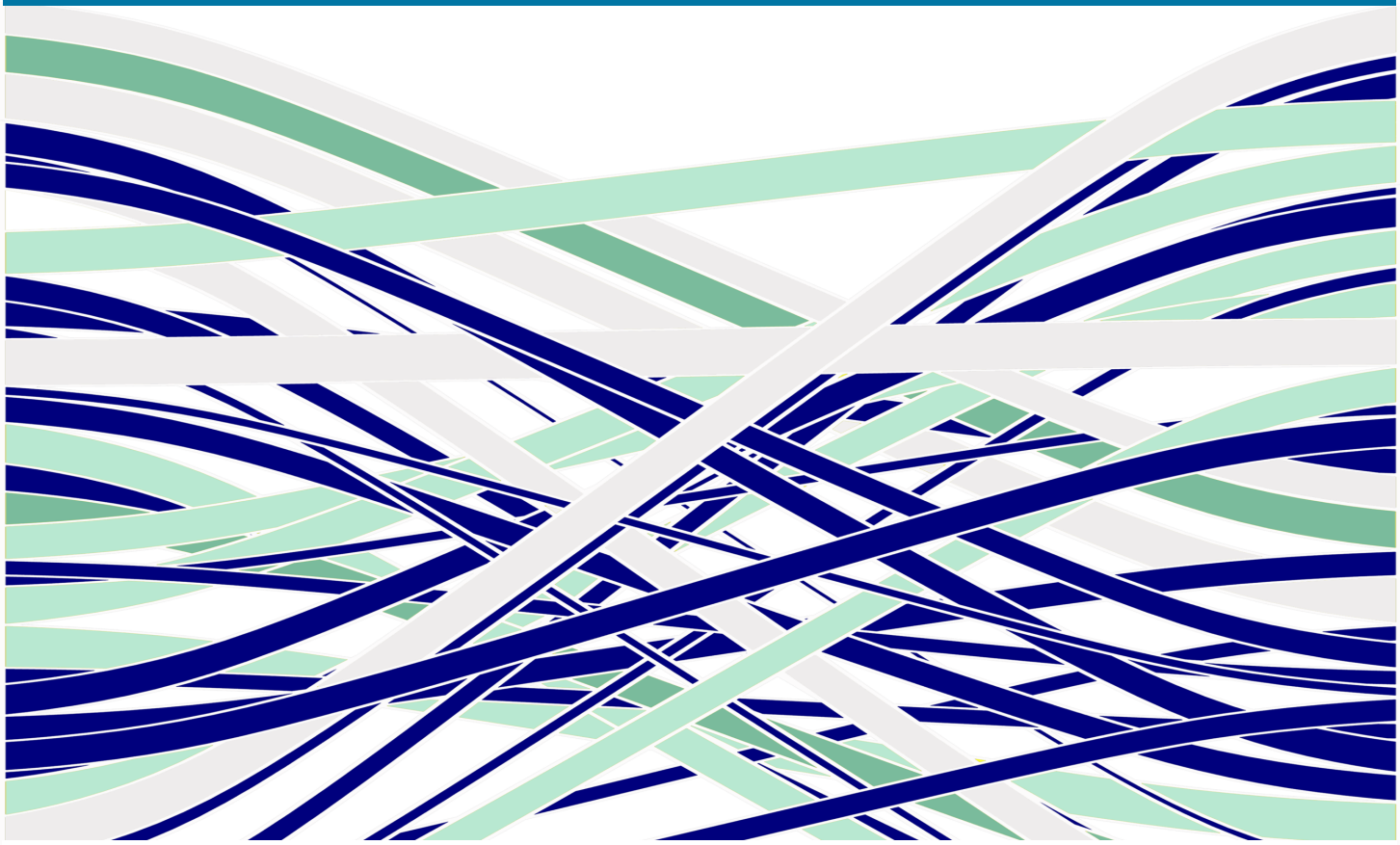
MUTATIONAL SCANNING SYMPOSIUM

VIRTUAL EVENT APRIL 5-7, 2021



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Atlas of Variant Effects

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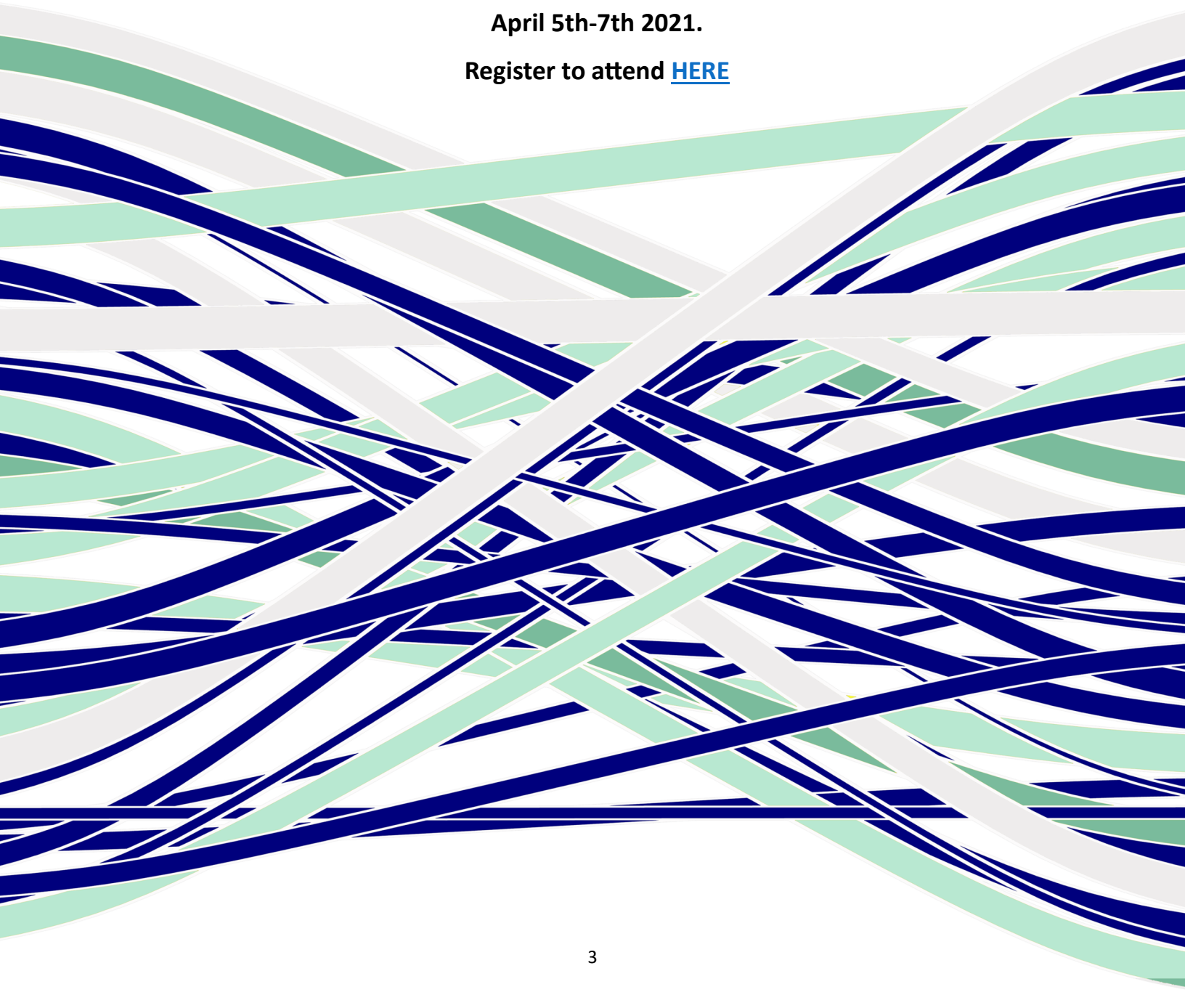
Multiplex Assays of Variant Effects

Multiplex Assays of Variant Effects (MAVEs) are key to variant interpretation and are transforming our understanding of the human genome. This annual symposium is sponsored by the Center for the Multiplex Assessment of Phenotype , Illumina, Octant, Wellcome Sanger, and the Brotman Baty Institute. Experts in the field of mutational scanning come from around the world meet to present their work and provide insights on the future of this science for this three-day event which will be held virtually,

April 5th-7th 2021.

Register to attend HERE



MUTATIONAL SCANNING SYMPOSIUM April 5-7 2021

April 5, 2021 Agenda

	All times Pacific Standard Time
Lea Starita, PhD | UW *Welcome, Opening Remarks*	**8:00 - 8:10 am**
Kim Reynolds, PhD | UTSW, Dallas (KEYNOTE/featured speaker) *Mapping sequence constraints in an essential metabolic enzyme*	**8:10 - 8:55 am**
Maitreya Dunham, PhD | UW *Deep mutational scanning of pharmacogenes using yeast activity assays.*	**8:55 - 9:20 am**
John Doench, PhD | Broad Institute *Development of pooled base editing screens of endogenous loci in mammalian cells.*	**9:20 - 9:45 am**
Break *(10min)* *Coffee Break / Short Stretch*	**9:45 - 9:55 am**
Martin Kampmann, PhD | USCF *Capturing disease-relevant protein conformations by deep mutational scanning*	**9:55 - 10:20 am**
Prashant Mali, PhD | UCSD *Engineering ADARs for precision transcriptome engineering.*	**10:20-10:45 am**
Break *(15min)* *Coffee Break / Short Stretch*	**10:45-11:00 am**
Matt Hurles | Wellcome Sanger & Doug Fowler | UW *Precision medicine at nucleotide resolution- The Atlas of Variant Effects Alliance*	**11:00-11:05 am**
Frederick (Fritz) Roth, PhD | University of Toronto and Prashant Mali, PhD | UCSD Experimental Technology and Standards (ETS)	**11:05-11:10 am**
Debora Marks, PhD | Harvard and Ben Lehner, PhD | CRGenomica Variant Scoring Tools, Methods and Standards (VSTMS)	**11:10-11:15 am**
Alan Rubin, PhD | WEHI, Australia and Maria Martin | EMBL-EBI Data Coordination and Dissemination (DCD)	**11:15-11:20 am**
Clare Turnbull, PhD | ICR, London and Lea Starita, PhD | UW Clinical Variant Interpretation (CVI)	**11:20 -11:25am**
Q & A breakout groups with each Workstream	**11:25 -11:40am**
Poster Session	**11:40- 1:00pm**
Optional Happy Hour/Social	**12:30- 1:00 pm**

MUTATIONAL SCANNING SYMPOSIUM April 5-7 2021

April 6, 2021 Agenda

	All times Pacific Standard Time
Ben Lehner, PhD | CRGenomica (KEYNOTE/featured speaker) *Solving structures and understanding genetic interactions using mutational scanning*	**8:00 - 8:45 am**
Eric Procko, PhD | University of Illinois *Engineering and modeling of receptors inspired by deep mutagenesis.*	**8:45 - 9:10 am**
Featured Abstracts Talk Block *(6 x 4 min)*	**9:10 - 9:40 am**
Break *(20min)* *Coffee Break / Short Stretch*	**9:40 - 10:00 am**
Rachel Karchin, PhD | Hopkins *CHASMplus for cancer-specific driver prediction and in silico saturation mutagenesis*	**10:00-10:25 am**
Tyler Starr, PhD | FHCRC *Deep mutational scanning and the evolution of SARS-related Coronavirus receptor binding*	**10:25-10:50 am**
Lea Starita, PhD | UW *Progress and Promise of MAVE for Clinical Variant Interpretation*	**10:50-11:15 am**
Doug Fowler, PhD | UW *Closing Remarks*	**11:15-11:30 am**
Happy Hour/Social	**11:30-12:00pm**

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MUTATIONAL SCANNING SYMPOSIUM April 5-7 2021

April 7, 2021 Agenda

All times Pacific Standard Time

Josh Cuperus, PhD | UW *Welcome, Opening Remarks*	**8:00 - 8:10 am**
Nuts and bolts of DMS	
Atina Cote, PhD | University of Toronto *Library Design, Construction, barcoding .*	**8:10 - 8:40 am**
Grace Anderson, PhD & Beatriz Adriana Osuna, PhD | Octant *Delivering libraries into mammalian cells*	**8:40 - 9:10 am**
Kenneth Matreyek, PhD | CWRU *How to design an appropriate selection method or DMS*	**9:10 - 9:40 am**
Break *(20min)* *Coffee Break / Short Stretch*	**9:40 - 10:00 am**
Application of mutational scanning	
Avtar Singh, PhD | MIT *Optical pooled Screening in mammalian cells*	**10:00-10:30 am**
Erika DeBenedictis, PhD | IPD, Seattle *DMS in Protein Design*	**10:30-11:00 am**
Meghan Garrett, PhC | FHCRC *Phage-DMS mapping of Antibody epitopes*	**11:00-11:30 am**
Concluding Remarks / Breakout sessions with speakers (Concurrent)	**11:30-12:00 pm**

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Keynote Speakers

BEN LEHNER, PH.D

Ben Lehner is Coordinator of the CRG Systems Biology program and an ICREA Professor. He has a degree and a PhD from the University of Cambridge and was a postdoctoral fellow at the Wellcome Sanger Institute. His lab works on basic questions in genetics such as incomplete penetrance, mutation rates and processes, epigenetic inheritance, genetic interactions and genetic prediction. An important focus at the moment is using deep mutagenesis to understand how mutations interact in proteins, RNAs and networks and to use these interactions to understand the energetics, in vivo structures, interactions and dynamics of ordered, disordered and aggregating macromolecules. Work in the lab has been recognized with the EMBO Gold Medal and the Bettencourt Prize for Life Sciences, amongst other awards.

KIMBERLY A. REYNOLDS, PH.D

Kimberly A. Reynolds is an Assistant Professor in the Green Center for Systems Biology at UT Southwestern Medical Center, in Dallas Texas. Kim's lab uses a combination of statistical genomics and high-throughput experiments to understand constraints on protein activity, abundance, and regulation inside the cell. Her group has used co-evolutionary analysis to engineer new allosteric regulation into proteins, and to identify metabolic enzyme pairs with constraints on relative expression. She is a Gordon and Betty Moore Foundation Data Driven Discovery Investigator, and recipient of a NSF CAREER award.

REAL-TIME ILLUSTRATIONS BY ALEX CAGAN

Alex Cagan is a post-doctoral researcher at the Wellcome Sanger Institute where he investigates evolutionary processes in somatic tissues. He is also a scientific illustrator most well-known for his live-sketching of scientific conference presentations. Alex will be using his tablet and stylus to create illustrated summaries of all the presentations at the meeting.

Grace R. Anderson, Ph.D

Grace is a systems-level cell biologist specializing in high-throughput genetic and pharmacological functional screening technologies. Broadly, they have always been driven to understand functional consequences of perturbed cellular states through the lens of cell health and signaling architecture. Prior to starting at Octant, Grace's research focused entirely in the oncology realm. They obtained their PhD in Molecular Cancer Biology from Duke University in the lab of Dr. Kris Wood. As a graduate student they uncovered mechanisms of anti-cancer drug resistance as well as deciphered mechanisms for how altered mitochondrial dynamics states can impact drug response across cancers that lack driver oncogenes.

Atina Cote, PhD

Atina earned her PhD in the Department of Molecular Genetics at the University of Toronto studying mechanisms of DNA palindrome instability under the supervision of Susanna Lewis. After her PhD, she worked in the lab of Tim Hughes where she contributed to the draft assembly of the Cannabis sativa genome. Atina is now a Scientific Associate in the lab of Fritz Roth where she has worked on several NGS-related projects and is currently developing tools to generate multiplexed assays of variant effect for genes involved in lipid disorders.

Josh Cuperus, Ph.D

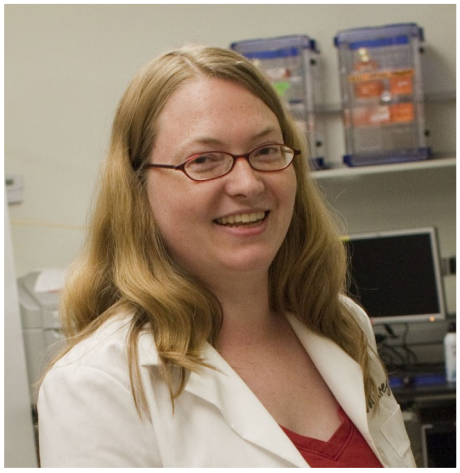
Dr. Josh Cuperus is an assistant professor in the department of Genome Sciences at the University of Washington. Dr. Cuperus did his Ph.D at Oregon State University with Dr. James Carrington, with a focus on small RNAs and technology development using next generation sequencing. Next he worked with Dr. Stan Fields with further emphasis on technology development and massively parallel assays in both yeast and plants. Now, Dr. Cuperus focuses on using high-throughput assays to help understand gene regulation in plant species, with focus on deciphering how and where cell-specific gene regulation occurs.

Erika DeBenedictis, Ph.D

Erika DeBenedictis is a postdoctoral researcher in the Baker lab using machine learning on experimental datasets to improve de novo design. Erika developed a platform for high-throughout continuous directed evolution and applied it to engineering biomolecules for genetic code expansion during her PhD at MIT biological engineering. She graduated cum laude from the California Institute of Technology with a Bachelor's in Computer Science. During undergraduate, she worked on topics in computational physics including space mission orbit design at the Jet Propulsion Laboratory, quantum computer compilation at Sandia National Laboratories, and computational protein design at D. E. Shaw Research. Erika is the recipient of numerous national awards, including first prize at the Intel Science Talent Search, the Davidson Fellowship, and the Ruth L. Kirschstein Predoctoral Fellowship.

John Doench, Ph.D

Since joining the Broad Institute in 2009, I have engaged in dozens of collaborations centered on functional genomics. As Director of R&D in the Genetic Perturbation Platform, I collaborate with a wide variety of research groups across many areas of biology, with a particular focus on understanding how gene dysfunction leads to disease. I have many years of experience in the development and use of functional genomic techniques, first with RNAi and more recently with CRISPR technology for genome-wide loss-of-function screening. Prior to joining the Broad, I received my Ph.D. in biology, training with Phil Sharp, and performed postdoctoral work at Harvard Medical School.

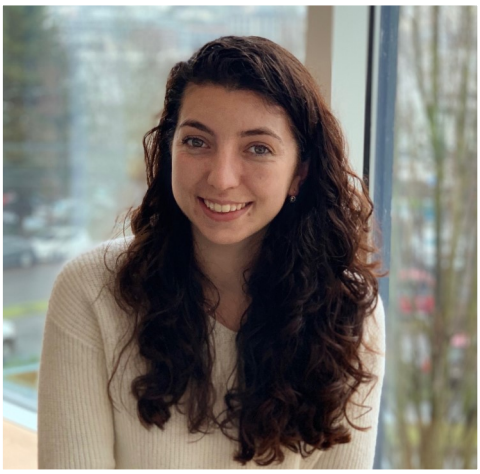


Maitreya Dunham, Ph.D.

Maitreya Dunham is a professor in the Genome Sciences department at University of Washington. Her lab uses yeast as a system to study genome evolution and genetic variation from both yeast and humans. Before coming to UW, she trained at MIT, Stanford, and Princeton.

Doug Fowler, Ph.D

Dr. Fowler is a leader in high-throughput, sequencing-based assays, and his lab has deep expertise in large-scale experimental approaches and computational analyses. He is now working to understand the effects of the millions of variants found in a typical human genome. Dr. Fowler is an Associate Professor of Genome Sciences and an Adjunct Associate Professor of Bioengineering at the University of Washington.



Meghan Garrett, Ph.D Candidate

I'm a graduate student in Julie Overbaugh's lab at Fred Hutch, where I study the antibody response to viruses such as HIV and SARS-CoV-2. To help accelerate isolation and characterization of new antibodies, I've combined DMS with phage display to create a system of finely mapping antibody epitopes and escape mutations. With this method I hope to aid in identifying new antibodies that bind to viral entry proteins. When I'm not in the lab, you can find me climbing rocks, baking cookies, or googling ggplot parameters.

Matt Hurles, PhD

Matt Hurles is a human geneticist focused on understanding the genetic architecture of severe developmental disorders. His lab combines large-scale genetic analysis of patient cohorts with modelling of pathogenic mutations in experimental model systems. Matt is passionate about sharing data to benefit patients and their families.

Martin Kampmann, Ph.D

Dr. Kampmann is an Associate Professor in the UCSF Department of Biochemistry and Biophysics and the Institute for Neurodegenerative Diseases, and an Investigator at the Chan Zuckerberg Biohub. He received his BA in Biochemistry from Cambridge University and his PhD in Biophysics/Cell Biology from Rockefeller University. The goal of Dr. Kampmann's research is to elucidate cellular mechanisms of brain disease and to develop new therapeutic strategies. He co-developed the CRISPRi and CRISPRa screening technologies, and his lab has pioneered CRISPR-based functional genomics in cell types derived from induced pluripotent stem cells (iPSCs). A major focus is the investigation of neurodegenerative diseases in human iPSC-derived neurons, astrocytes, and microglia, and 3D assembloids/organoids. Dr. Kampmann was named an NIH Director's New Innovator, an Allen Distinguished Investigator, a Chan Zuckerberg Biohub Investigator, and he received the CZI Ben Barres Early Career Acceleration Award.

Rachel Karchin, Ph.D

Dr. Karchin is a computational biologist who develops algorithms and software to analyze genomic variation data, tumor evolution, and the adaptive immune system. Her group has developed novel tools to identify pathogenic missense mutations, driver genes, multivariate biomarkers to inform cancer treatment, to model tumor evolution from next-generation sequencing data and to predict tumor neoantigens. She was the leader of the computational efforts to identify driver mutations for pioneering cancer sequencing projects at Johns Hopkins Sidney Kimmel Cancer Center, and co-led the TCGA PanCan Atlas Essential Genes and Drivers Analysis Working Group. In 2017, she was inducted into the College of Fellows of the American Institute for Medical and Biological Engineering for her contributions to translational computational biology.

Prashant Mali, Ph.D

Prashant Mali is a faculty member in the Department of Bioengineering at the University of California San Diego. His research is in the fields of synthetic biology and regenerative medicine, with a long-term focus on developing tools for enabling gene and cell based human therapeutics.

Deborah Marks, Ph.D

Debbie is a mathematician and computational biologist with a track record of using novel algorithms and statistics to successfully address unsolved biological problems. Her lab at Harvard is interested in developing methods in deep learning to address a wide range of biological challenges including predicting the effects of genetic variation and sequence design for biosynthetic applications.

Kenneth Matreyek , Ph.D

Kenneth Matreyek obtained a BSc in Microbiology, Immunology, and Molecular Genetics from the University of California Los Angeles. He went on to earn a PhD in Virology from Harvard University, studying the molecular interactions that HIV uses to enter the nucleus of infected cells before integrating its viral genome. For his dissertation, he discovered that HIV uses its protective capsid shell to interact with the intrinsically disordered domains present on the nuclear pore protein NUP153. For his postdoctoral training, he joined the laboratory of Dr. Douglas Fowler at the University of Washington. There, he applied mammalian cell engineering and synthetic biology to develop multiplex genetic methods to simultaneously characterize thousands of protein variants within cultured human cell models. As an American Cancer Society Postdoctoral Fellow, he characterized how germline and somatic missense variants of the PTEN tumor suppressor contributes to disease. He joined the Department of Pathology at Case Western Reserve University during the fall of 2019.

Beatriz Adriana Osuna, Ph.D

Bettie Osuna is a scientist on the deep mutational scanning team at Octant Bio. Before joining Octant, she completed her Ph.D. in Biochemistry at UCSF under the supervision of Dr. Joseph Bondy-Denomy. Her thesis work broadly focused on the functional and mechanistic characterization of molecular machines involved in bacterial immunity (CRISPR-Cas9 and viral anti-CRISPR proteins) and protein translation surveillance (ribosome quality control complexes).

Maria-Jesus Martin, Ph.D

Dr. Maria Martin leads the Protein Function Development team at EMBL-EBI. She is a world expert in the management of database resources with over twenty years of experience in developing protein sequence resources at EMBL-EBI. Since joining EMBL-EBI in 1996, she has been involved in the strategic planning, data analysis and development of many database resources at this institute with special focus on protein data and leading the bioinformatics aspects of the Universal Protein Resource (UniProt), the world leading database of classified and functionally annotated protein sequences. Additionally, she leads the GO Annotation development team and the Enzyme portal resource. Her interests include the study of novel methods for protein annotation and representation, the provision of quality annotation Reference Proteomes for the scientific community, and data analysis and visualization of protein data in the context of other –omics data i.e. proteomics and variation. She is key staff of the UniProt Consortium and an active member of the GO and QfO Consortia.

Erik Procko, Ph.D

Erik Procko is an Assistant Professor of Biochemistry at the University of Illinois. He completed his doctoral studies at Harvard University under the mentorship of Rachelle Gaudet, where he applied structural methods, biochemistry, and electrophysiology to investigate membrane protein mechanisms. During postdoctoral research with David Baker at the University of Washington, he computationally designed one of the first de novo proteins with function. Since beginning his independent position in 2014, his research program draws upon elements from his training to apply directed evolution and in vitro selections to model and engineer membrane protein systems. He has a particular focus on proteins involved in immunity (especially presentation of antigenic peptides by MHC molecules), virus infection (in particular the engineering of soluble decoy receptors that bind viral targets with affinity and specificity), and neuronal receptors and transporters.

Frederick (Fritz) Roth, Ph.D

Frederick (Fritz) Roth (U Toronto, Sinai Health) trained in physics and biology (UC Berkeley) and biophysics (Harvard). After early work on functional and motif enrichment in transcriptomic data, his team maps genetic and protein interactions and identifies damaging human variants.

Alan Rubin, Ph.D

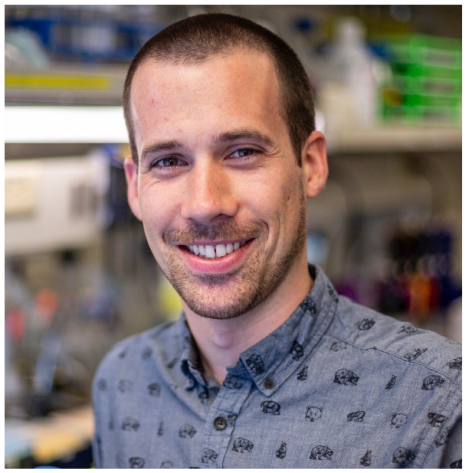
Dr. Rubin is a computational biologist at the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia. Alan's work focuses on developing new tools and approaches to analyze and interpret high-throughput genomics data.

Avtar Singh, Ph.D

Avtar Singh is a postdoctoral scholar in the Blainey lab at the Broad Institute, where he and others developed a technology for pooled image-based screens in mammalian systems. Optical pooled screens use in situ sequencing to demultiplex genetic perturbations from a pooled genetic library, enabling the use of high-content imaging as a phenotypic readout for pooled screens. Prior to the Broad Institute, Avtar was an NSF Graduate Research Fellow with Warren Zipfel at Cornell University where he developed methods for single-molecule stoichiometry analysis in engineered syncytia and an azimuthal scanning laser illumination platform for TIRF and super-resolution fluorescence microscopy.

Lea Starita, Ph.D

Dr. Starita is a Research Assistant Professor in the Department of Genome Sciences at the University of Washington and the Co-director of Brotman Baty Advanced Technology Lab. She earned her Ph.D. from Harvard Medical School before coming to the University of Washington to train in functional genomics with Stan Fields and Jay Shendure.



Tyler N. Starr, Ph.D.

Tyler Starr is a Damon Runyon Cancer Research Foundation Post-doctoral Fellow in Jesse Bloom's lab at the Fred Hutchinson Cancer Research Center, where he has used deep mutational scanning to understand the biochemistry, immunology, and evolution of the receptor-binding domain of the SARS-CoV-2 spike protein. Tyler completed his PhD in the lab of Joe Thornton, where he used mutational scanning techniques to characterize the features shaping trajectories of evolution in ancestrally reconstructed proteins.

Clare Turnbull, Ph.D

Professor Clare Turnbull is Professor of Translational Cancer Genetics in the Division of Genetics and Epidemiology at the Institute of Cancer Research, London. Her research spans statistical, population and public-health-related analyses of genetic cancer susceptibility and implementation of expanded genomic testing. She is currently rolling out a new £4.3 million Cancer Research UK(CRUK)-funded program: 'CanGene-CanVar: Data Resources, Clinical and Educational Tools to leverage Cancer Susceptibility Genetics for Early Detection and Prevention of Cancer' program.

Organizing Committee

Yashwanth Ashok
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University of Washington

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Project Manager
Brotman Baty Institute

Florence Chardon
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University of Washington

Jochen Weile
Roth Lab
University of Toronto

Jenny Xiao
Associate Director, Market Development
Illumina, Inc.

Daily Moderators

April 5: Flo Chardon, Moez Dawood, Sophie Moggridge, Doug Fowler, Aditya Chawla

April 6: Shawn Fayer, Andrej Patoski, Aditya Chawla

April 7: Flo Chardon, Daniel Tabet, Yash Ashok, Sophie Moggridge

Special thanks to Cristina Madeira Alexandre for banner design

Virtual Meeting Information

This three-day event will be held virtually, April 5th-7th, 2021.

Register to attend HERE

Poster session will be hosted on Gathertown

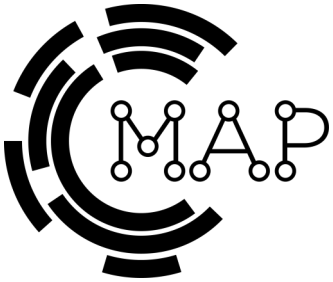
Attendees will need to create an avatar to participate.

The password to the poster session will be provided the day of the event.

The event will be live streamed on our YouTube channel

We encourage you to follow and interact with CMAP on Twitter and by using our event hashtag **#varianteffect21**

Many Thanks to our Sponsors



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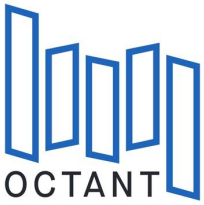

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