Variant effect mapping outreach and education program at the Center for the Multiplexed Assessment of Phenotype

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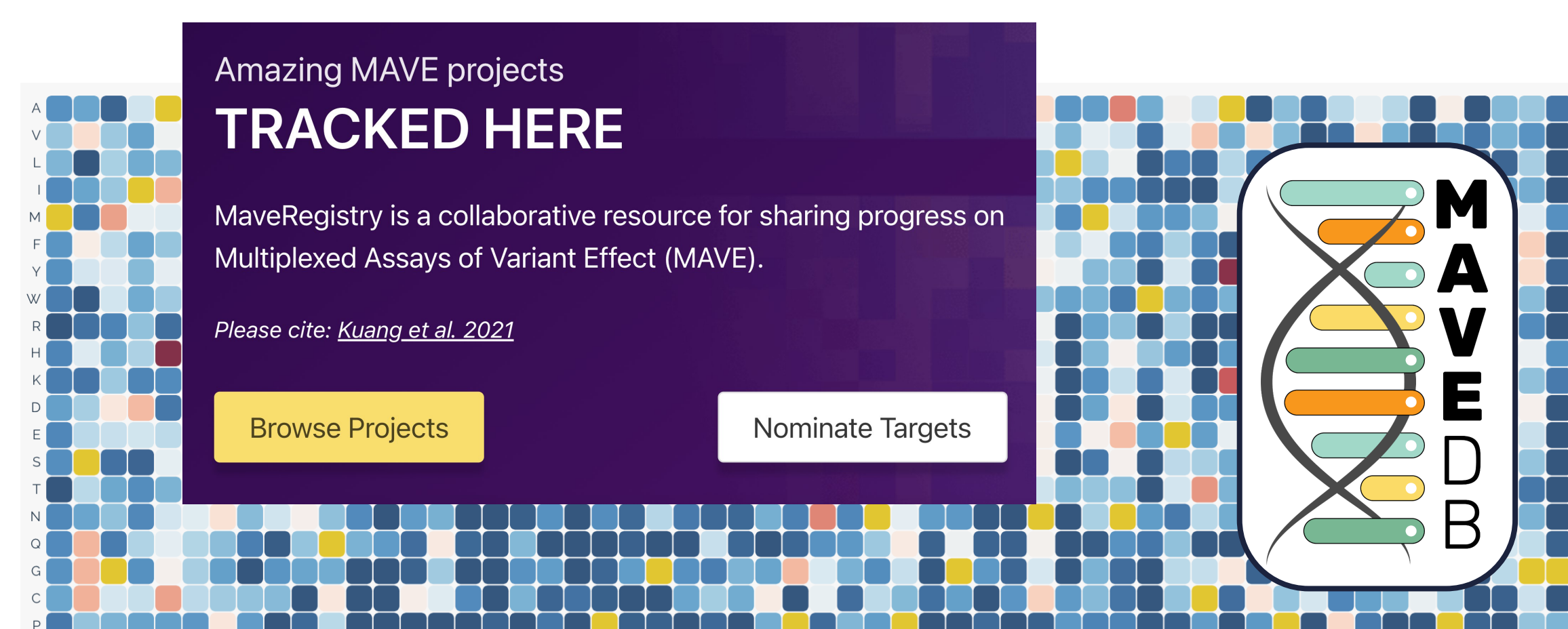
INTRODUCTION

The Center for the Multiplexed Assessment Phenotype (CMAP), is a Center of Excellence in Genome Science based at the University of Washington and the University of Toronto.

We build Multiplexed Assays of Variant Effect (MAVE) and mutational scanning technologies to enable proactive measurement of the functional effects of all possible single-nucleotide variants in a target gene. These methods offer a general, scalable way to understand how variants impact molecular and cellular phenotypes, and to resolve variants of uncertain significance (VUS) that arise when human genomes are sequenced.

CMAP's primary objectives are to 1) develop novel, scaleable and phenotypically complex technologies to assess the functional impact of single nucleotide variants in human genes 2) drive wide adoption of these methodologies 3) train early career experimentalists, clinical geneticists and data scientists to obtain and use large-scale functional data.

The technologies developed by our Center can shed light on the functional consequences of genetic variants and ultimately on the landscape of human genetic variation. By providing inclusive access to training and tools for making, depositing, obtaining, and using variant effects maps we are building a community that can take on the challenge of understanding how all of the billions of possible variants of the human genome impact phenotype and disease. Here we describe CMAP's outreach and education program.

CMAP offers short-term internships, postdocs as well as opportunities for undergraduates. Above: CMAP intern Moez Dawood and Dr. Lea Starita discussing a Saturation Genome Editing (SGE) project. Postdoc Curran Oi presenting work on whole organism Deep Mutational Scanning (DMS) at the CMAP all hands meeting.

Free educational content is available on our CMAP youtube page which includes presentations from the Mutational Scanning Symposium and Workshop as well as talks from the Variant Effect Seminar Series.

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2. Brotman Baty Institute for Precision Medicine, Seattle, WA, USA
3. The Donnelly Centre and Departments of Molecular Genetics and Computer Science, University of Toronto, Toronto, Ontario, Canada
4. Lunenfeld-Tanenbaum Research Institute, Sinai Health, Toronto, Ontario, Canada
5. Howard Hughes Medical Institute, Seattle, WA, USA
6. Bioinformatics Division, WEHI, Parkville, Australia
7. Department of Medical Biology, University of Melbourne, Parkville, Australia

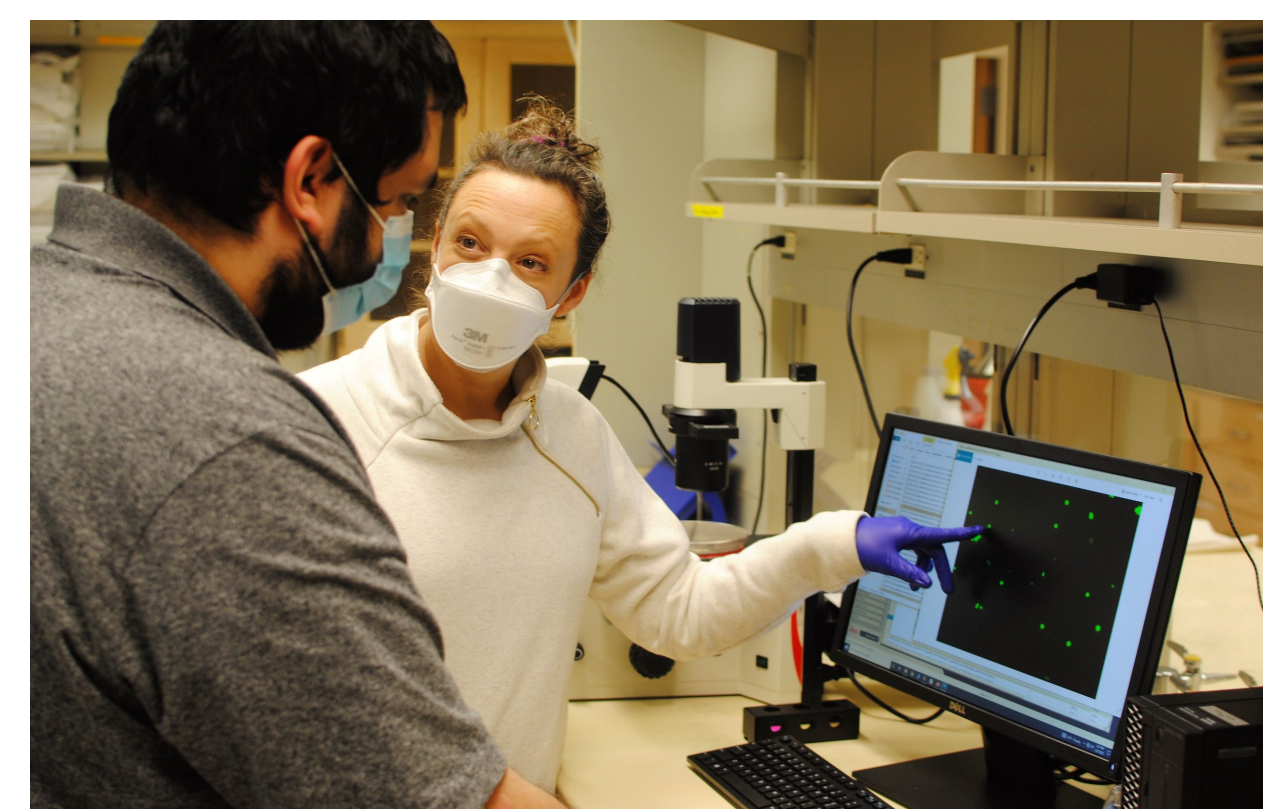## EDUCATION AND OUTREACH RESOURCES FOR VARIANT EFFECT MAPPING

We provide a suite of resources and tools for variant effect mapping. Resources include MaveRegistry, a platform to catalyze collaboration, reduce redundant efforts, allow stakeholders to nominate targets and enable tracking and sharing of progress on ongoing MAVE projects and MaveDB, a hub for the analysis and dissemination of MAVE datasets.

TYPE	Decription (and URL)
TRAINING (tailored to individuals interested in mastering CMAP-developed technologies)	
Technology Dissemination Internships 1-3mo duration	2 interns per year
Application-Focused Apprenticeships (Postdoc level) 1-2yr duration	1-2 fellows per year
Training Fund	Support for predocoral and postdoctoral research trainees working on high-risk, high-reward methods development in the field of functional genomics, 2 recipients in 2022
Summer Research Program REU (URM undergraduates)	The Department of Genome Sciences, provides summer research opportunities for undergraduate students. CMAP hosts ~ 5 students per year https://www.gs.washington.edu/academics/summer/gssummer/participants.htm
EDUCATION	
Mutational Scanning Symposium and Workshop	CMAP co-hosts the annual Mutational Scanning Symposium and Workshop (with 25 speakers, 10 lightning talks, 86 posters and over 362 attending, all from over 20 countries for the most recent hybrid event in Toronto, Canada). Brings together top international experts on mutational scanning. Held Annually https://www.varianteffect.org/mss2022
Variant Effect Seminar Series	Monthly seminar series where career scientists from around the globe share and discuss their research related to interpreting human genetic variation. Held virtually, free to the public https://www.varianteffect.org/seminar-series
Online resource_ Knowledgebase	Variant effect mapping resource knowledgebase https://www.varianteffect.org/resources
Educational Videos	Free educational content on the CMAP YouTube channel. Includes presentations from Mutational Scanning Symposium, Workshops and the Variant Effect Seminar Series. (over 300 subscribers, and 21,373 views) https://www.youtube.com/channel/UCdS-1bGBkOvAMYXkFZoAkIg
COMMUNITY, RESOURCES and TOOLKITS	
Atlas of Variant Effects (AVE) Alliance	Expands the community of scientists generating and using variant effect maps https://www.varianteffect.org/about
MaveDB	A public repository for variant effect maps https://www.mavedb.org/
MaveImpute	A web application and service for imputing and visualizing missense variant effect maps http://impute.varianteffect.org, https://github.com/joewuca/imputation
MaveQuest	A web resource for planning experimental tests of human variant effects https://mavequest.varianteffect.org
MaveRegistry	Collaborative resource for sharing progress on Variant Effect Mapping https://registry.varianteffect.org/
MaveVis	A visualization tool for variant effect maps in MaveDB http://vis.varianteffect.org https://github.com/VariantEffect/mavevis#readme
Enrich2	Software tool for processing, analyzing, and visualizing data from deep mutational scanning experiments https://github.com/FowlerLab/Enrich2
VARITY	Improved pathogenicity prediction for rare human missense variants http://varity.varianteffect.org/
CMAP Website	Information, recent news, manuscripts https://www.cmap.gs.washington.edu, https://www.cmap.gs.washington.edu/news, https://www.cmap.gs.washington.edu/publications
CMAP Twitter Account	https://twitter.com/CEGS_CMAP (@CEGS_CMAP) 476 Followers

MUTATIONAL SCANNING SYMPOSIUM

The Center's technologies have the potential to transform our understanding of the human genome. Our annual Mutational Scanning Symposium brings together top international experts on mutational scanning, who share their latest work and provide insights on the future of this science. The Symposium began four years ago as a local event in Seattle, and has grown each year, with generous support from funders and lots of work from organizers.
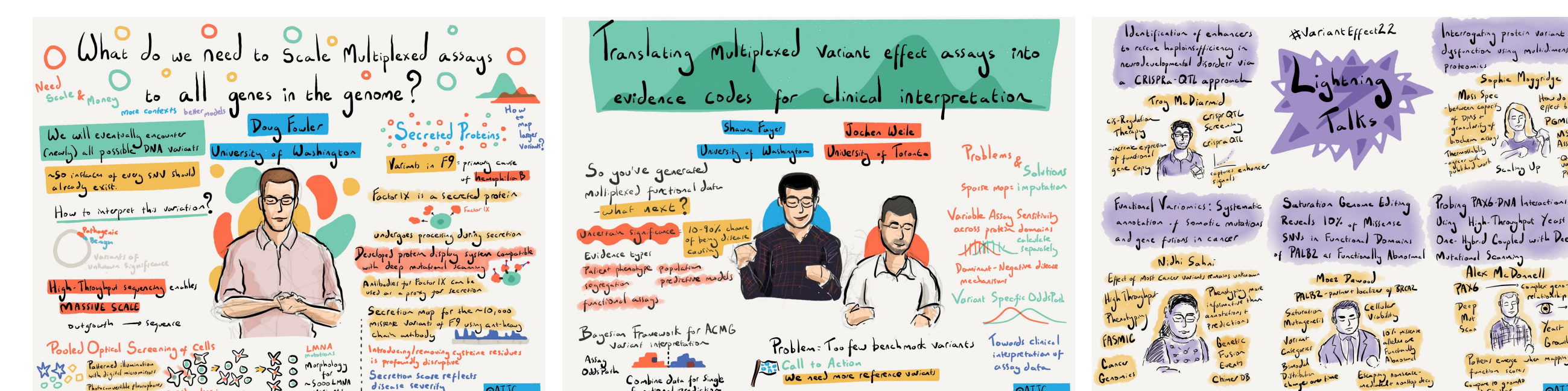
This year, the three day program included keynote lectures by Clare Turnbull and Doug Fowler, as well as 25 invited talks and 10 lightning talks selected from poster abstracts. Most speakers agreed to help us create a community resource by making their talks permanently available on our CMAP YouTube channel. In 2023, the Symposium will be in the UK at the Wellcome Sanger Institute. (Conference Illustrations by Alex Cagan).

We invite everyone to help solve the VUS problem
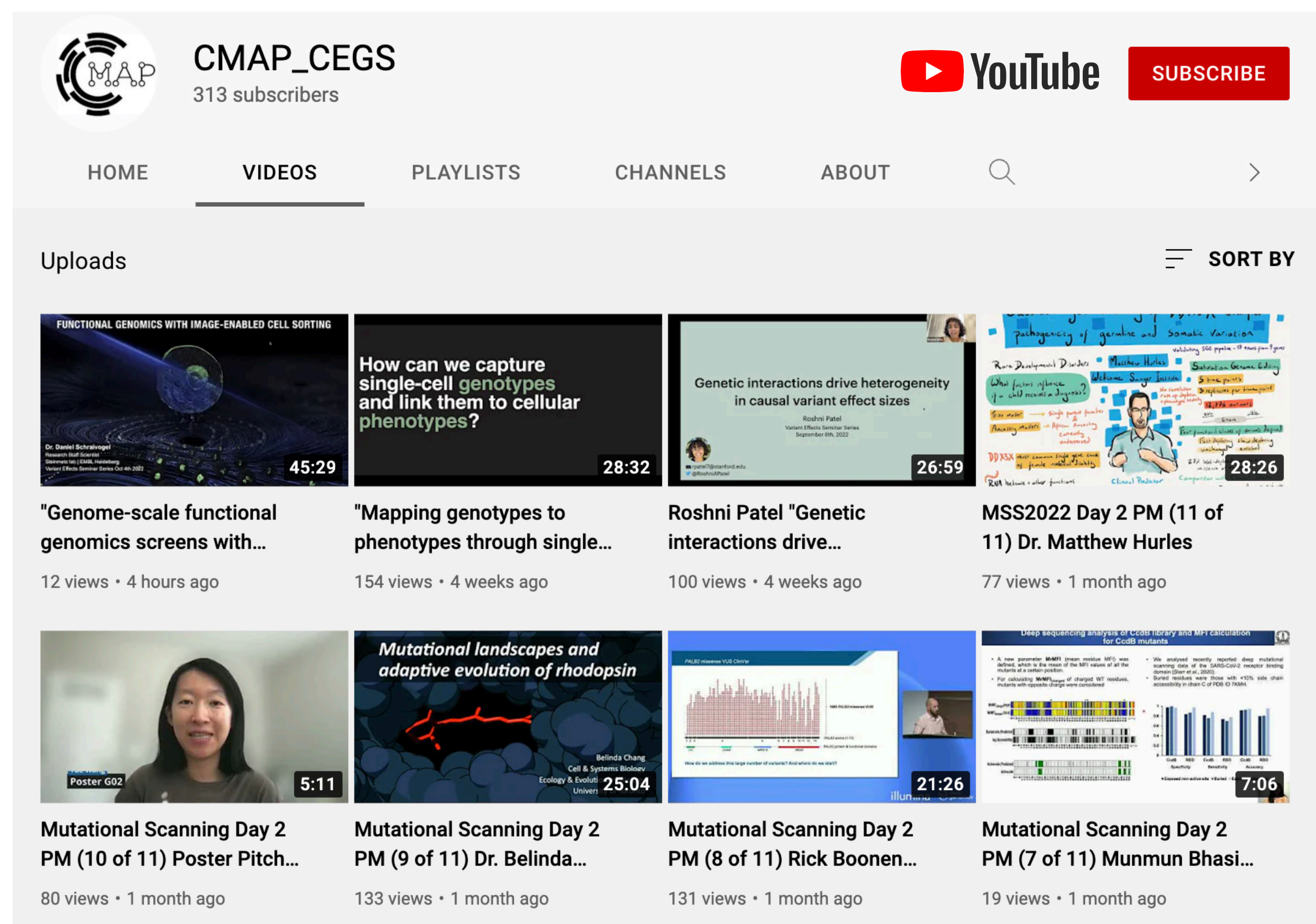
- Learn how to make a variant effect map!
- Watch educational videos!
- Deposit your Variant Effect Map data into MAVEDB
- Join our team! (Postdocs and Internships!)
- Attend and present at the Mutational Scanning Symposium
- Join our international MAVE Community user group