BIOGRAPHICAL SKETCH

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NAME: Russ B. Altman

eRA COMMONS USER NAME: ALTMAN.RUSS

POSITION TITLE: The Kenneth Fong Professor of Bioengineering, Genetics, Medicine, Biomedical Data Science, and (by courtesy) of Computer Science

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
Harvard College	A.B.	06/1983	Biochemistry & Molecular Biology
Stanford University Medical School	Ph.D.	06/1989	Medical Information Sciences
Stanford University Medical School	M.D.	06/1990	Medicine

A. Personal Statement

My area of professional expertise is biomedical informatics and data science and developing methods to analyze molecular, cellular, and organismal data of importance for problems in medicine and health. My specific application area of interest is drug action, including molecular, cellular, tissue, patient, and population-level understanding. I have a 29-year track record of mentoring students and postdocs. I provide 1:1 meetings every week, critical but supportive group meeting dynamics, and social events/retreats to build lab morale. We have moved to 100% BioRXiv submissions to help address rigor and reproducibility, and everyone who leaves the lab is expected to leave computational data, software, and other resources on simtk.org for dissemination. I conduct regular individual development plans with all students and postdocs in the lab and encourage experiences that help them prepare for life after their time at Stanford, such as internships. I especially focus on written and oral presentation skills, which are an area of expertise for me. (To wit: I teach an undergraduate writing class and I have a radio show on SiriuxXM/Apple Itunes “The Future of Everything.”). I served as the director of the Biomedical Informatics graduate program for 18 years and wrote 5 competitive renewals of that training grant, paying close attention to high-quality training and support. I served on the Biomedical Diversity Advisory Committee, focusing on maintaining a diverse student body in the Biosciences for 5 years, ending in 2019. I have been awarded the Stanford Mentorship Award and Stanford Teaching Award in 2000 and 2014, respectively. I lecture regularly in our program on how to write grants for K-awards and F-awards. I am proud of all the graduates from my lab; these include some who serve on the faculty at UCSF (Yeh), U. Peking (Wei), Princeton (Troyanskaya), U. Texas (Chang), Harvard (Raychaudhuri), UNC (Laederach), U. Washington (Mooney), Mt. Sinai (Percha), Columbia (Tatonetti) and others in industry at Personalis (Chen), Invitae (Mallory), Google (Liang), LinkedIn (Tang), Apple (Garten), 23andme (Wu), Qiagen (Felciano), and several startups that are still awaiting fame. Going forward with the BMI program, I will serve on the executive committee, attend the annual retreat, teach a core class (Intro to computational Biology), attend Tuesday talks, serve as an academic advisor and mentor MS and PHD students in research.

Ongoing projects that I would like to highlight include:

U01 FD005978 FDA (Co-PIs: Giacomini, Altman) Role: Co-PI
UCSF-Stanford Center of Excellence for Regulatory Science & Innovation 04/15/20014 – 8/31/2023

U24HG010615 NIH/NHGRI (Co-PIs: Klein, Whirl-Carrillo, Scott) Role: Co-I 04/03/2020 – 12/31/2025

PharmGKB: A Critical Knowledgebase for Personalized Medicine

Citations:

1. McInnes G, Dalton R, Sangkuhl K, Whirl-Carrillo M, Lee SB, Tsao PS, Gaedigk A, Altman RB, Woodahl EL. Transfer learning enables prediction of CYP2D6 haplotype function. PLoS Comput Biol. 2020 Nov 2;16(11):e1008399. PMID: 33137098; PMCID: PMC7660895.

2. Torng W, Altman RB. Graph Convolutional Neural Networks for Predicting Drug-Target Interactions. J Chem Inf Model. 2019 Oct 28;59(10):4131-4149. PMID: 31580672.

3. Yang L, Wang S, Altman RB. POPDx: an automated framework for patient phenotyping across 392 246 individuals in the UK Biobank study. J Am Med Inform Assoc. 2023 Jan 18;30(2):245-255. doi: 10.1093/jamia/ocac226. PMID: 36469791; PMCID: PMC9846671.

4. Kaushal A, Altman R, Langlotz C. Geographic Distribution of US Cohorts Used to Train Deep Learning Algorithms. JAMA. 2020 Sep 22;324(12):1212-1213. doi: 10.1001/jama.2020.12067. PMID: 32960230; PMCID: PMC7509620.

B. Positions, Scientific Appointments, and Honors

Research and/or Professional Experience

2020-	Advisory Panel to the *All of Us* Research Program
2019-	Associate Director, Stanford Institute for Human-Centered AI (HAI)
2018-	Attending, Pharmacogenomics Clinical Consult Service
2017-	International Advisory Board, Swiss Personalized Health Network
2016-	Founding Co-Editor-in-Chief (with M. Levitt) Annual Review of Biomedical Data Science
2016-	International Advisory Board, UK Biobank
2016-2019	Co-Chair, Burroughs Wellcome Foundation Careers at the Scientific Interface (CASI) Program
2016-2022	Member & Advisor, Chan-Zuckerberg Biohub
2015-2018	Co-Chair, Drug Forum of Institute of Medicine
2015-	Director, Stanford Predictives and Diagnostics Accelerator
2015-2022	Acting Chief, Systems Medicine Division, Department of Pediatrics
2013-2014	President, American Society for Clinical Pharmacology and Therapeutics
2013-2014	Chair, Science Board to the Food and Drug Administration
2007-2012	Chair, Department of Bioengineering, Stanford University
2000-2018	Director, Biomedical Informatics Program, Stanford University
2000-2002	President, International Society for Computational Biology
1999-2004	Associate Professor of Medicine (& Computer Science, by courtesy) tenure, Stanford University
1996-	Organizing Committee, Pacific Symposium on Biocomputing
1994-1995	Organizing Committee, 2nd & 3rd Intl. Conf. on Intelligent Systems for Molecular Biology
1993-1997	Member, Executive Steering Committee, San Diego Supercomputer Center
1992-1999	Assistant Professor of Medicine (& Computer Science, by courtesy), Stanford University
1990-1992	Intern and Resident, Stanford University Medical Center
1989-1992	Post-Doctoral fellow (part time). Prof. Oleg Jardetzky, Stanford Magnetic Resonance Laboratory
1984-1988	Graduate Research Assistant to Bruce G. Buchanan, Stanford Dept. of Computer Science
1982-1983	Undergraduate Research Assistant. Supervisor: Prof. Stephen C. Harrison, Harvard Department of Biochemistry and Molecular Biology
1996	Founding Board of Directors, International Society for Computational Biology (ISCB)
1982	Undergraduate Research Assistant. Supervisor: Prof. William N. Lipscomb, Nobel Laureate, Harvard Department of Chemistry

Honors and Awards

2023	Arthur Kornberg and Paul Berg Lifetime Achievement Award in Biomedical Sciences
2020	Stanford Biosciences Excellence in Graduate Teaching Award
2020	Tau Beta Pi Teaching Honor Roll
2014	Stanford Medical School Mentorship Award

2014 Fellow, American Association for the Advancement of Science
2010 Fellow, International Society for Computational Biology
2009 Fellow, American Institute of Medical and Biological Engineering
2009 Member, Institute of Medicine of the National Academies (now National Academy of Medicine)
2005 General Internal Medicine, Honorable Mention for Clinical Teaching
2000 Stanford Graduate Teaching Award
1999 Fellow, American College of Physicians
1998 Western Society for Clinical Investigation, Annual Young Investigator Award
1998 Fellow, American College of Medical Informatics
1997 U.S. Presidential Early Career Award for Scientists and Engineers (NIH)
1996 National Science Foundation CAREER Award
1993 Charles E. Culpeper Scholarship in Medical Science
1991 Howard Hughes Fellowship for Physicians
1987 Departmental Ph.D. oral exams passed "with high distinction"
1983 Phi Beta Kappa, Harvard College Chapter
1983 Summa Cum Laude, Harvard College
1983 NIH Medical Scientist Training Program pre-doctoral fellowship at Stanford

C. Contribution to Science
(A relatively comprehensive list of citations can be found at NCBI at:
https://www.ncbi.nlm.nih.gov/myncbi/russ.altman.2/bibliography/public/**)**

Five key areas of contribution over the last decade include:

1. I have contributed the field of **pharmacogenomics** as the founding PI, now Co-Investigator, of the Pharmacogenomics Knowledgebase (PharmGKB, http://www.pharmgkb.org/). PharmGKB is a premier human-curated knowledge base of how human genetic variation impacts drug response phenotypes. It annotates the literature, publishes review articles on drug pathways and genes of significance to pharmacogenomics, and is the basis for several clinical implementation research efforts, including the Clinical Pharmacogenetic Implementation Consortium guidelines (CPIC). We also have made primary contributions to PGx discovery.

a. McInnes G, Lavertu A, Sangkuhl K, Klein TE, Whirl-Carrillo M, Altman RB. Pharmacogenetics at Scale: An Analysis of the UK Biobank. Clin Pharmacol Ther. 2021 Jun;109(6):1528-1537. doi: 10.1002/cpt.2122. Epub 2020 Dec 17. PMID: 33237584; PMCID: PMC8144239.

b. McInnes G, Altman RB. Drug Response Pharmacogenetics for 200,000 UK Biobank Participants. Pac Symp Biocomput. 2021;26:184-195. PMID: 33691016; PMCID: PMC7951365.

c. International Warfarin Pharmacogenetics Consortium; Klein TE, Altman RB, Eriksson N, Gage BF, Kimmel SE, Lee MT, Limdi NA, Page D, Roden DM, Wagner MJ, Caldwell MD, Johnson JA. Estimation of the warfarin dose with clinical and pharmacogenetic data. N Engl J Med. 2009 Feb 19;360(8):753-64. doi: 10.1056/NEJMoa0809329. Erratum in: N Engl J Med. 2009 Oct 15;361(16):1613. PMID: 19228618; PMCID: PMC2722908.

d. Johnson JA, Gong L, Whirl-Carrillo M, Gage BF, Scott SA, Stein CM, Anderson JL, Kimmel SE, Lee MT, Pirmohamed M, Wadelius M, Klein TE, Altman RB; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C9 and VKORC1 genotypes and warfarin dosing. Clin Pharmacol Ther. 2011 Oct;90(4):625-9. doi: 10.1038/clpt.2011.185. Epub 2011 Sep 7. PMID: 21900891; PMCID: PMC3187550.

2. My group has led in the creation of **methods to analyze the scientific literature**, in support of extracting information about the relationship between genes, drugs and phenotypes (in particular, diseases). These are the critical entities for our work in pharmacogenomics and translational medicine. There is a large volume of

unstructured knowledge in the published literature, and too often it is not captured and integrated optimally in the creation and testing of hypotheses. Our work has focused on extracting high quality, semantically clear relationships between key entities. We have focused on both abstracts in PubMED as well as full text, as available. We have released recently a compendium of more than 2 million high quality and typed relationships between genes, drugs and diseases. We have also shown the ability of novel text mining algorithms to search full text to find relationships between entities. We have then used these extracted relationships to support curation of PharmGKB and the generation of networks that can be used to understand the systematic response to drugs.

a. Percha B, Altman RB. A global network of biomedical relationships derived from text. Bioinformatics. 2018 Aug 1;34(15):2614-2624. doi: 10.1093/bioinformatics/bty114. PubMed PMID: 29490008; PubMed Central PMCID: PMC6061699.

b. Sosa DN, Altman RB. Contexts and contradictions: a roadmap for computational drug repurposing with knowledge inference. Brief Bioinform. 2022 Jul 18;23(4):bbac268. doi: 10.1093/bib/bbac268. PMID: 35817308; PMCID: PMC9294417.

c. Mallory EK, Zhang C, Ré C, Altman RB. Large-scale extraction of gene interactions from full-text literature using DeepDive. Bioinformatics. 2016 Jan 1;32(1):106-13. doi: 10.1093/bioinformatics/btv476. Epub 2015 Sep 3. PubMed PMID: 26338771; PubMed Central PMCID: PMC4681986.

d. Mallory EK, de Rochemonteix M, Ratner A, Acharya A, Re C, Bright RA, Altman RB. Extracting chemical reactions from text using Snorkel. BMC Bioinformatics. 2020 May 27;21(1):217. doi: 10.1186/s12859-020-03542-1. PMID: 32460703; PMCID: PMC7251675.

3. My group has created a suite of programs for **recognizing the molecular functions of proteins**, particularly with respect to drug binding, druggability and drug design. We have created and applied programs for assessing pocket similarity, druggability, maximum tolerated dose, and side effect associations by analyzing protein features (active and binding sites) and applying network and other algorithms to make these inferences. We have used these to recognize novel off-target interactions that explain side effects. Recently, we have created a fast neural network representation (COLLAPSE) for characterizing structural microenvironments within proteins that can be used for mutation assessment, protein interface recognition and functional site recognition.

a. Derry A, Altman RB. COLLAPSE: A representation learning framework for identification and characterization of protein structural sites. Protein Sci. 2023 Feb;32(2):e4541. doi: 10.1002/pro.4541. PMID: 36519247; PMCID: PMC9847082.

b. Lo YC, Cormier O, Liu T, Nettles KW, Katzenellenbogen JA, Stearns T, Altman RB. Pocket similarity identifies selective estrogen receptor modulators as microtubule modulators at the taxane site. Nat Commun. 2019 Mar 4;10(1):1033. doi: 10.1038/s41467-019-08965-w. PMID: 30833575; PMCID: PMC6399299.

c. Liu T, Altman RB. Relating Essential Proteins to Drug Side-Effects Using Canonical Component Analysis: A Structure-Based Approach. J Chem Inf Model. 2015 Jul 27;55(7):1483-94. doi: 10.1021/acs.jcim.5b00030. Epub 2015 Jul 16. PMID: 26121262; PMCID: PMC4875781.

d. Liu T, Altman RB. Using multiple microenvironments to find similar ligand-binding sites: application to kinase inhibitor binding. PLoS Comput Biol. 2011 Dec;7(12):e1002326. doi: 10.1371/journal.pcbi.1002326. Epub 2011 Dec 29. PMID: 22219723; PMCID: PMC3248393.

4. Our group has engaged in a program of **translational bioinformatics** to show how systems pharmacology approaches can be used to understand the relationship of molecular mechanism to adverse events. We have shown that we can link data mining of the FDA adverse events database and electronic medical records to extract and validate novel and unexpected drug interactions. We have used crowdsourcing to prioritize adverse events based on their severity. We have created algorithms for linking molecular networks to drugs and diseases in order to generate and understand pathways of drug response, and how drug interactions may

result from intersections of underlying molecular mechanisms of individual drug responses. In recent work cited below, we have created methods for analyzing cytokine response, defining disease subtypes, creating personalized treatment plans based on expression data,

a. Liu T, Wang S, Wornow M, Altman RB. Construction of disease-specific cytokine profiles by associating disease genes with immune responses. PLoS Comput Biol. 2022 Apr 11;18(4):e1009497. doi: 10.1371/journal.pcbi.1009497. PMID: 35404985; PMCID: PMC9022887.

b. Liu T, Han L, Tilley M, Afzelius L, Maciejewski M, Jelinsky S, Tian C, McIntyre M; 23andMe Research Team; Bing N, Hung K, Altman RB. Distinct clinical phenotypes for Crohn's disease derived from patient surveys. BMC Gastroenterol. 2021 Apr 9;21(1):160. doi: 10.1186/s12876-021-01740-6. PMID: 33836648; PMCID: PMC8034169.

c. Han L, Sayyid ZN, Altman RB. Modeling drug response using network-based personalized treatment prediction (NetPTP) with applications to inflammatory bowel disease. PLoS Comput Biol. 2021 Feb 5;17(2):e1008631. doi:10.1371/journal.pcbi.1008631. PMID: 33544718; PMCID: PMC7891788.

d. Han L, Maciejewski M, Brockel C, Afzelius L, Altman RB. Mendelian Disease Associations Reveal Novel Insights into Inflammatory Bowel Disease. Inflamm Bowel Dis. 2018 Feb 15;24(3):471-481. doi: 10.1093/ibd/izx087. PMID: 29462399; PMCID: PMC6037048.

5. We have helped demonstrate **how whole human genomes can be annotated**, and the issues of genome annotation in the context of next generation sequencing. This leadership has been through highly collaborative papers showing the first clinical analysis of a whole human genome, the analysis of a family quartet of genomes, an analysis of a series of genomes with an analysis of accuracy, and papers on the appropriate interpretation and triage of variations discovered in genome sequencing applications, both for pharmacogenomics and more broadly. We have recently focused on the analysis of Pharmacogenomics profiles of populations in biobanks.

a. McInnes G, Sharo AG, Koleske ML, Brown JEH, Norstad M, Adhikari AN, Wang S, Brenner SE, Halpern J, Koenig BA, Magnus DC, Gallagher RC, Giacomini KM, Altman RB. Opportunities and challenges for the computational interpretation of rare variation in clinically important genes. Am J Hum Genet. 2021 Apr 1;108(4):535-548. PMID: 33798442; PMCID:PMC8059338.

b. Ashley EA, Butte AJ, Wheeler MT, Chen R, Klein TE, Dewey FE, Dudley JT, Ormond KE, Pavlovic A, Morgan AA, Pushkarev D, Neff NF, Hudgins L, Gong L, Hodges LM, Berlin DS, Thorn CF, Sangkuhl K, Hebert JM, Woon M, Sagreiya H Whaley R, Knowles JW, Chou MF, Thakuria JV, Rosenbaum AM, Zaranek AW, Church GM, Greely HT, Quake SR, Altman RB. Clinical assessment incorporating a personal genome. Lancet. 2010 May 1;375(9725):1525-35. doi: 10.1016/S0140-6736(10)60452-7. PMID: 20435227; PMCID: PMC2937184.

c. Dewey FE, Grove ME, Pan C, Goldstein BA, Bernstein JA, Chaib H, Merker JD, Goldfeder RL, Enns GM, David SP, Pakdaman N, Ormond KE, Caleshu C, Kingham K, Klein TE, Whirl-Carrillo M, Sakamoto K, Wheeler MT, Butte AJ, Ford JM, Boxer L, Ioannidis JP, Yeung AC, Altman RB, Assimes TL, Snyder M, Ashley EA, Quertermous T. Clinical interpretation and implications of whole-genome sequencing. JAMA. 2014 Mar 12;311(10):1035-45. doi: 10.1001/jama.2014.1717. PMID: 24618965; PMCID: PMC4119063.

d. MacArthur DG, Manolio TA, Dimmock DP, Rehm HL, Shendure J, Abecasis GR, Adams DR, Altman RB, Antonarakis SE, Ashley EA, Barrett JC, Biesecker LG, Conrad DF, Cooper GM, Cox NJ, Daly MJ, Gerstein MB, Goldstein DB, Hirschhorn JN, Leal SM, Pennacchio LA, Stamatoyannopoulos JA, Sunyaev SR, Valle D, Voight BF, Winckler W, Gunter C. Guidelines for investigating causality of sequence variants in human disease. Nature. 2014 Apr 24;508(7497):469-76. doi: 10.1038/nature13127. PMID: 24759409; PMCID: PMC4180223.