BIOGRAPHICAL SKETCH

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NAME: Whirl-Carrillo, Michelle

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

POSITION TITLE: PharmGKB Co-PI and Director

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)*	Completion Date MM/YYYY	FIELD OF STUDY
Massachusetts Institute of Technology, Cambridge, MA	SB	05/1993	Biology
Stanford University, Stanford, CA	PHD	01/2003	Biophysics

A. Personal Statement

My work focuses on pharmacogenomics, the study of the impact of genetics on drug response, and its application to personalized medicine and personal genomics. I am the Co-PI and Director of the PharmGKB (Pharmacogenomics Knowledge Base) in the Department of Biomedical Data Science at Stanford University. My research ranges from basic science studying gene-variant-drug associations at PharmGKB to translation of pharmacogenomics information into the clinical setting. I am particularly interested in translation of human genome sequencing data (whole genome and exome) to pharmacogenomic-based therapeutic recommendations that are actionable in the clinic. I am a Clinical Pharmacogenetics Implementation Consortium (CPIC) Steering Committee member, the coordinator of the Stanford CPIC group and the co-Director of the CPIC Informatics Working Group which works to reduce barriers to implementing the CPIC guidelines in the clinical electronic environment, in part by addressing Clinical Decision Support (CDS) in Electronic Health Record (EHR). I am also a co-investigator of PharmCAT, which seeks to enable the translation of raw patient genotype or sequencing results into diplotypes and clinical guidance. This project leverages the curated pharmacogenomics knowledge from CPIC, PharmGKB and PharmVar to create patient-specific reports that are informative to clinicians. I am a member of the PharmVar Steering Committee and multiple PharmVar gene expert panels. I coordinate information across the PharmVar, PharmGKB, CPIC and PharmCAT projects to maintain consistency of pharmacogenetic gene nomenclature and harmonize allele definition and function terminology/assignment. Additionally, I work with the Clinical Genome Resource (ClinGen) to move forward integration of pharmacogenomics into clinical genomic medicine as the co-Chair of the Pharmacogenomics Working Group. I also work with ClinVar to create representation of pharmacogenomic data into the predominantly disease genomics resource. I have published over 100 peer-reviewed manuscripts and book chapters on pharmacogenomics and knowledge resources.

Citations:

1. **Whirl-Carrillo M**, McDonagh EM, Hebert JM, Gong L, Sangkuhl K, Thorn CF, Altman RB, Klein TE. Pharmacogenomics knowledge for personalized medicine. Clin Pharmacol Ther. 2012 Oct;92(4):414-7. PubMed PMID: 22992668; PubMed Central PMCID: PMC3660037.
2. Sangkuhl K[1], **Whirl-Carrillo M[1]**, Whaley RM, Woon M, Lavertu A, Altman RB, Carter L, Verma A, Ritchie MD, Klein TE. Pharmacogenomics Clinical Annotation Tool (PharmCAT). Clin Pharmacol Ther. 2019 Jul;107(1):203-210. PubMed PMID: 31306493; PubMed Central PMCID: PMC6977333. ([1]Joint first authors)

3. **Whirl-Carrillo M**, Huddart R, Gong L, Sangkuhl K, Thorn CF, Whaley R, Klein TE. An Evidence-Based Framework for Evaluation Pharmacogenomic Knowledge for Personalized Medicine. Clin Pharmacol Ther. 2021 110(3):559-562. PubMed PMID: 34216021; PubMed Central PMCID: PMC8457105.

B. Positions, Scientific Appointments and Honors

2022 - present Co-PI, PharmGKB, Stanford University
2019 - present Director, PharmGKB, Stanford University
2014 - 2019 Associate Director, PharmGKB, Stanford University
2009 - 2014 Assistant Director, PharmGKB, Stanford University
2008 - 2009 Curation Manager, 23andMe, Inc.
2007 - 2008 Research Scientist/Lead Curator, PharmGKB, Stanford University
2002 - 2007 Research Scientist/Scientific Curator, PharmGKB, Stanford University

C. Contributions to Science

1. I am the Co-PI and Director of the Pharmacogenomics Knowledge Base (PharmGKB, https://www.pharmgkb.org). PharmGKB is the premier knowledge resource regarding the impact of genetic variation on drug response and contains thousands of manually curated gene-variant-drug relationships. I have led or co-led the development of all PharmGKB curation processes and overseen the evaluation of manual curation and natural language processing (NLP)/text mining methods for annotation of the scientific literature. I have done extensive work in knowledge modeling and terminology/ontology development for pharmacogenomics. I have constructed knowledge models for multiple types of data annotations in PharmGKB, including annotated drug labels from international regulatory agencies, and variant and clinical annotations that identify and summarize specific variant-drug associations and their meta-data. I co-developed a terminology for classifying subjects of pharmacogenomics studies by biogeographical group. My early work focused on the development of knowledge models and informatics tools to capture gene-drug relationships, raw genotype and phenotype data, and pathway knowledge. I co-developed the PharmGKB XML schema description of genotype, sequencing and SNP-discovery data; constructed data models for pharmacogenomic phenotype information; developed a preliminary ontology for data annotation; and co-designed the format and development process for the iconic PharmGKB drug-centered pathways.

    a. **Whirl-Carrillo M**, Woon M, Thorn CF, Klein TE, Altman RB. An XML-based interchange format for genotype-phenotype data. Hum Mutat. 2008 Feb;29(2):212-9. PubMed PMID: 17994540.
    b. **Whirl-Carrillo M**, McDonagh EM, Hebert JM, Gong L, Sangkuhl K, Thorn CF, Altman RB, Klein TE. Pharmacogenomics knowledge for personalized medicine. Clin Pharmacol Ther. 2012 Oct;92(4):414-7. PubMed PMID: 22992668; PubMed Central PMCID: PMC3660037.
    c. Lever J, Barbarino JM, Gong L, Huddart R, Sangkuhl K, Whaley R, **Whirl-Carrillo M**, Woon M, Klein TE, Altman RB. PGxMine: Text mining for curation of PharmGKB. Pacific Symposium on Biocomputing 2020; 25:611-622. PubMed PMID: 31797632.
    d. **Whirl-Carrillo M**, Huddart R, Gong L, Sangkuhl K, Thorn CF, Whaley R, Klein TE. An Evidence-Based Framework for Evaluation Pharmacogenomic Knowledge for Personalized Medicine. Clin Pharmacol Ther. 2021 110(3):559-562. PubMed PMID: 34216021; PubMed Central PMCID: PMC8457105.

2. I am co-investigator of the Pharmacogenomics Clinical Annotation Tool (PharmCAT). I worked with the team to develop a software tool that leverages CPIC, PharmGKB and PharmVar information to enable translation of patients' genomes to actionable clinical reports which will be able to be imported into the electronic health record (EHR). Previously, I manually annotated some of the first human genomes to be published with pharmacogenomic information, including the first family quartet. I applied my knowledge and experience from developing a manual PGx annotation process to the creation of PharmCAT's algorithm. Unlike the hugely time-consuming manual annotation process, PharmCAT can analyze a genome in seconds and is scalable so that it can annotate thousands of biobank sequences at a time.

a. Dewey FE, Chen R, Ormond KE, Caleshu C, Karczewski KJ, **Whirl-Carrillo M**, Wheeler MT, Dudley JT, Byrnes JK, Cornejo OE, Knowles JW, Woon M, Sangkuhl K, Gong L, Thorn CF, Hebert JM, Capriotti E, David SP, Pavlovic A, West A, Thakuria JV, Ball MP, Zaranek AW, Rehm HL, Church GM, West JS, Bustamante CD, Snyder M, Altman RB, Klein TE, Butte AJ, Ashley EA. Phased whole-genome genetic risk in a family quartet using a major allele reference sequence. PLoS Genet. 2011 Sep;7(9):e1002280. PubMed PMID: 21935354; PubMed Central PMCID: PMC3174201.

b. Chen R, Mias GI, Li-Pook-Than J, Lam H, Jiang L, Chen R, Miriami E, Karczewski K, Hariharan M, Dewey FE, Lin S, Habegger L, Clark MJ, Balasubramanian S, Cheng Y, O'Huallachain M, Dudley J, Hillenmeyer S, Haraksingh R, Sharon D, Euskirchen G, Lacroute P, Bettinger K, Im H, Boyle AP, Kasowski M, Grubert F, Seki S, Garcia M, **Whirl-Carrillo M**, Gallardo M, Blasco MA, Greenberg PL, Snyder P, Klein TE, Altman RB, Butte A, Ashley EA, Nadeau K, Gerstein M, Tang H, Snyder M. Personal omics profiling reveals dynamic molecular medical phenotypes. Cell 2012 148(6): 1293-1307. PubMed PMID: 22424236; PubMed Central PMCID: PMC3341616.

c. Sangkuhl K[1], **Whirl-Carrillo M[1]**, Whaley RM, Woon M, Lavertu A, Altman RB, Carter L, Verma A, Ritchie MD, Klein TE. Pharmacogenomics Clinical Annotation Tool (PharmCAT). Clin Pharmacol Ther. 2019 Jul;107(1):203-210. PubMed PMID: 31306493; PubMed Central PMCID: PMC6977333. ([1]Joint first authors)

d. McInnes G, Lavertu A, Sangkuhl K, Klein TE, **Whirl-Carrillo M**, Altman RB (2020). Pharmacogenetics at Scale: An Analysis of the UK Biobank. *Clinical Pharmacology and Therapeutics*,109(6):1528-1537.PubMed PMID: 33237584; PubMed Central PMCID: PMC8144239.

3. I am co-Director of the Clinical Pharmacogenetics Implementation Consortium (CPIC) Informatics Working Group, Stanford CPIC coordinator and a Steering Committee member and have been part of CPIC since its inception. I worked with the CPIC PIs to develop the original guideline standards. With CPIC, I have worked to create standardized terminology for pharmacogene allele functionality and phenotype terms that can be used across platforms for the return of pharmacogenetic test results. We have also developed resources to support clinical decision support (CDS) for CPIC guideline implementation. I worked with a professional software developer to create a database and API to store all CPIC materials including prescribing recommendations and supplemental resources to enable querying of data, making it more accessible to electronic health record (EHR) systems. We continue to work to develop resources that will support clinical implementation of guidelines in the EHR. I have co-authored multiple CPIC guidelines and guideline updates.

   a. Hoffman JM, Dunnenberger HM, Kevin Hicks J, Caudle KE, **Whirl Carrillo M**, Freimuth RR, Williams MS, Klein TE, Peterson JF. Developing knowledge resources to support precision medicine: principles from the Clinical Pharmacogenetics Implementation Consortium (CPIC). J Am Med Inform Assoc. 2016 Jul;23(4):796-801. PubMed PMID: 27026620; PubMed Central PMCID: PMC6080683.

   b. Caudle KE, Gammal RS, **Whirl-Carrillo M**, Hoffman JM, Relling MV, Klein TE. Evidence and resources to implement pharmacogenetic knowledge for precision medicine. Am J Health Syst Pharm. 2016 Dec 1;73(23):1977-1985. PubMed PMID: 27864205; PubMed Central PMCID: PMC5117674.

   c. Caudle KE, Dunnenberger HM, Freimuth RR, Peterson JF, Burlison JD, **Whirl-Carrillo M**, Scott SA, Rehm HL, Williams MS, Klein TE, Relling MV, Hoffman JM. Standardizing terms for clinical pharmacogenetic test results: consensus terms from the Clinical Pharmacogenetics Implementation Consortium (CPIC). Genet Med. 2017 Feb;19(2):215-223. PubMed PMID: 27441996; PubMed Central PMCID: PMC5253119.

   d. Caudle KE, Sangkuhl K, **Whirl-Carrillo M**, Swen JJ, Haidar CE, Klein TE, Gammal RS, Relling MV, Scott SA, Hertz DL, Guchelaar HJ, Gaedigk A. Standardizing CYP2D6 Genotype to Phenotype Translation: Consensus Recommendations from the Clinical Pharmacogenetics Implementation Consortium and Dutch Pharmacogenetics Working Group. 2020 Jan;13(1):116-124. PubMed PMID: 31647186; PubMed Central PMCID: PMC6951851.

4. I have worked collaboratively on many pharmacogenomics research projects. As part of the PharmVar steering committee and multiple PharmVar gene expert panels, I focus on gene allele nomenclature. I have worked with the PharmVar project from its formation, contributing to the extensive rule-based system for assigning allele nomenclature, gene-level documentation and the development of “core” allele definitions. I have also worked on nomenclature projects with the CDC concerning pharmacogenomic test result reports. I represent CPIC and PharmGKB on the Association for Molecular Pathology (AMP) pharmacogenetic guideline workgroup, which works to define variants that should be included on pharmacogenomic testing panels.

    a. Kalman LV, Agúndez J, Appell ML, Black JL, Bell GC, Boukouvala S, Bruckner C, Bruford E, Caudle K, Coulthard SA, Daly AK, Del Tredici A, den Dunnen JT, Drozda K, Everts RE, Flockhart D, Freimuth RR, Gaedigk A, Hachad H, Hartshorne T, Ingelman-Sundberg M, Klein TE, Lauschke VM, Maglott DR, McLeod HL, McMillin GA, Meyer UA, Müller DJ, Nickerson DA, Oetting WS, Pacanowski M, Pratt VM, Relling MV, Roberts A, Rubinstein WS, Sangkuhl K, Schwab M, Scott SA, Sim SC, Thirumaran RK, Toji LH, Tyndale RF, van Schaik R, **Whirl-Carrillo M**, Yeo K, Zanger UM. Pharmacogenetic allele nomenclature: International workgroup recommendations for test result reporting. Clin Pharmacol Ther. 2016 Feb;99(2):172-85. PubMed PMID: 26479518; PubMed Central PMCID: PMC4724253.
    b. Gaedigk A, **Whirl-Carrillo M**, Pratt VM, Miller NA, Klein TE. PharmVar and the Landscape of Pharmacogenetic Resources. Clin Pharmacol Ther. 2020 Jan;107(1):43-46. PubMed PMID: 31758698; PubMed Central PMCID: PMC6925620.
    c. Pratt VM, Cavallari LH, Del Tredici AL, Hachad H, Ji Y, Moyer AM, Scott SA, **Whirl-Carrillo M**, Weck KE. Recommendations for Clinical CYP2C9 Genotyping Allele Selection: A Joint Recommendation of the Association for Molecular Pathology and College of American Pathologists. J Mol Diagn. 2019 Sep;21(5):746-755. PubMed PMID: 31075510; PubMed Central PMCID: PMC7057225.
    d. Desta Z, El-Boraie A, Gong L, Somogyi AA, Lauschke VM, Dandara C, Klein K, Miller NA, Klein TE, Tyndale RF, **Whirl-Carrillo M**, Gaedigk A. PharmVar GeneFocus: CYP2B6. Clin Pharmacol Ther. 2021 110(1):82-97. PubMed PMID: 33448339; PubMed Central PCMID: PMC8693800.

5. My graduate work focused on constructing and assessing molecular models of RNA, including the E.coli 30S ribosomal subunit, based on published biochemical and molecular experimental data. At the time, the x-ray crystal structure of the ribosome had proved difficult to elucidate so distance data gathered from experimental methods was the available knowledge and models were the best estimation. Subsequently, several ribosomal structures were resolved through x-ray crystallography, which allowed us to retrospectively assess the quality of the experimental distance data that had been previously reported in the literature. Distance measurements continued to be instrumental in understanding the dynamics of the ribosome not revealed by static structures.

    a. Gabashvili IS, **Whirl-Carrillo M**, Bada M, Banatao DR, Altman RB. Ribosomal dynamics inferred from variations in experimental measurements. RNA. 2003 Nov;9(11):1301-7. PubMed PMID: 14561879; PubMed Central PMCID: PMC1287051.
    b. **Whirl-Carrillo M**, Gabashvili IS, Bada M, Banatao DR, Altman RB. Mining biochemical information: lessons taught by the ribosome. RNA. 2002 Mar;8(3):279-89. PubMed PMID: 12003488; PubMed Central PMCID: PMC1370250.
    c. Joseph S, **Whirl ML**, Kondo D, Noller HF, Altman RB. Calculation of the relative geometry of tRNAs in the ribosome from directed hydroxyl-radical probing data. RNA. 2000 Feb;6(2):220-32. PubMed PMID: 10688361; PubMed Central PMCID: PMC1369908.