## BIOGRAPHICAL SKETCH

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NAME: D.C. Rao

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

POSITION TITLE: Professor 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 |
|---|---|---|---|
| Indian Statistical Institute, Calcutta, India | B. Stat. | 1967 | Statistics/Math |
| Indian Statistical Institute, Calcutta, India | M. Stat. | 1968 | Math Genetics & Probability |
| Indian Statistical Institute, Calcutta, India | Ph.D. | 1971 | Statistical Genetics |

**A. Personal Statement**

I am a Professor of Biostatistics, Genetics, Psychiatry, and Mathematics, and the Director of the Division of Biostatistics at Washington University in St. Louis, School of Medicine. My major research interest is genetic epidemiology of common complex human diseases, with particular interests in cardiovascular (CVD) and metabolic diseases and their risk factors, notably blood pressure and hypertension, lipids, insulin resistance, diabetes, and obesity. My research in CVD genetics has been supported by multiple grants from the NHLBI. I have served or currently serve as the PI of the Data Coordinating Centers (DCC) for several NHLBI-sponsored multi-center family and genetic studies. I have published extensively in the area of cardiovascular genetic epidemiology.

My research interest in Gene-Environment Interactions (GxE) is life-long, starting with gene-age interactions in the "unmeasured genotype" era, continuing into the GWAS era, and lately focusing on gene-lifestyle interactions in substantially large multi-ancestry populations. It originated with a simple gene-age interaction model where parent-child correlation was modeled as a function of child's age (#1 below). This was extended into a path analysis (structural equations) model where "heritability" was modeled as a function of age, still dealing with latent genotypes (#2). The same hypothesis was pursued in a GWAS setting leveraging CHARGE, GBPGen, and ICBP resources (#3). Funded by another NHLBI R01 (HL107552), we pursued several gene-lifestyle interaction publications using dbGaP data. These investigations formed the basis for launching an expanded investigation of interactions (HL118305) (#4). Recognizing the limited power of the current investigations for identifying interactions, this proposal seeks to overcome the power barrier by relying on three large biobanks. With this background, I believe that I am well qualified to lead this project.


1. **Rao DC**, MacLean C, Morton NE and Yee S. Analysis of family resemblance. V. Height and Weight in Northeastern Brazil. American Journal of Human Genetics. 1975 27:509-520. PMCID: PMC1762799
2. Province MA and **Rao DC**. A new model for the resolution of cultural and biological inheritance in the presence of temporal trends: Application to systolic blood pressure. Genetic Epidemiology.1985 2:363-374. PMID: 3841327
3. Simino J*, Shi G*,……, Chakravarti A*, **Rao DC***. Gene-age interactions in blood pressure regulation: A large-scale investigation using the CHARGE, Global BPgen, and ICBP consortia. American Journal of Human Genetics. 2014 95(1):24-38. **Authors contributed equally*. PMCID: PMC4085636

4. **Rao DC,** Sung YJ, Winkler TW, Schwander K, Borecki I, Cupples LA, Gauderman WJ, Rice K, Munroe PB, Psaty BM; CHARGE Gene-Lifestyle Interactions Working Group. Multiancestry Study of Gene-Lifestyle Interactions for Cardiovascular Traits in 610 475 Individuals From 124 Cohorts: Design and Rationale. *Circ Cardiovasc Genet.* 2017 Jun;10(3). pii: e001649. doi: 10.1161/CIRCGENETICS.116.001649. PMCID: PMC5476223

**B. Positions and Honors**

**Positions and Employment**

| | |
|---|---|
| 1971-1972 | Post-Doctoral Fellow, Dept. of Probability and Statistics, University of Sheffield, England |
| 1972-1978 | Assistant Geneticist, Population Genetics Laboratory, University of Hawaii, Honolulu, HI, USA |
| 1978-1980 | Associate Geneticist, Population Genetics Laboratory, University of Hawaii, Honolulu, HI, USA |
| 1980-1982 | Associate Professor and Director, Division of Biostatistics, Department of Preventive Medicine; Associate Professor in Psychiatry and Genetics; Adjunct Associate Professor in Mathematics, Washington University, St. Louis, MO USA |
| 1982-present | Professor and Director, Division of Biostatistics, Professor in Psychiatry and Genetics, Adjunct Professor in Mathematics, Washington University, St. Louis, MO, USA |
| 2002-present | Program Director, Genetic Epidemiology Masters of Science (GEMS) Training Program, Washington University in St. Louis, MO, USA |
| 2004-2010 | Program Co-Director, Ph.D. Program in "Human and Statistical Genetics", Division of Biology and Biomedical Sciences, Washington University in St. Louis, MO, USA |
| 2006-present | Program Director, Summer Institute Program to Increase Diversity in Cardiovascular Genetic Epidemiology: SIPID and PRIDE |
| 2011-present | Program Director, Master of Science in Biostatistics (MSIBS) Training Program, Washington University in St. Louis, MO, USA |

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**Honors**

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|---|---|
| 1996 | President, International Genetic Epidemiology Society (IGES) |
| 1997 | "IGES Leadership Award" from the International Genetic Epidemiology Society (IGES) |
| 2005 | "Champion of Public Health", Awarded by the School of Public Health and Tropical Medicine, Tulane University, New Orleans |
| 2012 | Fellow of the American Association for the Advancement of Science (AAAS) |
| 2013 | Fellow of the American Statistical Association (ASA) |

**C. Contributions to Science**

1. **Path Analysis (Structural Equation Models): Introduced Likelihood Theory and Hypothesis Testing**: My early publications addressed significant challenges in the analysis of nature-nurture issues. While estimates of familial correlations were available for a number of human traits, optimal methods of analysis (model fitting) were lacking. My early research made significant contributions to the analysis of quantitative traits, qualitative traits, as well as multivariate data by introducing likelihood approaches and hypothesis testing (which led to major extensions of the modelling framework as genetic epidemiology was growing). I led this methodological research in collaboration with other colleagues (most notably my post-doctoral Mentor, Dr. Newton Morton).

   a. **Rao DC**, Morton NE and Yee S. Analysis of family resemblance. II. A linear model for familial correlation. American Journal of Human Genetics. 1974 26:331-359. PMCID: PMC1762612

   b. **Rao DC**, Morton NE, Gottesman II and Lew R. Path analysis of qualitative data on pairs of

relatives: Application to schizophrenia. Human Heredity. 1981 31:325-333. PMID: 7333621

c. **Rao DC**, McGue M, Wette R and Glueck CJ. "Path analysis in genetic epidemiology" In: Human Population Genetics: The Pittsburgh Symposium, (ed. A. Chakravarti), Van Nostrand Reinhold Company, Inc., Stroudsburg, PA, 1984 pp 35-81.

2. **Linkage Analysis**: **Mapping Function and Gene Mapping using Pair-Wise LOD Score Data:** Through most of the 1970's, linkage analysis was largely limited to the detection of linkage through significant LOD scores between a trait (locus) and a measured marker, or the use of mapping functions based on fixed levels of interference between the loci. My early research also made significant contributions to linkage methodology by introducing a general mapping function incorporating arbitrary levels of interference (by introducing an estimable parameter). These publications also introduced a maximum likelihood approach to gene mapping whereby pairwise LOD score data were used to generate linear genetic maps. These publications, which I led in collaboration with my colleagues, influenced several developments in the field.

   a. **Rao DC**, Morton NE, Lindsten J, Hulten M and Yee S. A mapping function for man. Human Heredity. 1977 27:99-104. PMID: 863463
   b. **Rao DC**, Keats BJB, Morton NE, Yee S and Lew R. Variability in human linkage data. American Journal of Human Genetics. 1978 30:516-529. PMCID: PMC1685598
   c. **Rao DC**, Keats BJB, Lalouel JM, Morton NE and Yee S. A maximum likelihood map of chromosome 1. American Journal of Human Genetics. 1979 31:680-696. PMCID: PMC1686048

3. **Genetic Basis of Cardio-Metabolic Traits:** In addition to the methodological contributions described in the preceding sections, I have either led or directed numerous investigations of the genetic basis of cardio- metabolic traits throughout my career. These publications made significant contributions to and, in turn, benefitted from the vast literature preceding the GWAS era.

   a. **Rao DC**, Morton NE, Glueck CJ, Laskarzewski PM and Russell JM. Heterogeneity between populations for multifactorial inheritance of plasma lipids. American Journal of Human Genetics.1983 35:468-483.
   b. Kraja AT, Lawson HA, Arnett DK, Borecki, IB, Broeckel U, de las Fuentes L, Hunt SC, Province MA, Cheverud J, **Rao DC**. Obesity-Insulin Targeted Genes in the 3p26-25 Region in Human Studies and LG/J and SM/J Mice. Metabolism. 2012 61(8):1129-1141. PMCID: PMC3586585.
   c. Simino J, Sung YJ, Kume R, Schwander K, **Rao DC.** Gene-alcohol interactions identify several novel blood pressure loci including a promising locus near SLC16A9. Front Genet. 2013; 4:277. **PMID: 24376456**.
   d. Basson JJ, de las Fuentes L, **Rao DC.** Single Nucleotide Polymorphism-Single Nucleotide Polymorphism Interactions Among Inflammation Genes in the Genetic Architechture of Blood Pressure in the Framingham Heart Study. Am J Hypertens 2015. 28(2):248-55. doi: 10.1093/ajh/hpu132. **PMID: 25063733**

4. **Gene-Environment Interactions**: I have had a life-long interest in GxE interactions, starting with gene- age interactions in the unmeasured genotype era and continuing into the present GWAS era, and expanding into gene-lifestyle interactions in large multi-ancestry populations. I have led or directed most of these studies.

   a. Province MA and **Rao DC**. A new model for the resolution of cultural and biological inheritance in the presence of temporal trends: Application to systolic blood pressure. Genetic Epidemiology.1985 2:363-374.
   b. Simino J*, Shi G*, …, Chakravarti A*, **Rao DC***. Gene-age interactions in blood pressure regulation: A large-scale investigation using the CHARGE, Global BPgen, and ICBP consortia. American Journal of Human Genetics. 2014; 95(1):24-38. **Authors contributed equally*. PMCID: PMC4085636
   c. **Rao DC,** Sung YJ, Winkler TW, Schwander K, Borecki I, Cupples LA, Gauderman WJ, Rice K, Munroe PB, Psaty BM; CHARGE Gene-Lifestyle Interactions Working Group. Multiancestry Study of Gene-Lifestyle Interactions for Cardiovascular Traits in 610 475 Individuals From 124 Cohorts:

Design and Rationale. *Circ Cardiovasc Genet.* 2017 Jun;10(3). pii: e001649. doi: 10.1161/CIRCGENETICS.116.001649. PMCID: PMC5476223

d. Sung YJ, Winkler TW, de las Fuentes L, Bentley AR, Brown MR, Kraja AT, Schwander K, Ntalla I, **……**, Caulfield MJ, Elliott P, Rice K, Munroe PB, Morrison AC, Cupples LA, **Rao DC**, Chasman DI. A Large-Scale Multi-ancestry Genome-wide Study Accounting for Smoking Behavior Identifies Multiple Significant Loci for Blood Pressure. *Am J Hum Genet.* 2018 Mar 1;102(3):375-400. doi: 10.1016/j.ajhg.2018.01.015. Epub 2018 Feb 15. PMCID: PMC5985266

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

R01 HL118305 Rao, D.C. 1/15/2014 **-**12/31/2018 (NCE)
NIH/NHLBI

A Multi-Ethnic Study of Gene-Lifestyle Interactions in Cardiovascular Traits

The primary goal of the proposed research is to leverage existing GWAS and Exome Chip data in 25 large multi-ethnic cohorts to discover additional genetic loci for cardiovascular traits by modeling gene-lifestyle interactions, using pleiotropy analysis of correlated traits, and pathway analysis. The investigation will be carried out in 150,765 samples of European Americans, African Americans, Hispanic Americans, and Asians. Approximately equal sample sizes will be used for replication.

Role: PI

R25HL105400 Rao, D.C. 9/1/2014 **-** 12/31/2023
NIH/NHLBI

PRIDE Summer Institute in Cardiovascular Disease Comorbidities, Genetics and Epidemiology (CVD-CGE)

Training and mentoring a diverse biomedical research workforce in state-of-the-art approaches to research in cardiovascular diseases is of considerable public health importance. A highly desirable added benefit is that the trained scientists are more likely to succeed in their research efforts to deal with health disparities among racial and ethnic groups.

Role: PI

T32HL091823 Rao, D.C. 9/15/2008 **-** 8/31/2020 (NCE)
NIH/NHLBI

Post-Doctoral Research Training in Genetic Epidemiology

This renewal application for Post-Doctoral Research Training in Genetic Epidemiology is requesting funds for continued support of 4 post-doc slots each year for 5 years. Trainees will come with an MD or MD/PhD or a PhD degree. Half of the trainees will complete a master's degree and receive in-depth training in genetic epidemiology, statistical genetics, and bioinformatics. The centerpiece of this young program is an Individualized Training Pathway (ITP), customized around the strengths and weaknesses of each trainee.
Role: PI

**Recently Ended**

R01 HL055673 Rao, D.C. 4/1/2013 **-**3/31/2019 (NCE)

NIH/NHLBI University of Kentucky

HyperGEN: Genetics of Left Ventricular Hypertrophy

Black people tend to have an enlarged left ventricle more commonly than those in other race groups, putting them at greater risk for having potentially fatal cardiovascular diseases. Enlarged left ventricles are caused, at least in part, by a person's genes. This study seeks to discover which genetic factors may cause an enlarged heart; this may ultimately lead to new diagnoses and treatments to help lower cardiovascular disease risk in blacks.

Role: Subcontract PI