BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Mancuso, Nicholas

eRA COMMONS USER NAME (credential, e.g., agency login): MANCUSO2

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Georgia State University	BS	05/2007	Computer Science
Georgia State University	PHD	08/2014	Computer Science
University of California Los Angeles, Los Angeles, CALIFORNIA	Postdoctoral Fellow	03/2019	Statistical Genetics

A. Personal Statement

I am an assistant professor in the Center of Genetic Epidemiology and Department of Preventive Medicine at the Keck School of Medicine at University of Southern California. I have a Ph.D. in computer science from Georgia State University where my work focused on developing algorithms (kGEM, VirA, BioA) to reconstruct the underlying virus haplotypes of a heterogeneous infection (e.g., hepatitis C or human immunodeficiency virus) from noisy short-read sequencing data (advised by Dr. Alex Zelikovsky at GSU and Dr. Yury Khudyakov at the CDC). During my post-doctoral training under Dr. Bogdan Pasaniuc at UCLA, I developed novel computational and statistical approaches (RHOGE, FOCUS) to elucidate the role of genetics in common disease risk. Several representative papers include:

1. Mancuso N, Freund MK, Johnson R, Shi H, Kichaev G, Gusev A, Pasaniuc B. Probabilistic fine-mapping of transcriptome-wide association studies. Nat Genet. 2019 Apr;51(4):675-682. PubMed PMID: 30926970.
2. Mancuso N, Gayther S, Gusev A, Zheng W, Penney K, Kote-Jarai Z, Eeles R, Freedman M, Haiman C, Pasaniuc B. Large-scale transcriptome-wide association study identifies new prostate cancer risk regions. Nature Communications. 2018 October 4; 9(1):-.
3. Mancuso N, Shi H, Goddard P, Kichaev G, Gusev A, Pasaniuc B. Integrating Gene Expression with Summary Association Statistics to Identify Genes Associated with 30 Complex Traits. Am J Hum Genet. 2017 Mar 2;100(3):473-487. PubMed PMID: 28238358; PubMed Central PMCID: PMC5339290.
4. Mancuso N, Rohland N, Rand K, Tandon A, Allen A, Quinque D, Mallick S, Li H, Stram A, Sheng X, Kote-Jarai Z, Easton D, Eeles R, Le Marchand L, Lubwama A, Stram D, Watya S, Conti D, Henderson B, Haiman C, Pasaniuc B, Reich D. The contribution of rare variation to prostate cancer heritability. Nature Genetics. 2015 November 16; 48(1):30-35.

B. Positions and Honors

Positions and Employment

2007 - 2010 Software Engineer, Catalyst Technologies, Atlanta, GA
2010 - 2014 Graduate Research Assistant, Dept of Computer Science, Georgia State University, Atlanta, GA

2012 - 2014	Intern, Division of Viral Hepatitis, Centers for Disease Control and Prevention, Atlanta, GA
2014 - 2019	Post-doctoral Fellow, UNIVERSITY OF CALIFORNIA LOS ANGELES
2019 -	Assistant Professor, University of Southern California, Los Angeles, CA

Other Experience and Professional Memberships

2019 -	Member, International Genetic Epidemiology Society

Honors

2011 - 2012	Research Fellowship, Molecular Basis for Disease, Georgia State University
2012	Tuition Scholarship, Summer Institute in Statistical Genetics, Dept of Biostatistics, University of Washington, Seattle
2012 - 2014	Research Fellowship, Second Century Initiative Program, Georgia State University

C. Contribution to Science

1. My graduate-degree research focused on developing computational methods to reconstruct virus haploids from a heterogeneous infection from modern high-throughput sequencing reads. Given the high mutation rate of RNA-based viruses, the haploid group (infection) is a closely related population, making it difficult to differentiate between sequencing errors and mutations. I developed and implemented several combinatorial-based methods to perform this task, which scale well for large sequencing datasets. This toolset enables researchers to exploit the complex haploid network present in HCV or HIV infections in developing targeted drugs or studying immune escape response.

    a. Mangul S, Wu NC, Mancuso N, Zelikovsky A, Sun R, Eskin E. Accurate viral population assembly from ultra-deep sequencing data. Bioinformatics. 2014 Jun 15;30(12):i329-37. PubMed PMID: 24932001; PubMed Central PMCID: PMC4058922.

    b. Skums P, Mancuso N, Artyomenko A, Tork B, Mandoiu I, Khudyakov Y, Zelikovsky A. Reconstruction of viral population structure from next-generation sequencing data using multicommodity flows. BMC Bioinformatics. 2013;14 Suppl 9:S2. PubMed PMID: 23902469; PubMed Central PMCID: PMC3698000.

    c. Mancuso N, Tork B, Skums P, Ganova-Raeva L, Măndoiu I, Zelikovsky A. Reconstructing viral quasispecies from NGS amplicon reads. In Silico Biol. 2011-2012;11(5-6):237-49. PubMed PMID: 23202425.

2. My postdoctoral research focused on developing statistical methods measuring the contribution from rare genetic variation to disease risk across diverse populations. Genome-wide association studies (GWAS) are typically performed using genotyping arrays, which probe primarily common genetic variants. In contrast, modern sequencing platforms enable investigating the impact of both rare and common genetic variation on disease risk. In this setting, we found that rare variants contribute significantly to risk of prostate cancer in men of African descent. Our results suggest that risk variants were driven to low frequencies as the result of selective pressure. We found through a novel simulation- based strategy a significant coupling between selection and prostate cancer risk.

    a. Mancuso N, Rohland N, Rand KA, Tandon A, Allen A, Quinque D, Mallick S, Li H, Stram A, Sheng X, Kote-Jarai Z, Easton DF, Eeles RA, Le Marchand L, Lubwama A, Stram D, Watya S, Conti DV, Henderson B, Haiman CA, Pasaniuc B, Reich D. The contribution of rare variation to prostate cancer heritability. Nat Genet. 2016 Jan;48(1):30-5. PubMed PMID: 26569126.

3. Genome-wide association studies (GWAS) quantify the contribution of common genetic variation to complex trait or disease risk. However, GWAS results provide regions where there is reliable evidence of genetics influencing downstream trait but cannot provide a mechanism. Large-scale efforts quantifying the impact of genetic variation on molecular features, such as gene expression, provide a systematic approach to identify and prioritize possible disease mechanisms (i.e. genes).

My work has focused on developing computational methods in this post-GWAS setting.

a. Mancuso N, Gayther S, Gusev A, Zheng W, Penney KL, Kote-Jarai Z, Eeles R, Freedman M, Haiman C, Pasaniuc B. Large-scale transcriptome-wide association study identifies new prostate cancer risk regions. Nat Commun. 2018 Oct 4;9(1):4079. PubMed PMID: 30287866; PubMed Central PMCID: PMC6172280.
b. Freund MK, Burch KS, Shi H, Mancuso N, Kichaev G, Garske KM, Pan DZ, Miao Z, Mohlke KL, Laakso M, Pajukanta P, Pasaniuc B, Arboleda VA. Phenotype-Specific Enrichment of Mendelian Disorder Genes near GWAS Regions across 62 Complex Traits. Am J Hum Genet. 2018 Oct 4;103(4):535-552. PubMed PMID: 30290150; PubMed Central PMCID: PMC6174356.
c. Gusev A, Mancuso N, Won H, Kousi M, Finucane HK, Reshef Y, Song L, Safi A, McCarroll S, Neale BM, Ophoff RA, O'Donovan MC, Crawford GE, Geschwind DH, Katsanis N, Sullivan PF, Pasaniuc B, Price AL. Transcriptome-wide association study of schizophrenia and chromatin activity yields mechanistic disease insights. Nat Genet. 2018 Apr;50(4):538-548. PubMed PMID: 29632383; PubMed Central PMCID: PMC5942893.
d. Mancuso N, Shi H, Goddard P, Kichaev G, Gusev A, Pasaniuc B. Integrating Gene Expression with Summary Association Statistics to Identify Genes Associated with 30 Complex Traits. Am J Hum Genet. 2017 Mar 2;100(3):473-487. PubMed PMID: 28238358; PubMed Central PMCID: PMC5339290.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

T32 NS048004-13 FREIMER, NELSON B. (PI) 07/15/04-06/30/20
Training Grant in Neurobehavioral Genetics
Role: TA