	Colby Sandate	TSRI	Substrate engagement by the microtubule severing enzyme spastin
	Short Break		
	Venera Weinhardt	LBNL	Probing phase separation by soft x-ray tomography
	Vasudha Srivastava	UCSF	Oncogene-induced changes in mammary tissue structure and mechanics
	Jonathan Leano	UCSF	Inroads to packaging neurotransmitters
	Seth Axen	UCSF	Determining the information content of second harmonic generation spectroscopy for modeling conformational changes of macromolecules
	Mohamed Elshenawy	UC Berkeley	Cargo adaptors regulate the stepping and force generation of human dynein/dynactin complex
	Adolfo Cuesta	UCSF	Developing lysine-targeted covalent probes of the Hsp90 family
	Christian Bache Billesboelle	UCSF	Molecular mechanisms of the hepcidin-ferroportin axis
20:30 – 22:00	**Reception with Buffet**		**Poolside**

World Molecular Engineering Network (WMEN) CABO XXVIII, May 5 - 8, 2018

Sunday Morning, May 6, 2018			**Structure and Biology of Cellular Processes (Chair: Carolyn Larabell)**
09:00	Gabriel Lander	TSRI CA	Size and resolution limits using conventional EM methods
09:20	Jeffrey Lengyel	FEI	Cryo-tomography: merging of structural and cellular biology
09:40	Danielle Grotjahn	TSRI CA	It takes two to cargo: mechanisms of cytoplasmic dynein regulation revealed by cryo-electron tomography
10:00	Ahmet Yildiz	UC Berkeley	The mechanism of dynein's directionality
10:20	**Break**		
10:40	Carolyn Larabell	UCSF	Cellular CT scans: New views, new insights
11:00	Zev Gartner	UCSF	Building tissues to understand how tissues build themselves
11:20	Seemay Chou	UCSF	Weapons to probes: using toxins to study bacterial cell wall structure
11:40	Andrej Sali	UCSF	Integrative structure and functional anatomy of a nuclear pore complex
Sunday Afternoon, May 6, 2018			**Chemical Biology (Chair: Dennis Wolan)**
16:00	Phil Dawson	TSRI CA	Making new connections in protein chemistry
16:20	Jack Taunton	UCSF	Small-molecule interrogation of proteostasis
16:40	Dennis Wolan	TSRI CA	A dipeptidyl aminopeptidase from a commensal bacterium degrades human antimicrobial peptides
17:00	Matthew Francis	UC Berkeley	Chemically modified viral capsids for in vivo delivery applications
17:20	**Break**		
			Membrane Proteins (Chair: Robert Fletterick)
18:00	Mark Yeager	University of Virginia	"Ball-and-Chain" mechanism for pH-gating of gap junction channels revealed by CryoEM, crosslinking and HDX mass spectrometry
18:20	Robert Stroud	UCSF	How a voltage sensor works to activate an ion channel
18:40	Jian Payandeh	Genentech	Structural basis for dual-mode inhibition of an ABC transporter
19:00	Aashish Manglik	UCSF	Structural dynamics of opioid action
20:00 – 22:30	*Sponsor Dinner, by invitation only – The Rib*		
Monday Morning, May 7, 2018			**Sponsors (Chair: Andrej Sali)**
09:00	Andrea Cochran	Genentech	Unraveling the biology of bromodomain reader modules
09:20	Kyle Landgraf and Paul Marinec	Reflexion	Beyond antibodies: targeting VEGF and PD-1 with synthetic D-proteins
09:40	David L. Sloane	Nektar	NKTR-255: A new player in immune-oncology
10:00	**Break**		

World Molecular Engineering Network (WMEN) CABO XXVIII, May 5 - 8, 2018

Monday Morning, May 7, 2018 (continued)			**Sponsors (Chair: Andrej Sali)**
10:20	Glen Spraggon	GNF	Kinetoplastid growth inhibitors from molecules to cells
10:40	Eswar Narayan	DuPont Pioneer	Trait discovery & applications in Ag Biotech
11:00	Tom Evans	New England Biolabs	Cappable-seq: using next-generation sequencing as a lens into RNA dynamics
11:20	Debanu Das	Accelero Biostructures	New paradigms for high-throughput protein X-ray crystallography in small molecule and biologics drug discovery
11:40	Jill Chrencik	Merck	Protein engineering strategies for drug discovery of difficult targets
Monday Afternoon, May 7, 2018			**Nucleic Acids, Nucleic Acid Binding Proteins & Complexes (Chair: Katrin Karbstein)**
16:00	Robert Fletterick	UCSF	Nurr1 nuclear receptor
16:20	Kendall Nettles	TSRI FL	Structural rules for allostery in the steroid receptors
16:40	Doug Kojetin	TSRI FL	A structural mechanism for directing inverse agonism of PPARγ
17:00	David Millar	TSRI CA	Functional coordination in DNA polymerases
17:20	**Break**		
17:40	Katrin Karbstein	TSRI FL	Quality control in 40S ribosome assembly
			Immunology and Microbial Pathogens (Chair: Jim Paulson)
18:00	Jim Paulson	TSRI CA	Putting the brakes on mast cells
18:20	Ian Wilson	TSRI CA	Neutralizing antibodies and vaccine design for malaria
Tuesday Morning, May 8, 2018			**Computation, Proteomics, Systems Biology and Design (Chair: Robert Stroud)**
08:50	Martin Kampmann	UCSF	Molecular and cellular determinants of protein aggregation in neurodegenerative diseases
09:10	Hao Li	UCSF	Systems biology of cellular aging
09:30	John Yates	TSRI CA	“Molecular Painting” using mass spectrometry
09:50	**Break**		
10:10	Elizabeth Getzoff	TSRI CA	The clock is ticking
10:30	Michel Sanner	TSRI CA	Advances in peptide docking
10:50	Art Olson	TSRI CA	Modeling and visualizing cellular environments
11:10	**Ian Wilson and Andrej Sali**		**Closing Remarks**

In order to protect individual rights and promote discussion, it is a requirement of the Scripps-UCSF WMEN CABO Annual Meeting 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 the Conference acknowledges and agrees to these restrictions as a condition of attending the Conference.

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

WMEN Conference
San Jose del Cabo

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Supervisor: Aashish Manglik
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Presentation: Molecular Mechanisms of the Hepcidin-Ferroportin Axis

Impressions: Group size was pretty optimal and the program had a good mix of speakers. I found most of the talks highly relevant to my own work and well aligned with the conference theme. I got thoughtful feedback on my work and met someone that turned into a new collaborator. The conference was generally very well organized and the length was perfect. I'm very positive about having attended.
Location: Very nice venue and great conference room. One downside is that the hotel was large and I missed the spontaneous conversations that happen at smaller venues where you run into people over meals.
Other: Unfortunately, I missed the dinner on the first night. There was an announcement after the last talk that I didn't quite hear, and the program only said "dinner poolside", hotel staff didn't know the location. Maybe you should send directions by e-mail.
Thanks for a great conference!

Name: Christopher Cottrell
Supervisor: Andrew Ward
Department: Integrative Structural and Computational Biology/The Scripps Research Institute
Mailing address: The Scripps Research Institute, 10550 N. Torrey Pines Rd. La Jolla CA 92037
Email address: cchris@scripps.edu
Phone number: 858-784-7504

Presentation: My research focuses on using structural biology to inform vaccine design. I presented data showing how we used cryoEM structures of HIV envelope protein in complex with vaccine-elicited antibodies to engineer a series of HIV Env immunogens designed to focus the immune response to a specific epitope.

Impressions: The meeting was great! I was very happy to have been able to attend. The PI talks were informative and the keynote was amazing! Specifically, the keynote highlighted several successful stories of going from basic science discoveries to translational therapies. I have no changes to recommend.

Name: Mohamed Elshenawy
Supervisor: Ahmet Yildiz
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Presentation: My research focuses on understanding the role of cargo adaptors on regulating functions of dynein. Activation of dynein motility requires its assembly with dynactin and one of several cargo adaptors proteins. We found that the complexes formed with some cargo adaptors primarily recruit two dyneins, and they are faster and stronger than complexes that recruit a single dynein. The faster velocity of these complexes was due to its faster stepping rate, while we found that artificial coupling of multiple dyneins accounts for the increase in the collective force production. Additionally, complexes formed with two dyneins compete more efficiently against kinesin-1 in a one-to-one mechanical competition. We demonstrate a mechanistic basis for how different cargo adaptors modulate dynein,Äôs mechanical properties to perform a wide range of cellular functions.

Impressions: I was fortunate to have the opportunity to attend WMEN meeting and interact with all these outstanding researchers. The presentations were all informative and the discussions after the presentation were inspiring and provided an excellent opportunity for exchange of ideas and views. I believe that the meeting in its current format is great and I would recommend no change in it.

Name: Robert Fletterick
Department: UCSF
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Phone number: 415-298-3060

Overview: The meeting was broadly focused exceptional Structure and Cellular Biology. The core of many presentations was chemistry and biochemistry. The range of science was great but the participants were focused on making their presentations clear to all. I appreciated the enthusiasm of both the presenters and the audience.

Presentation: I spoke about the structure and mechanism of the nuclear receptor Nurr1, a potent and important regulator of life and death on neurons that signal with dopamine. Parkinson Disease relates to the functioning of these neurons. The neurotransmitter dopamine derives from tyrosine and is carefully regulated through its metabolism and locations in synapses and within neurons. It is strangely reactive by poorly understood chemistry. Nurr1 controls the function and fate of neurons but no one had identified the hormone agent that through binding to Nurr1, alters the transcription programs in neurons. By selective biophysical binding studies, a chemical was identified which is a semi stable metabolite of dopamine.
I showed by differential scanning fluorimetry that the metabolite of dopamine, dihydroxy indole, DHI, binds to Nurr1 and stabilizes it. I showed that the binding is reversibly covalent using surface plasmon resonance with an apparent Kd of about 5 micromolar. Determination of the three dimensional structure using X-ray crystallography revealed DHI covalently bound to a specific Cys S atom. Calculations using quantum mechanics to model the mechanism of thiolate S atom attacking the DHI suggested that the two hydroxyl groups oxidized to quinone, and that the resident molecule was IQ- Indole quinone. The free energy barrier of the reversible covalent association is of the order 6 Kcal/mole. Finally I showed through reporter assays and a zebra fish assay that DHI affects transcription of endogenous genes under control of Nurr1. This work was done with Pam England and Matt Jacobson and colleagues at UCSF.

Impressions: Fabulous meeting. Everyone participated and interacted. The talks were mostly well-timed and well-presented. I appreciated being at the excellent hotel and being able to meet with and

dine with participants. The organization of the meeting and travel was 5 star. The rooms, meals and seminar room were first rate.

Name: Matthew B. Francis
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Phone number: 510-643-9915

Overview: This was my second time attending this conference. Like last time, I met with many different faculty members and I was able to identify a couple of postdocs who might be interesting candidates for future faculty hires.

Presentation: Synthetically Modified Viral Capsids for In Vivo Delivery Applications

Impressions: I had a terrific time learning about the research activities at UCSF and Scripps. The event was a great networking opportunity, and the location was terrific!

Name: Danielle Grotjahn
Supervisor: Gabriel Lander
Department: Department of Integrated Structural and Computational Biology, The Scripps Research Institute
Mailing address: 10550 North Torrey Pines Road, TPC-19 La Jolla, California 92037
Email address: grotjahn@scripps.edu
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Presentation: My research takes a structural approach to understand regulatory mechanisms by which the cytoplasmic dynein-dynactin motor protein complex transports cellular cargo along microtubules. Using cryo-electron tomography and the development of a novel subtomogram averaging approach, I solved the first three-dimensional reconstruction of the dynein-dynactin complex, and showed that dynactin recruits and activates two dynein complexes for efficient microtubule-based motility.

Impressions: Overall, I thought the meeting this year was fantastic. I really enjoyed Pete Schultz's keynote lecture. I think the session chairs could be a little bit more diligent on time management, as many of the presentations went over their allotted time. Perhaps the time limit for presentations should be emphasized more prior to the meeting. Other than that, it was a great mix of interesting science and beautiful weather.

Name: Martin Kampmann
Department: UCSF
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Overview: The Kampmann lab develops and uses innovative technologies to understand cellular and molecular mechanisms of human diseases, and to discover new therapeutic strategies.
A major focus of our research are diseases associated with protein misfolding, such as neurodegenerative diseases. We ask how cells maintain their proteins in a functional and balanced state. In human cells, this is accomplished by a network of over 1,000 different factors called the proteostasis network. Our goal is to understand how this network functions, and how it is challenged and rewired in disease states, including neurodegenerative diseases and cancer.
Our functional genomics technology, which integrates CRISPR/Cas9-based control of gene function and large-scale genetic interaction maps, enables us to elucidate dynamic networks and to pinpoint nodes that are potential therapeutic targets. CRISPRi and CRISPRa genetic screens in cells derived from human induced pluripotent stem cells (hiPSCs) can reveal mechanisms of disease-associated genes and of selective vulnerability of specific cell types. We use biochemistry, biophysics and cell biology to "zoom in" on individual nodes of the network and to reveal their mechanism of action.

Presentation: Molecular and cellular determinants of protein aggregation in neurodegenerative diseases

Impressions: This was my first time at the WMEN meeting - it was a fantastic opportunity to learn about research by the other investigators and for many informal discussions, and making of new connections.

Name: Emine Kaya
Department: Global Blood Therapeutics
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Overview: We at GBT are using the power of small molecule drugs to address molecular mechanisms in non-malignant blood-borne diseases. We have a clinical candidate small molecule (Voxelotor) in Phase III, which prevents polymerization of HbS and thereby eases downstream pathophysiology of Sickle Cell Disease.

Presentation: N/A

Impressions: The meeting was very well structured and had an optimal number of attendees. I liked the fact that different talk formats were offered to give all attendees (postdocs/grad students, PIs as well as industry sponsors) a chance to present. The location is great and made it very easy to get in touch with other attendees to discuss collaborations.

Name: Jack Kirsch
Department: QB3 Institute
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Overview: Great as always, both in depth and scope. Every talk had at least something useful for each audience member.

Presentation: I am retired and didn't present.
Impressions: Social and professional interactions were plentiful and profitable.

Name: Douglas Kojetin
Department: Department of Integrative Structural and Computational Biology
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130 Scripps Way, Jupiter, Florida, 33458
Email address: dkojetin@scripps.edu
Phone number: 561-228-2298

Overview: My research uses methods in structural biology, biochemistry, and molecular pharmacology towards understanding the mechanism of action of nuclear receptor ligands.

Presentation: We discovered a new structural mechanism for directing inverse agonism of the nuclear receptor PPARγ. Our findings, which were presented at this year's Cabo meeting, could lead to the development of a novel class of synthetic PPARγ ligands.

Impressions: This was my first year at the Cabo meeting, and it was excellent on all accounts. The science was amazing and included a blend of young and experienced investigators, and the opportunities to hear from and meet scientists in industry was great as well. I especially enjoyed hearing several talks related to nuclear receptor structure-function.

Name: Gabriel C Lander
Department: DISCoBio, TSRI
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Phone number: 858-784-8793

Overview: This is an excellent meeting that assembles world-renowned scientists and emerging leaders in the field in a relaxing and beautiful resort environment that encourages one-on-one scientific discussions. The small size of the meeting, the informal nature of the talks, the free time in the afternoons, are all conducive to, and often lead to, successful and prolific collaborations. The attendees are mainly structural biologists, and I enjoy learning about the newest developments in structure determination methodologies and interpretation, as the diversity in approaches and techniques that are presented always prompts new ideas for the ongoing projects in my lab. There are also numerous exceptional non-structural researchers who attend this meeting, which broadens the scope of the lectures and further encourages multidisciplinary discussion and collaboration.

Presentation: Technical and methodological advances in single-particle cryo-electron microscopy (cryo-EM) have expanded the technique into a resolution regime that was previously only attainable by X-ray crystallography. Although single-particle cryo-EM has proven to be a useful technique for determining the structures of biomedically relevant molecules at near-atomic resolution, nearly 98% of the structures resolved to better than 4 Å resolution have been determined using 300 keV transmission electron microscopes (TEMs). I discussed our recent work, which showed that it is possible to obtain cryo-EM reconstructions of macromolecular complexes to better than 3 Å resolution using a 200 keV

TEM. These structures are of sufficient quality to unambiguously assign amino acid rotameric conformations and identify ordered water molecules and bound cofactors, features previously thought only to be resolvable using TEMs operating at 300 keV.
Determining the high-resolution structures of sub-100 kDa complexes that have been recalcitrant to crystallization has also been a long-term goal of the cryo-EM community. Recently, the Volta Phase Plate has used to solve the structures of numerous small biological specimens, and it is now widely accepted that resolving small-sized samples is only possible with a phase plate. I also presented evidence that it is possible to solve high-resolution structures of asymmetric, conformationally flexible specimens that are smaller than 100 kDa using conventional cryo-EM methodologies at 200 keV, without the need for a phase plate or energy filter.
Impressions: Every year this meeting seems to get better, and this meeting was no exception. I say without reservation that this is the best meeting I attend all year. I'm exposed to more interesting and applicable science in Cabo than in most other conferences, and I always return to lab energized and enthusiastic, eager to push my lab members to branch aspects of their projects in new directions.

Name: Kyle Landgraf
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Overview: Reflexion is pioneering the development of D-protein therapeutics. We utilize mirror-image phage display to discover synthetic d-proteins that act to antagonize specific disease related targets. The advantages of D-protein therapeutics, compared to their L-protein counterparts, include lack of immunogenicity, resistance to protease mediated degradation, better tissue penetration and uptake into the brain. Our overall goal is to design superior D-protein drugs for oncology and neurological disease.

Presentation: The presentation focused on a technology background describing d-proteins and the use of mirror-image phage display, as well as updates on two programs targeting VEGF and PD-1. Data were presented on the feasibility of synthesizing VEGF and PD-1 in D-form and the initial discovery of D-protein binders to these targets. Further optimization of these hits will be carried out this year and preclinical data supporting the development of this compounds as therapeutics will be discussed next year.

Impressions: The WMEN meeting is an excellent forum for fantastic scientific presentations and discussions. The group size is perfect and should not get too much larger if the intimate setting is to be maintained. The location offers a relaxing environment and opportunities to combine a few days of vacation before/after the meeting. The length of the meeting is perfect and the 20 min talk slots are also ideal. The mix of industry and academic talks is ideal and this style should be maintained.

Name: Jeffrey Lengyel
Department: Thermo Fisher Scientific/Electron Microscopy
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Phone number: 503-560-9184

Overview: In the EM LS division of Thermo Fisher Scientific, we are leaders in electron microscopy including cryoEM. We are constantly developing new workflows and instruments to address biological questions.

Presentation: I presented on recent technological and technical advancements in the application of cryo-electron tomography to imaging of eukaryotic cells. In order to perform cryo-electron tomography first requires the thinning of vitrified cells in a specialized dual-beam in order to general lamellas. These lamellas are then transferred to a cryo-TEM for tomographic imaging.

Impressions: Location: Excellent
Number of participants: Excellent
Length of meeting: Very good.
I thought it was a very good meeting that facilitated excellent scientific discussion. My only comment is some speakers presentations were long and the session chairs could be more judicious with enforcing timing.

Name: David Millar
Department: Integrative Structural & Computational Biology, The Scripps Research Institute
Mailing address: 10550 N. Torrey Pines Rd. La Jolla CA 92037
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Phone number: 858-784-9870

Overview: My lab is engaged in the development and application of single-molecule fluorescence spectroscopy. Currently, there are three main projects. (1) Understanding functional coordination in multi-functional DNA polymerases, (2) Dissecting ligand activation mechanisms of chemokine receptors, and (3) Elucidating the assembly pathway of the HIV-1 Gag polyprotein.

Presentation: My presentation focused on functional coordination in DNA polymerase I, an enzyme responsible for Okazaki fragment processing and DNA base excision repair. Pol I contains three distinct enzymatic activities within a single polypeptide. Previous structural studies have shown that the active sites are widely separated in different subdomains, but there is no understanding of how the three sites work together to ensure accurate and efficient DNA replication and repair. We have devised a single-molecule FRET system that distinguishes among the three distinct modes of DNA binding. Using this system, we have shown that a DNA substrate can switch repeatedly between all three active sites during a single encounter with Pol I. Kinetic analysis of the single-molecule records reveals the temporal coordination between the various site-switching events. The results are proving insights into the physical mechanisms underlying functional coordination.

Impressions: This is a highly informative meeting that continues to be a highlight of my calendar each year. I have attended all of the previous meetings, so I have gained an historical perspective on the meeting. Amazingly, the meeting gets better each year! The quality of the science and participants is world class. The inclusion of new attendees each year ensures that the meeting remains vibrant and is also a testament to the broad appeal of the meeting. The relaxed setting in San Jose del Cabo encourages informal interactions among the participants, while the Hyatt Ziva provides a comfortable and convenient venue for the meeting. May the meeting continue to flourish!

Name: Arthur Olson
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Phone number: 858-784-9702

Overview: Excellent meeting. Everyone gets to talk. Great tradition for almost 30 years. Venue is among the best over all of this time.

Presentation: My presentation covered recent developments in our work to build, visualize and interact with models of cellular environments at the molecular level. I discussed the "instant" CellPACK program which enables construction of such environments in seconds, and some of the algorithmic improvements for building and fibrous structures such as DNA and RNA into these environments.

Impressions: As usual, great science and interesting discussions. Lots of collegiality.

Name: James Paulson
Department: Department of Molecular Medicine, The Scripps Research Institute
Mailing address: 10550 N. Torrey Pines Road, MB202 La Jolla, CA 92037
Email address: jpaulson@scripps.edu
Phone number: 858-784-9634

Overview: Chemical Glycobiology. My lab studies glycan-binding proteins that mediate cell surface biology from the recognition of host cell receptors by influenza virus and other pathogens, to the regulation of immune cell responses involved in distinguishing between self and non-self. Our group is multidisciplinary with expertise ranging from carbohydrate chemistry to mouse biology, and we are particularly interested in understanding protein-glycan interactions and mechanisms underlying their biology at the molecular level.

Presentation: Exploiting inhibitory Siglecs to desensitize mast cells and suppress allergic responses. We have developed a nanoparticle platform that displays an allergen/antigen and a high-affinity ligand of a mast cell Siglec that is designed to recruit this inhibitory receptor to the immunological synapse when the allergen/antigen is recognized by an antibody bound to the mast cell Fc receptor. When injected into a mouse, the recruitment of the Siglec prevents antigen-mediated mast cell-induced anaphylaxis and mast cells are desensitized to subsequent antigen challenge. The results show promise for invoking Siglec mediated suppression of mast cell responses in a therapeutic setting.

Impressions: The meeting is consistently a highlight of my year. Last year, I couldn't go because of a conflict, so was determined to not let that happen again. The high quality of the science, networking with colleagues, getting to better know students and postdocs from other labs, coupled with the relaxed setting and time to enjoy it is truly unique. Highly recommended to everyone.

Name: Cristina Puchades
Supervisor: Gabriel Lander
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Presentation: Making mitochondria great again: Protein quality control in the inner membrane
Impressions: Awesome!

Name: Andrej Sali
Department: Bioengineering and Therapeutic Sciences
Mailing address: 1700 4th St, San Francisco, CA 94158
Email address: sali@salilab.org
Phone number: 415 514 4227

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 understand the cell, we need to know the structures of its macromolecular assemblies. Determining these structures generally requires pure samples of the studied assemblies. Here, I described how we obtained the structure of the Nup82 subcomplex of the nuclear pore complex, using integrative structure determination based on electron microscopy, chemical cross-linking, and assorted other data.
Impressions: Informative and enjoyable!

Name: Colby Sandate
Supervisor: Gabe Lander
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Presentation: The AAA+ ATPase spastin is implicated in remodeling the cytoskeleton through microtubule severing. I presented a cryo-EM structure of the spastin hexamer bound to a poly-glutamic acid substrate. Our ~3.3 √Ö resolution structure reveals how nucleotide and substrate binding organizes spastin protomers, suggesting a potential mechanism of spastin-mediated microtubule depolymerization.
Impressions: I was very impressed by the quality of the science presented at this meeting. I thought our small group size was intimate and great for producing conversation between the attendees. I would have enjoyed having more grad students around, however.
I do think the session chairs could have done a better job at ensuring that the presenters did not go over their allocated time. One of our sessions went over by nearly 45 minutes!

Name: Michel Sanner
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Overview: My lab is focused on developing computational methods for predicting interactions between biological molecules. Specifically we have been developing AutoDockFR for including receptor flexibility into automated docking experiments. We are also actively developing a new method for docking peptides into biological macromolecules. Finally, we are working computational techniques for modelling the mesoscale. We have developed several software programs in this area, including: cellPACK and cellVIEW

Presentation: My presentation was entitled: Advances in peptide docking. I presented a new data set of protein peptide complexes that we constructed and curated. While building this data set we took special care to characterize and quantify crystal contacts and provide receptors in their biologically active form. I then described our approach for peptide docking based on the protein folding tool CRANKITE and described its current performance.

Impressions: Every aspect of this meeting was outstanding, including the science, the attendance, the opportunities for informal discussions and the hotel.

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Overview: I've been hearing about this conference ever since I was a post-doc with Charly Craik and Elliott Sigal in the early 1990s, and this was my first opportunity to attend. It lived up to its reputation as being an exciting overview of first-rate, cutting-edge structural biology, in a beautiful setting. Although the presentation schedule was packed, there was some time to mingle and interact in smaller groups.

Presentation: My presentation was "NKTR-255: A new player in immuno-oncology". The top presentations that stand out in my memory were: Gabriel Lander's talk on cryo EM, Zev Gartner's talk on tissue self-organization, Andrej Sali's talk on the nuclear pore structures, Debanu Das's talk on high-throughput crystallography, and Martin Kampmann's talk on tauopathies. These presentations really stood out, however, all of the presentations were fascinating and very well-done.

Impressions: I was honored to attend this meeting and participate in such a meeting. My only constructive feedback would be to somehow schedule in more "mingling" time, or more "directed" social interactions (as opposed to just "free time"). Thank you for organizing this conference.

Name: Angelo Solania
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Presentation: My research focuses on developing inhibitors selective for individual caspase family members. A lead inhibitor was validated using in vitro kinetic measurements and activity-based probe profiling experiments. The caspase-3 selective inhibitor protected against apoptosis to the same degree as pan-caspase inhibitor Ac-DEVD-KE. Analysis of apoptotic jurkats with caspase-3 selective inhibitor display normal caspase maturation, unlike treatment with Ac-DEVD-KE, which leads to the general suppression of caspase maturation.

Impressions: I really enjoyed my first time attending the WMEN Cabo meeting. I found the resort to be extremely hospitable and enjoyed being able to interface with many graduate students and PIs. I think Dr. Schultz gave a really interesting keynote and I learned a lot about the nuances of both cryo EM and x-ray crystallography. I was really excited to hear about Merck's expansion in the Bay Area. I would recommend no changes in the meeting. Specifically, I was very pleased with the timing of the incoming flight which allowed us some time to settle in and eat before the beginning of the first session.

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 and small molecule based therapeutics using structure and computation to guide the discovery. Projects range from protein engineering to the development of bioactive organic molecules by structure-aided drug design with all activities closely coupled to the adoption and development of new technologies.

Presentation: Kinetoplastids are a widespread group of single cell flagellated protozoa. A number of species belonging to the Trypanasome and Leishmania families spend parts of their life cycle within mammalian cells. Contagion of human cells by these parasites leads to a number of diseases such as African sleeping sickness, Chagas disease and Leishmaniasis; all of which represent large unmet medical needs.
GNF, has been seeking to address the challenges associated with treating these infections by the identification of novel small molecule compounds and their associated molecular targets, capable of both specificity and lethality to the disease causing kinetoplastids.
The talk focused on the discovery of one such compound series and its target, the subsequent development of a potent pan-kinetoplastid inhibitor and the work to unravel the molecular and cellular mechanism of the lead candidates via high resolution Cryo-EM and whole cell Soft X-ray Tomography.

Impressions: The WMEN conference provided a wide but coherent mix of novel structural biology presentations covering everything from chemical biology to Cryo-EM and single cell imaging.
The format and location of the meeting is outstanding and provides an optimal setting for education, collaboration and active discussion with scientific leaders from a range of molecular engineering disciplines.

Name: Robert M. Stroud
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Overview: The main project in my laboratory discussed concerned the structural determinations of an ion channel TPC1 and two transmembrane transporters. One was a glucose transporter GLUT1 with various drugs bound as potential anticancer therapeutics. This was a first for transporters of this class. The second was a structure of a homolog of VGLUTs, vesicular glutamate transporters of key importance for the nervous system.

Presentation: The mechanism was defined in structures that show how the channel and transporters work and are sensitive to voltage, and to transported nutrients. Protein crystal structure has a key role in the understanding of an essential process in cell biology. New channels and transporters from human disease connections and from human brain are basis for drug design.

Impressions: Impressions of the Meeting:
Location: Excellent.
Number of participants: Good size
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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Presentation: Probing phase separation by soft x-ray tomography

Impressions: Overall the meeting was great. The only thing I did not like is that the conference and talks did not start on time and never ended on time.

Name: Ian A. Wilson
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Overview: My lab works on immune recognition of microbial antigens, such as HIV, HCV, influenza virus and *P. falciparum,* by broadly neutralizing antibodies. Our goal is to use the information on how antibodies bind to sites of vulnerability on these viruses or malaria parasite for structure- assisted design of vaccines and therapeutics.

Presentation: I presented our recent malaria work on protective antibodies to the major surface antigen, the circumsporozoite protein (CSP) on *P. falciparum.* These antibodies were derived from vaccination with the RTS,S vaccine and recognize NANP repeats that form the central portion of CSP. These antibodies bind to 2 to 3 repeats. The actual structural motif is NPNA , which forms a type 1 beta-turn or an Asn pseudo turn. When the antibodies bind to a soluble expressed CSP construct, multiple antibodies bind and stabilize an unusual extended spiral structure of the NANP repeats, as visualized by electron microscopy by my colleague Andrew Ward and his group at Scripps. We are using this information on how antibodies recognize CSP for structure-assisted vaccine design to try to either improve existing vaccines, such as RTS,S, or design new vaccines.

Impressions: Another great meeting with fabulous talks, including a great keynote from Pete Schultz and the always interesting and entertaining short talks from the grad. students and postdocs. This meeting always encourages great interactions with all participants. The location is great and the hotel looks after us well.

Name: Dennis Wolan
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Overview: Our laboratory employs an array of biochemical, cellular, biophysical, and high-throughput screening methodologies in the identification of the diverse assortment and types of bacterial proteins that are produced within normal and diseased distal gut microbiomes, in the development of small molecules as probes to elucidate essential commensal bacterial proteins, and as novel therapeutics to modulate the activity of important enzymes in microbiome-related pathogenesis.

Presentation: A dipeptidyl aminopeptidase from a commensal bacterium degrades human antimicrobial peptides.With a panel of chemical biological and structure-based approaches, we

demonstrated the substrate specificity of a secreted protease from commensal bacteria. We ultimately showed that the protease hydrolyzes a panel of human antimicrobial peptides found in the gut and therefore posit that secretion of this enzyme permits gut colonization by inactivation of host antimicrobial peptides.

Impressions: As always, this meeting was a fantastic opportunity to see the cutting-edge work being performed by colleagues at TSRI, UCSF, and UCB. I've now established several collaborations with UCSF faculty as a result of my interactions and presentations

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Name: Ke Yang
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Presentation: "Structural basis of cooperativity in a hematopoietic transcription factor:coactivator ternary complex"
My work focuses on elucidating the detailed molecular mechanisms by which the human T-cell leukemia virus I basic leucine zipper protein (HBZ) controls the transcription of viral and cellular genes. HBZ is uniformly expressed in all infected cells and plays a central role in leukemogenesis and proliferation of transformed adult T-cell leukemia (ATL) cells. Through its interactions with the KIX domain of the transcriptional coactivators CBP and p300, HBZ deregulates transcriptional programs involved in hematopoietic differentiation. We describe the crystal structure of a complex formed between KIX, the HBZ activation domain, and the cellular transcription factor c-Myb. By binding to KIX to form a ternary complex, HBZ allosterically stabilizes the interaction between KIX and c-Myb. These studies provide new molecular insights into the mechanism by which HBZ interferes with hematopoietic signaling pathways and promotes T cell proliferation.
Impressions: I enjoyed every aspect of the meeting! I was exposed to a wide range of inspiring science from multidisciplinary endeavors in drug discovery to cutting-edge applications of techniques in structural biology. The small group size enabled a lot of interactions among attendees, and it was wonderful to be able to hear everyone talk. The venue was amazing. As a graduate student, I greatly appreciate the opportunity to present my research and receive constructive feedback from others. It was a truly incredible experience for me.

Name: John Yates
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Overview: this was my first WMEN meeting consequently i didn't know what to expect. As a scientific meeting, I thought it was excellent. My only suggestion would be to try to create an activity onthe first day to stimulate interactions among participants as a means to break twice early.

Presentation: Molecular Painting of the proteome.

Impressions: The meeting site was nice although very self contained. Good and bad to that of course. The food was good, the rooms were good. Overall the site and meeting were excellent.

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Presentation: I talked about my thesis project, sulfur-fluoride exchange enabled radiolabeling of aryl fluorosulfate. We discovered by NMR saturation transfer technique that the fluoride exchange reaction between aryl fluorosulfate and anionic fluoride was fast. By employing [18F]fluoride, we were able to incorporate the positron-emitting nucleus into organic molecules in late stage. Radiolabeled compounds were dosed to live mice to study biological problems, such as distribution of soluble epoxide hydrolase, and formation of amyloid plaques in brain.

Impressions: The Cabo meeting is uniquely exciting for a graduate student. I have never presented my research to such a prestige audience wearing sandals. The talks by faculty from all institutions and scientists from sponsors were fantastic. I learned a lot from the presentations and conversations out of the conference room. For future meetings, I suggest longer time (8 or 10 minutes) for graduate students. One can hardly cover the essentials of his/her research in 5 minutes.