2024 Featured Symposia (as of May 2024)

Thursday, November 7, 8:00 - 9:30 AM

AJHG at 75: Looking to the future of human genetics research
Moderator: Bruce R. Korf, MD/PhD, University of Alabama at Birmingham

Audience: Researchers
Topic: Complex Traits
Track: Basic or Translational Research; Clinical Research; Diversity, Equity, and Inclusion

Session Description: This year marks the 75th anniversary of the American Journal of Human Genetics. From its inception, the Journal has had the mission of publishing high quality peer-reviewed research across the spectrum of human genetics. The contents of the journal are always evolving along with the fast-paced progression of human genetics research in general. This session is intended to use recent trends in papers published in the Journal to stimulate discussion on major areas of exciting development in human genetics research in the near-term future. The editor-in-chief, Dr. Bruce Korf will provide context on the history of the journal, following which four speakers who have published papers in the Journal in the recent past will comment on how they see the future of four areas of research: rare disease diagnosis and treatment, understanding the genetic contributors to common disease, genetic studies of human evolution, and genetics research in lower and middle income countries. The session will conclude with a panel discussion that will entertain questions and comments from the audience.

Learning Objectives:
1. Explain new genomic testing approaches will increase diagnostic yield on diagnosis of genetic disorders
2. Describe approaches to definition of the genetic contribution to common disease and how these can be used to advance public health
3. Summarize obstacles to implementation of genomics research in lower and middle income regions and some of the approaches to overcome these obstacles
4. Explain how human evolutionary studies can provide insights that inform current human population genetics

Speakers:
Rare Disease Diagnosis and Treatment. Danny Miller, MD/PhD, University of Washington
Genomics of Common Disorders. Eimear Kenny, PhD, Icahn School of Medicine at Mount Sinai
Genetics Research in Low- and Middle-Income Settings. Elizabeth Atkinson, PhD, Baylor College of Medicine
Genetic Studies of Human Evolution. Lluis Quintana-Murci, PhD, Pasteur Institute and College de France

Thursday, November 7, 8:00 - 9:30 AM

Balancing open science and patient privacy in the era of precision medicine
Moderators: Gamze Gursoy, PhD, Columbia University; Thomas Lehner, PhD, New York Genome Center (NYGC)

Audience: Researchers
Topic: Genetic Counseling, ELSI, Education, and Health Services Research
Track: Ethical, Legal, and Social Issues; Other

Session Description: In the rapidly evolving field of genomic medicine, balancing the essential need for data sharing with the critical imperative of protecting patient privacy presents an unprecedented challenge. The utilization of deeply personal genetic, demographic, lifestyle, and health information to customize medical care heightens the importance of securing sensitive data against unauthorized access and misuse. These privacy and security concerns are pertinent across patient care and research domains, each bringing distinct challenges and demands. This symposium aims to dissect the intricate balance between these challenges and the opportunities they present. We aim to shed light on innovative strategies that safeguard patient privacy and data security while fostering the collaborative exchange of scientific knowledge. Through four engaging talks, we will delve into the hurdles to enhancing diversity and participation in genetic research, deploying robust security and privacy frameworks for data sharing, and computing within large biobanks, research consortia, and healthcare systems. Additionally, we will address the ethical, legal, and social ramifications of data sharing in this field. Through a moderated panel discussion and Q&A session, we will navigate the complexities of these critical issues, gaining insights into both the challenges and the cutting-edge practices that promise to advance precision medicine responsibly and in a scientifically robust manner.

Learning Objectives:
1. Identify challenges of sharing genetics data in biobanks and large-scale consortia
2. Evaluate security and privacy frameworks for data sharing and computing
3. Highlight challenges and opportunities for enhancing diversity and participation in genetic research
4. Explore ethical, legal, and social implications of data sharing

Speakers:
Stewardship and Sharing: Balancing genomic privacy and research advances in the context of psychiatric genetics. Lea Davis, PhD, Vanderbilt Univ Med Center
Human Pangenome(s) in the Cloud: Seeking Balance between Utility and Privacy. Alice Popejoy, PhD, University of California, Davis
Technical approaches to balance patient privacy and shared analytic utility. John Wilbanks, BA, Broad Institute of MIT and Harvard
Secure and federated quantitative trait loci mapping with privateQTL. Yoolim Annie Choi, BA, Columbia University

Thursday, November 7, 8:00 - 9:30 AM

Contributions of tandem repeats to human variation, traits, and disease
Moderators: David L. Nelson, PhD, Baylor College of Medicine; Emily G. Allen, PhD, Emory University School of Medicine

Audience: Researchers
Topic: Genetic, Genomic, and Epigenomic Resources and Databases
Track: Basic or Translational Research

Session Description: Short tandem repeats (STRs) are abundant in the human genome and are estimated to compose as much as 7% of our DNA. STRs are motifs of DNA 2-6 nucleotides in length repeated up to thousands of times. At many loci, STRs show considerable population polymorphism, with variable length and sequence features such as interruption and alternative motifs. Since 1991, some 60 STR loci have been found to contribute to monogenic disorders, notably many neurodegenerative and neurodevelopmental syndromes such as Huntington Disease and Fragile X syndrome. Understanding the number and nature of STRs in the human genome and their contributions to normal variation and common disease has been challenging due to limitations with genome sequence analysis. Recent technological advancements in collecting and analyzing DNA sequence data are beginning to overcome these limitations. In this session, four leading groups will present their latest approaches to characterizing genome-wide STRs and identifying associations with phenotypic data in large collections of human genomes. From these presentations, it will be apparent that the contribution of polymorphic variation at STRs is large for both rare and common diseases, and that methods to measure their impact have matured sufficiently to no longer overlook STRs in studies of human genetic variation.

Learning Objectives:
1. Identify best practices for analyzing tandem repeats
2. Reproduce the diversity in tandem repeats
3. Analyze the genome-wide genetic and epigenetic variation in tandem repeat regions
4. Indicate the role of this type of variation in human variation, traits and disease

Speakers:
Profiling genetic and epigenetic variation in and around tandem repeat regions. Egor Dolzhenko, PhD, Pacific Biosciences of California
Cataloguing of CGG Short Tandem Repeats Reveals an Overrepresentation of Expansions in Neurodevelopmental Disorders. Dale Annear, PhD, University of Antwerp
Genomic approaches for studying the role of tandem repeat expansions in human disease. Andrew Sharp, PhD, Icahn School of Medicine at Mount Sinai
Tandem repeats make widespread contributions to complex traits. Melissa Gymrek, PhD, University of California, San Diego

Thursday, November 7, 8:00 - 9:30 AM

Unveiling genetic mysteries: RNA editing's breakthrough in disease and gene therapy
Moderators: Xinshu Xiao, PhD, University of California Los Angeles; Michael S. Breen, PhD, Icahn School of Medicine at Mount Sinai

Audience: Researchers
Topic: Molecular Effects of Genetic Variation
Track: Basic or Translational Research

Session Description: With the ever-growing catalog of disease loci identified by genome-wide association studies, the demand increases for interpretation of these genetic variants through interacting layers of gene regulation. Novel disease mechanisms have been appreciated by the adoption of quantitative trait loci (QTL) analysis, and expansion from expression QTLs to consider other consequential molecular phenotypes, such as A-to-I RNA editing. A-to-I RNA editing is an abundant post-transcriptional modification, whose dysregulation in diseases ranging from cancer to neurological disorders has been well characterized. Studying the genetic regulation of A-to-I editing by cis-acting variants (edQTL) has demonstrated A-to-I editing mediates a substantial amount of disease risk for autoimmune and inflammatory diseases and supported a causal role of RNA editing in psychiatric disorders. As a therapeutic tool, targeted RNA editing has the potential to recode RNA sequence and modulate gene expression and splicing, thus representing therapeutic potential for rare, protein-altering variants along with non-coding GWAS variants. How will advancing our knowledge of RNA editing and its role in gene regulation clarify mechanisms underlying complex traits and diseases? What is the potential of RNA therapeutics from these insights? This session will feature research ranging from molecular dissection of disease mechanisms, statistical genetics approaches, and development of targeted RNA editing therapeutics.

Learning Objectives:
1. Summarize genetic disease insights gained from RNA editing studies
2. Share research that has resolved missing heritability from GWAS
3. Highlight technological advancements in RNA therapeutics
4. Translate the application of these tools to their own research interests

Speakers:
ADAR1 Inhibitors: Novel Cancer Therapeutics and Immunotherapy Synergyzers. Kazuko Nishikura, PhD, The Wistar Institute
RNA Editing: Innate Immunity and Autoinflammatory Disease. Jin Billy Li, PhD, Stanford University
Massive-scale meta-analysis of genetic regulation of RNA editing in the human brain identifies new risk genes and mechanisms for neurological disease. Winston H. Cuddleston, PhD, Icahn School of Medicine at Mount Sinai
Enhanced ADAR Activity in Inefficiently Edited Substrates using Chemical Modifications of Oligonucleotides. Aashrita Manjunath, BS, University of California, Davis

Thursday, November 7, 8:00 - 9:30 AM

TOPMed 10-year anniversary: Ongoing success and future directions
Moderators: Tamar Sofer, PhD, Beth Israel Deaconess Medical Center / Harvard Medical School; Weiniu Gan, PhD, National Heart Lung and Blood Institute

Audience: Researchers
Topic: Complex Traits
Track: Basic or Translational Research

Session Description: The Trans-Omics in Precision Medicine (TOPMed) project of the National Heart, Lung, and Blood Institute (NHLBI) has supported genomic data generation and harmonization for many U.S. and international-based studies. These include deep whole-genome sequencing (WGS) data and omics datasets. TOPMed is one of the largest resources of WGS and omics (>180,000 WGS, >70,000 funded methylation, RNA-seq, and metabolomics assays, >40,000 proteomics). Importantly, the TOPMed program focuses on data collection from under-studied and under-represented populations such as Hispanic and Latino individuals in the U.S., African, and African American individuals. This session will highlight the 10th anniversary of the TOPMed program and focus on the future use of the TOPMed resource by the broader research community. The session will begin with an "overview of TOPMed" talk by Dr. Gan, the NHLBI program director who oversees TOPMed, describing the vision that motivated TOPMed, highlight major TOPMed milestones, and introduce the vision for the next step of TOPMed. Dr. Gan will also cover the current process for accessing TOPMed data and ideas to improve the process. Four talks will follow highlighting findings enabled by TOPMed: insights into genetic diversity, selection, and population dynamics from large scale sequencing, and findings from integration of omics and genetics. A panel discussion will introduce additional achievements, gaps, and outline to the community how they can use this massive resource.

Learning Objectives:
1. Describe inference and implications of genetic effects at the population levels from ultra-rare genetic variants
2. Identify mechanisms by which trans-eQTLs impact gene expression
3. Examine genetic influences on circulating metabolites with diverse populations via a novel, large multi-ancestry harmonized metabolomics data set
4. State new findings about how proteins causally affect other proteins in human plasma and use of genetic data to infer these relationships

Speakers:
Patterns of ultra-rare genetic variation from high coverage whole genome sequencing of over 150,000 diverse individuals. Miguel Guardado, BS, University of California, San Francisco
Cross-cohort e/sQTL analyses of 6,602 multi-ethnic TOPMed whole blood RNA-seq samplesnominate genes and mechanisms underlying trans-eQTLs. Laura Scott, PhD, MPH, University of Michigan
Genetic Architecture of Circulating Metabolites and Its Impact on Health from Trans-Omics for Precision Medicine (TOPMed) Program. Nannan Wang, PhD, UTHealth Houston School of Public Health
The Integration of Genomic and Proteomic Profiling Data in TOPMed to Identify Protein-Protein Pathway Partners in Human Plasma. Aaron Eisman, PhD, MD, Yale New Haven Hospital

Thursday, November 7, 8:00 - 9:30 AM

Advances in artificial intelligence tools to improve clinical diagnoses and medical genetics education with an emphasis on diverse datasets
Moderators: Gholson J. Lyon, MD/PhD, Institute for Basic Research in Developmental Disabilities; Tzung-Chien Hsieh, PhD, University Hospital of Bonn

Audience: Researchers
Topic: Mendelian Phenotypes
Track: Basic or Translational Research; Clinical Research

Session Description: This session will explore the use of Artificial Intelligence (AI), Deep Learning (DL), and Large Language Models (LLM) in diagnosing rare disorders and their role in educating the next generation of geneticists. Many rare disorders exhibit distinct physical manifestations crucial for diagnosis. However, European-biased training data limits performance for individuals of non-European ancestry. In response to this challenge, the first talk will introduce the GestaltMatcher Database (GMDB) as a global reference medical imaging database showcasing the phenotypic variability of rare diseases across diverse populations. By analyzing facial images and clinical notes, the second talk will investigate how GestaltMML, powered by Multimodal Machine Learning (MML), aids in diagnosing patients with rare disorders. The third talk will highlight rare eye diseases, specifically inherited retinal diseases (IRDs), which present a formidable challenge and can lead to blindness. We will introduce Eye2Gene, a DL algorithm for streamlining IRD diagnosis via retina scan analysis. The last talk will discuss using DL techniques to enhance the education of clinical geneticists in recognizing genetic conditions more effectively by leveraging generative AI and explainable AI approaches to provide comprehensive insights into genetic conditions. Talks will describe confounders in AI model training and how diverse demographics in datasets (e.g., ancestry, age, and sex) improve accuracy for all patients.

Learning Objectives:
1. Apply artificial intelligence to facial photographs and rare genetic disorders
2. Perform large language models and multi-modal machine learning for next-generation phenotyping
3. Illustrate Eye2Gene for fundoscopy imaging analysis, to assist variant interpretation
4. Propose collecting image data from diverse populations

Speakers:
GestaltMatcher Database - A global reference for the phenotypic variability of rare diseases in humans. Shahida Moosa, MD/PhD, Tygerberg Hospital
Multimodal Machine Learning Combining Facial Images and Clinical Texts Improves Diagnosis of Rare Genetic Diseases. Da Wu, PhD, University of Pennsylvania
Eye2Gene - next generation phenotyping using artificial intelligence to predict the genetic diagnosis in inherited retinal diseases. Ismail Moghul, PhD, University College London
Deep Learning for Genomics Education. Rebekah Waikel, PhD, NHGRI

Thursday, November 7, 8:00 - 9:30 AM

Human genetic mosaicism: Diversity within individuals
Moderators: Christopher Grochowski, PhD, Baylor College of Medicine; Claudia Gonzaga-Jauregui, PhD, Universidad Nacional Autónoma de México (UNAM)

Audience: Researchers
Topic: Molecular Effects of Genetic Variation
Track: Basic or Translational Research; Clinical Research

Session Description: Human genetic mosaicism is the presence of populations of cells with different genetic compositions, within a single individual. Originally studied within cancer, the occurrence of mosaic somatic variation has remained understudied. This variation can arise at a single nucleotide or encompass chromosomal aberrations and may be present at varying levels in different tissues and has been shown to play a critical role in the development of several human diseases. Despite its significance, the detection, validation, and subsequent interpretation of a potentially mosaic variation within sequencing data remains a challenge in both the research and clinical settings. This session will highlight research in the field and will begin with an introduction to the topic with an emphasis on the formation within a cellular lineage and will detail the pathogenic consequence within a disease state. The second speaker will review the topic in a bioinformatics focused lens; explaining the development of tools to detect mosaic variation within sequencing data. Our next speaker will present the challenges in detection/interpretation of mosaic variants in a diagnostic setting and its implications for family counseling. The last speaker will highlight the ambitions of the newly formed NIH consortium Somatic Mosaicism across Human Tissues (SMaHT) that will develop new tools/methodologies to understand this underappreciated type of variation and how it may influence the pathogenesis of disease.

Learning Objectives:
1. Summarize the formation of somatic mosaicism in the human body
2. Identify how mosaicism can lead to a disease state
3. Evaluate the challenges in detecting and interpreting mosaicism diagnostically
4. Define the Somatic Mosaicism across Human Tissues (SMaHT) consortium's goal in understanding human mosaicism

Speakers:
Formation of genomic mosaicism: somatic mutation in the human brain. Christopher Walsh, MD/PhD, Boston Children's Hospital
Detection of mosaic structural variation with Sniffles2. Luis Paulin, PhD, Baylor College of Medicine
Understanding mosaicism in a diagnostic setting. Laura Conlin, PhD, Children's Hospital of Philadelphia
Charting the Landscape of Somatic Mutations: The SMaHT Consortium's goal for Understanding Human Tissue Variability. Tim Coorens, PhD, Broad Institute of MIT and Harvard

Thursday, November 7, 8:00 - 9:30 AM

The Alzheimer's Disease Sequencing Project (ADSP): A paradigm for identifying genetically driven therapeutics for a global complex disease
Moderators: Anthony Griswold, PhD, University of Miami; Biniyam Ayele, MD, College of Health Sciences, Addis Ababa University

Audience: Researchers
Topic: Complex Traits
Track: Basic or Translational Research

Session Description: Clinical trials are far more likely to succeed when supported by genetic evidence. Thus, across complex diseases affecting millions worldwide, large-scale collaborative projects are needed to accelerate identifying targets for treatment. This session will describe a model for such an initiative, The Alzheimer's Disease Sequencing Project (ADSP), initiated by the National Institute on Aging in 2012 to accelerate the development of effective treatments for Alzheimer's disease and related dementias. The ADSP leverages whole genome sequencing with an integrated infrastructure for sample acquisition, data generation, data harmonization, and rapid data sharing. This is a global collaborative initiative that includes the collating and harmonizing of rich phenotypic information from across the globe including resource limited communities in the US along with cooperative efforts in the Caribbean, South America, Africa, and South and East Asia. Incorporating multi-omics, biomarkers, and cellular and animal modeling has hastened the development of genetically driven targets currently in clinical trials including TREM2, MS4A4A, MS4A6A, and APOE. This session will briefly highlight the history and emphasize the current and future prospectives of the ADSP and how it can serve as a model for other consortia in identifying new and potential therapeutic developments through international collaboration, inclusion of diversity, functional analysis, and exploration of clinical targets.

Learning Objectives:
1. Analyze the history and evolution of the ADSP and its progress towards genetically driven therapeutic targets
2. Identify the complexities of phenotypic harmonization required in recruiting and including diverse populations in genetic studies
3. State the utilization of functional genomics approaches in identifying new disease genes
4. Recognize the trajectory of genetic discoveries to cell and animal model evaluation of potential therapies

Speakers:
From Gene Discovery to Clinical Trials: The Alzheimer's Disease Sequencing Project's progress towards therapeutic targets. Margaret Pericak-Vance, PhD, University of Miami
The ADSP Phenotype Harmonization Consortium: Aggregating phenotyping data across the globe. Logan Dumitrescu, PhD, Vanderbilt University Medical Center
Extending the Approaches of the ADSP into Functional Genomics: Characterizing New Potential Targets with Proteogenomic Analysis of Cerebrospinal Fluid Identifies Neurologically Relevant Regulation and Informs Causal Proteins for Alzheimer's Disease. Carlos Cruchaga, PhD, Washington University
This Mission of the ADSP to Identify Genetically Driven Therapeutic Targets for AD: Using Cell and Animal Models of MS4A as a Case Study of Translating AD Genetics to Therapies. Alexandra Munch, BA, Icahn School of Medicine at Mount Sinai

Friday, November 8, 8:00 - 9:30 AM

Model organisms to the rescue: Next generation animal models for precise phenotyping of complex diseases
Moderators: Ashish Kapoor, PhD, UTHealth Houston; Hilda Chubaryov, BS, NYU School of Medicine

Audience: Researchers
Topic: Molecular Effects of Genetic Variation
Track: Basic or Translational Research

Session Description: Sequencing studies have led to vast catalogs of disease-associated variants, but functional studies aimed at understanding their effects on specific cellular processes underlying diseases are lagging. Hence, there is a growing need to create targeted and humanized animal models to interrogate the effects of these variants in specific cell types and at specific time points during development or aging. In this session we will bring together four talks focused on utilizing invertebrate and vertebrate model systems to model the cellular and molecular phenotypes of complex and undiagnosed diseases. The first speaker will talk about using humanized aneuploid mouse models of Down syndrome (DS) to uncover changes in the enteric nervous system of DS patients. The second speaker will touch upon using humanized Drosophila models to classify uncharacterized human variants from genome sequencing for multiple undiagnosed diseases. The third speaker will highlight the use of Zebrafish to test for genetic variants and as a small molecule screening tool to identify therapeutic agents for Retinitis Pigmentosa. Finally, we will have a talk about the Macaque Genotype and Phenotype Resource, which allows for identification of macaques harboring mutations that recapitulate multiple human rare genetic diseases, providing novel disease models. Our session plans to give a comprehensive tour of the current state of animal model system research helping to untangle the complexity of complex diseases.

Learning Objectives:
1. Describe efforts to generate targeted models in invertebrate and vertebrate systems, including non-human primates, to model complex human diseases
2. Explain ongoing challenges in selecting and optimizing the modification of disease loci in various model systems
3. Describe the unique challenges and opportunities in generating non-coding variants and functionalizing weak effect size variants in model systems
4. Analyze these models for their potential to be used for drug screens and other therapeutic interventions

Speakers:
Humanized mouse models to discover genetic and molecular changes in enteric nervous system of Down syndrome patients. Sumantra Chatterjee, PhD, NYU School of Medicine
Model Organisms Screening In Undiagnosed Diseases. Michael Wangler, MD, Baylor College of Medicine
Advancing Retinitis Pigmentosa Research: The value of zebrafish in disease modeling and drug discovery. Liyun Zhang, PhD, Johns Hopkins University
The Macaque Genotype and Phenotype Resource (mGAP): Aggregating genomic data to interpret naturally occurring and engineered variation in macaques to develop novel disease models. Benjamin Bimber, PhD, Oregon Health & Science University

Friday, November 8, 8:00 - 9:30 AM

Not only transcription intermediates: The roles of R-loops in genome stability and brain disease
Moderators: Bing Yao, PhD, Emory University; Rebecca Meyer-Schuman, PhD, Baylor College of Medicine

Audience: Researchers
Topic: Epigenetics
Track: Basic or Translational Research

Session Description: R-loops are three-stranded structures consisting of a DNA:RNA hybrid and the non-template single-stranded DNA frequently form during transcription. R-loops were found to play critical roles in regulation of gene expression, initiation of DNA replication, and maintenance of genome stability. These structures can become sources of DNA damage and genome instability when their homeostasis is disrupted. Investigations of R-loops have linked them to many brain diseases, including repeat expansion disorders, amyotrophic lateral sclerosis (ALS), and Aicardi–Goutières syndrome (AGS). In repeat expansion diseases such as Fragile X and Huntington's, excessive R-loop formation contributes to genome instability. In addition, TAR DNA-binding protein 43 (TDP-43) loss-of-function, a hallmark of ALS and Alzheimer's disease, has been shown to disrupt R-loop genome-wide homeostasis and lead to transcriptional dysregulation in genes and transposable elements by coordinating with the covalent DNA modification 5-hydroxymethylcytosine (5hmC). While exciting progress have been made to shed light on the importance of R-loops in the brain, how R-loops are regulated and their precise mechanistic roles in brain functions and diseases are not fully understood. In this session, we invite world renown leaders in the field of R-loop biology to present their cutting-edge results to advance our understanding of this critical genomic structure in human health and diseases.

Learning Objectives:
1. Examine the basic forces that drive R-loop formation and maintenance
2. Analyze the changes in transcription patterns, R-loops, and protein modifications associated with ATM deficiency
3. Evaluate the roles of RNA-binding proteins in modulating R-loop homeostasis in neurological disorders
4. Investigate the relationship between R-loops and G-quadruplex, and their roles in facilitating long-range chromatin interactions

Speakers:
Understanding R-loop structures and the role of altered R-loop metabolism in human disorders. Frédéric L. Chédin, PhD, University of California, Davis
Transcription, R-loops, and DNA damage in ATM-deficient cells and tissues. Tanya T. Paull, PhD, The University of Texas at Austin
Regulation of genome folding by R-loops and G-quadruplexes. Kavitha Sarma, PhD, The Wistar Institute
RNA-binding proteins regulate the expression of genes and transposable elements through the coordination between R-loops and DNA modification in neurological disorders. Yingzi Hou, PhD, Emory Univeristy

Friday, November 8, 8:00 - 9:30 AM

For the children: Genomics to improve the health of pediatric patients and their families
Moderators: Daniel Koboldt, MS, Nationwide Children's Hospital; Ninad Oak, PhD, St. Jude Children's Research Hospital

Audience: Researchers
Topic: Omics Technologies
Track: Basic or Translational Research

Session Description: Pediatric diseases are a major source of childhood morbidity and mortality, often with lifelong health consequences. Many, if not most, have genetic underpinnings. Thus, advances in genomic technologies can improve the diagnosis, treatment, and long-term surveillance of these conditions. In this session, researchers and clinician-scientists from leading children's hospitals in North America will discuss how genomics can improve outcomes for diverse pediatric conditions ranging from congenital disorders to cancers. The strategies presented have common elements, such as integrative analysis and leveraging large public datasets, that are broadly useful to the field. Dr. Aldinger will lead off with her work on integrative genomic and phenotypic analysis of neurodevelopmental disorders as the preclinical framework for precision therapeutics. Dr. Ramadesikan will share translational multi-omics research to improve the diagnosis and management of pediatric disorders. Dr. Wang will take a deeper dive into an epidemiological study of pediatric cancer survivors that informed the full allelic spectrum of genetic architecture of pediatric ALL susceptibility. Lastly, Dr. Schlien will describe a strategy for comparing patient bulk RNA-seq data to large reference datasets such as TreeHouse with machine learning to diagnose and stratify pediatric tumors. The session will end with a panel discussion on promise and perils of pediatric genomics in the 21st century.

Learning Objectives:
1. Examine the role of genomic testing in the diagnosis, treatment, and surveillance of neurodevelopmental disorders and cancers in children
2. Apply multi-omics approaches, machine learning, and large datasets to improve the diagnostic yield and prognostic value of clinical genetic testing
3. Integrate high-quality genomic and clinical data from pediatric patients to unravel disease biology and identify targets for precision therapeutics
4. Translate novel insights into the genetic origins and long-term consequences of pediatric disorders to the clinic to improve health outcomes

Speakers:
Connecting the dots between genetic malformations and acquired disruptions. Kimberly Aldinger, PhD, University of Washington/SCRI
Translational research at a children's hospital: From gene discovery to diagnosis for diverse pediatric conditions. Swetha Ramadesikan, PhD, Nationwide Children's Hospital
Genetic risk of pediatric acute lymphoblastic leukemia: harnessing the data from the St. Jude Lifetime Cohort and the Childhood Cancer Survivor Study. Zhaoming Wang, PhD, St. Jude Children's Research Hospital
Towards a universal diagnostic platform for childhood cancer. Adam Shlien, PhD, The Hospital for Sick Children

Friday, November 8, 8:00 - 9:30 AM

Improving health equity in genomics: Interventions and implementation efforts to address disparities in genetic services research
Moderators: Alanna Kulchak Rahm, PhD, NHGRI; Kimberly Kaphingst, PhD, University of Utah

Audience: Researchers
Topic: Genetic Counseling, ELSI, Education, and Health Services Research
Track: Diversity, Equity, and Inclusion; Ethical, Legal, and Social Issues

Session Description: This session will describe intervention and implementation efforts in the digital space designed to address barriers to genetic service access and delivery across patient, clinician and/or system levels. Presentations will showcase disparities identified in research (by race, ethnicity, language, health literacy, and rurality), attempts to address disparities identified, and highlight DEI aspects to prioritize for the use of digital applications in genomic medicine. Speaker one will describe two patient-level intervention studies and review differential uptake, development and use of digital tools for and challenges identified in equitable return and access to genetic results. Speaker two will describe the perceptions of diverse patients and strategies employed to overcome identified disparities within a multi-level study to identify primary care patients meeting criteria for cancer genetic evaluation via algorithm and comparing two models of service delivery. Speaker three will present disparities identified from a system-level trial of engagement strategies for hereditary cancer across 12 clinical sites. The final speaker will review DEI in digital genomic tools and utilize the presented findings to highlight opportunities and priorities to attend to DEI in the development, evaluation, and use of digital tools for genomic medicine. A panel discussion will synthesize findings, promote discussion, and provide guidance for the field.

Learning Objectives:
1. Identify factors that may explain racial/ethnic disparities observed in uptake of genetic testing, genetic results and digital alternatives
2. Apply tools and methods to identify and address disparities and adapt to local populations and barriers
3. Describe how biases in engagement across strategies and interventions can influence the reach and representation of patients
4. Propose best practices to attend to DEI in the development, evaluation, and use of digital tools for genomic medicine

Speakers:
Disparities in uptake of genetic research results and use of digital tools in the RESPECT Studies. Angela Bradbury, MD, University of Pennsylvania
Designing and addressing equity in identification and delivery of cancer genetic services. Daniel Chavez-Yenter, MPH, University of Utah
Differential reach by engagement approach in population-based screening for hereditary cancer. Catharine Wang, PhD, Boston University School of Public Health
Mitigating disparities in genomics research & clinical testing: Rethinking our approaches. Yvonne Bombard, PhD, University of Toronto

Friday, November 8, 8:00 - 9:30 AM

How do we describe and ascribe clinical significance to the non-coding genome?
Moderators: Wen-Hann Tan, BMBS, Boston Children's Hospital; Annelise Mah-Som, MD/PhD, Havard Medical Genetics Training Program

Audience: Clinicians
Topic: Molecular Effects of Genetic Variation
Track: Basic or Translational Research; Clinical Research

Session Description: Genomic sequencing has been used within the clinic for over a decade, yet our understanding of clinically significant genetic variation is largely limited to the protein-coding genome. Although international efforts are underway to systematically interrogate which non-coding genetic variants are clinically significant, translating these findings into clinical medicine remains a challenge. In this session, we will synthesize the literature on hundreds of clinically significant non-coding genetic variants that are known to cause Mendelian conditions via the disruption of gene regulatory elements. In addition, we will discuss the barriers that exist for describing these non-coding variants, as well as ascribing clinical significance to them. Specifically, we will go over challenges that are encountered when assigning nomenclature to regions outside of what is commonly defined as a “gene”. We will then explore challenges with annotating and summarizing the functional impact and clinical significance of non-coding variants within clinically-facing databases like ClinVar. Finally, we will provide examples of syndrome discovery in the Genomics England 100,000 Genomes Project using the recent ACMG/AMP guidelines for interpretation of non-coding variants. The session will end with a panel discussion that will explore how we can overcome these barriers to translate ongoing efforts to annotate the function of the non-coding genome into clinical medicine.

Learning Objectives:
1. Recognize our current knowledge of how non-coding variants contribute to Mendelian conditions
2. Summarize the current naming strategies for elements of the human genome
3. Evaluate how existing guidelines can be adapted for classifying non-coding variation
4. Identify critical data elements to describe functional effects of a variant in a database

Speakers:
How do alterations in gene regulatory elements cause Mendelian diseases? Andrew Stergachis, MD/PhD, University of Washington
How should we name non-coding elements? Elspeth Bruford, PhD, University of Cambridge
How do we represent functional effects of non-coding variants in public databases? Melissa Landrum, PhD, NCBI/NLM/NIH
How do we identify, annotate, and clinically classify variants in the non-coding genome? Nicola Whiffin, PhD, University of Oxford

Friday, November 8, 8:00 - 9:30 AM

Aging, clonal hematopoiesis, and our health
Moderators: Zhi Yu, MB/PhD, Broad Institute of MIT and Harvard; Kristin Ardlie, PhD, Broad Institute of MIT and Harvard

Audience: Researchers
Topic: Evolutionary and Population Genetics
Track: Basic or Translational Research; Clinical Research

Session Description: Over our lifespan, our normal cells continuously acquire somatic mutations, with profound implications for our health. Clonal hematopoiesis - expansions due to somatic mutations in the blood-forming system - has especially captured the attention of both the scientific community and the public in recent years. This surge in interest stems from the ability to detect these mutations through sequencing of blood, enabling large-scale population studies. Furthermore, in those studies, clonal hematopoiesis has been shown to be prevalent among senior individuals and associated with a wide spectrum of diseases, from cancer to cardiovascular diseases and many other disorders. This session aims to introduce the concept of somatic mutation and its association with aging across diverse species (Dr. Alex Cagan) and then delve deeper into clonal hematopoiesis in humans, exploring its biology and broad impact on our health across diverse populations (Dr. Alex Bick), methodological advancement and considerations (Dr. Po-Ru Loh), and clinical management for diverse patients (Dr. Kelly Bolton). Insights and new results will be shared by four leading researchers in the respective fields, along with informative live illustrating of all talks by Dr. Alex Cagan to further facilitate the delivery of the content. Each presentation will last 15 minutes, followed by a 30-minute interactive panel discussion and Q&A, offering attendees a unique opportunity to interact directly with these experts.

Learning Objectives:
1. State what somatic mutation is and how aging drives somatic mutation development across diverse species
2. Recognize the biological processes underpinning clonal hematopoiesis and health consequences in multi-ancestry populations
3. Highlight technical and methodological advancements in detecting and analyzing clonal hematopoiesis at the population level
4. State clinical implications of somatic mutations in general and clonal hematopoiesis in particular

Speakers:
The role of somatic mutations in aging: across the lifespan and across species. Alex Cagan, PhD, University of Cambridge
Clonal expansion: leveraging biobank scale data to identify molecular mechanisms and non-oncologic disease consequences. Alexander Bick, MD/PhD, Vanderbilt University Medical Center
Computational methods for detecting clonal hematopoiesis in biobank cohorts. Po-Ru Loh, PhD, Brigham and Women's Hospital
Determinates of Clonal Hematopoiesis Progression to Hematologic Malignancy. Kelly Bolton, MD/PhD, Washington University in St. Louis

Friday, November 8, 8:00 - 9:30 AM

Cross-examining the rare and common variant architecture of psychiatric conditions, brain structure, and function
Moderators: David Glahn, PhD, Boston Children's Hospital; Sarah Medland, PhD, QIMR Berghofer

Audience: Researchers
Topic: Complex Traits
Track: Basic or Translational Research

Session Description: While rare and common variants contribute to the risk of psychiatric conditions and affect brain structure, these different research fields mostly operate in silos. The symposium will cross-examine the risk conferred by rare and common variants for psychiatric conditions and ask how these variants affect brain structure measured by Magnetic Resonance imaging (MRI) in humans. We will illuminate how recent strides in functional genomics are forging connections between psychiatric and neuroimaging genetics to infer how large-scale brain networks may underlie the association between genomic variants and psychiatric conditions. The first presentations will discuss the combined risk conferred by rare and common variants (CNVs) for a broad range of psychiatric disorders. While it is known that CNVs show substantial pleiotropic effects, preferential risk for any given psychiatric condition remains unclear. We will show how many major psychiatric disorders share common etiologic pathways, but diagnostic outcome varies according to how gain and loss of function of neurodevelopmental and synaptic processes are spatially distributed in the developing brain. The last presentations will examine the overlapping polygenic architecture between psychopathology and cortical brain structure. Opportunities and limitations of the current large-scale brain MRI datasets and methods to investigate shared genetic contributions across psychiatric conditions and brain structure will be discussed.

Learning Objectives:
1. Summarize the association of rare CNVs across psychiatric conditions
2. Evaluate the preferential effects of CNVs on particular psychiatric conditions
3. Evaluate the shared genetic underpinnings between psychiatric disorders and structural phenotypes of the cerebral cortex
4. Highlight the convergence between the rare and common variants architecture of psychiatric conditions

Speakers:
Functional-based association study of rare CNVs across six psychiatric disorders identifies common biological components but distinctly different genetic effects in autism and schizophrenia. Worrawat Engchuan, PhD, The Hospital for Sick Children
The combined effects of recurrent CNVs and polygenic risk on psychiatric traits. Molly Sacks, BA, University of California, San Diego
New insights into the overlapping genetic architecture of neuropsychiatric disorders and morphology of the human cerebral cortex. Zhiqiang Sha, PhD, University of Pennsylvania
Rare Copy Number Variant architecture of the cortical organization of the human brain. Kuldeep Kumar, PhD, University of Montreal

Friday, November 8, 8:00 - 9:30 AM

Face the facts: The impact of advances in data science on translational research
Moderators: Joseph G. Hacia, PhD, University of Southern California; Abimbola Oladayo, PhD, BDS, MPH, University of Iowa

Audience: Researchers
Topic: Genetic, Genomic, and Epigenomic Resources and Databases
Track: Basic or Translational Research

Session Description: The translational science spectrum, which encompasses basic, preclinical, and clinical research as well as clinical implementation and public health, is being transformed by the use of data science methods to analyze big data. Here, we will review unpublished progress towards applying emerging data science methods, including artificial intelligence and machine learning (AI/ML), to accelerate translational research. Special emphasis is placed on deep data research involving craniofacial traits and medical conditions to provide a general platform for discussing the relevance of data science to a broad multidisciplinary audience. Our first presentation will discuss developments in the FaceBase Consortium whose mission is to advance craniofacial research through the generation and wide dissemination of multi-omics data and facial imaging. Our second presentation discusses the application of advances in big data analytics in medical imaging to elucidate genetic contributions towards heterogeneity in human facial morphological traits. Our third presentation focuses on the use of data science methods to accelerate preclinical and public health studies of a ubiquitous dental condition on a global scale. Our final presentation discusses the pivotal role of community engagement to generate deep data for public health research. Overall, the Symposium will highlight opportunities for using novel and existing data science methods to maximize the impact big data has on global health.

Learning Objectives:
1. Explain how data science methods and big data can be leveraged to address the unmet needs of translational and patient-centered biomedical research
2. Assess how data science methods can enhance the clinical research and implementation stages of translational science research
3. Discuss how data science can be leveraged to improve public health by enhancing efforts to prevent, diagnose, and treat common and rare diseases
4. Discuss how research communities can embrace, integrate, and strengthen DEIA in the translational science spectrum

Speakers:
FaceBase: A Community-Driven Hub for Data-Intensive Research. Alejandro Bugacov, PhD, USC Information Sciences Institute
Big data analytics in medical imaging to investigate craniofacial phenotypes. Meng Yuan, MS, KULeuven
Data science approaches to identify genetic risk factors for common medical conditions in diverse multiethnic populations. Simon Haworth, PhD, University of Bristol
Community engagement in translational research and global public health. Azeez Butali, DDS, PhD, University of Iowa