

Association of Genetic Variants With Primary Open-Angle Glaucoma Among Individuals With African Ancestry

Genetics of Glaucoma in People of African Descent (GGLAD) Consortium, Hauser MA (1,2,3,4) , Allingham RR (2,3,4) , Aung T (3,4,5,6) , Van Der Heide CJ (7) , Taylor KD (8,9) , Rotter JI (8) , Wang SJ (10) , Bonnemaier PWM (11,12,13) , Williams SE (14) , Abdullahi SM (15) , Abu-Amero KK (16) , Anderson MG (7) , Akafo S (17) , Alhassan MB (15) , Asimadu I (18) , Ayyagari R (19) , Bakayoko S (20,21) , Nyamsi PB (22) , Bowden DW (23) , Bromley WC (24) , Budenz DL (25) , Carmichael TR (14) , Challa P (2) , Chen YI (8,9) , Chuka-Okosa CM (26) , Cooke Bailey JN (27,28) , Costa VP (29) , Cruz DA (30) , DuBiner H (31) , Ervin JF (32) , Feldman RM (33) , Flamme-Wiese M (7) , Gaasterland DE (34) , Garnai SJ (35) , Girkin CA (36) , Guirou N (20,21) , Guo X (8) , Haines JL (27,28) , Hammond CJ (37) , Herndon L (2) , Hoffmann TJ (38,39) , Hulette CM (10) , Hydera A (40) , Igo RP Jr (27) , Jorgenson E (41) , Kabwe J (42) , Kilangalanga NJ (42) , Kizor-Akaraiwe N (18,43) , Kuchtey RW (44) , Lamari H (45) , Li Z (46) , Liebmann JM (47) , Liu Y (48,49,50) , Loos RJF (51,52) , Melo MB (53) , Moroi SE (35) , Msosa JM (54) , Mullins RF (7) , Nadkarni G (51,55) , Napo A (20,21) , Ng MCY (23) , Nunes HF (53) , Obeng-Nyarkoh E (24) , Okeke A (56) , Okeke S (18,43) , Olaniyi O (15) , Olawoye O (57) , Oliveira MB (53) , Pasquale LR (58,59) , Perez-Grossmann RA (60) , Pericak-Vance MA (61) , Qin X (62) , Ramsay M (63) , Resnikoff S (64,65) , Richards JE (35,66) , Schimiti RB (67) , Sim KS (46) , Sponsel WE (68,69) , Svidnicki PV (53) , Thiadens AAHJ (11,13) , Uche NJ (26,43) , van Duijn CM (11,70) , de Vasconcellos JPC (29) , Wiggs JL (71,72) , Zangwill LM (19) , Risch N (38,39,41) , Milea D (3,4,5) , Ashaye A (57) , Klaver CCW (11,13,73) , Weinreb RN (19) , Ashley Koch AE (1) , Fingert JH (7) , Khor CC (3,46)

1 Department of Medicine, Duke University, Durham, North Carolina.

2 Department of Ophthalmology, Duke University, Durham, North Carolina.

3 Singapore Eye Research Institute, Singapore.

4 Duke-NUS Medical School, Singapore.

5 Singapore National Eye Center, Singapore.

6 Department of Ophthalmology, Young Loo Lin School of Medicine, Singapore.

7 Carver College of Medicine, Department of Ophthalmology and Visual Sciences, University of Iowa, Iowa City.

8 The Institute for Translational Genomics and Population Sciences, Department of Pediatrics, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, California.

9 Department of Pediatrics, Harbor-University of California, Los Angeles Medical Center, Torrance.

10 Department of Pathology, Duke University, Durham, North Carolina.

11 Department of Epidemiology, Erasmus MC, Rotterdam, the Netherlands.

12 Rotterdam Eye Hospital, Rotterdam, the Netherlands.

13 Department of Ophthalmology, Erasmus MC, Rotterdam, the Netherlands.

14 Division of Ophthalmology, Department of Neurosciences, University of the Witwatersrand, Johannesburg, South Africa.

15 National Eye Centre, Kaduna, Nigeria.

16 Department of Ophthalmology, College of Medicine, King Saud University, Riyadh, Saudi Arabia.

17 Unit of Ophthalmology, Department of Surgery, University of Ghana Medical School, Accra, Ghana.

18 Department of Ophthalmology, ESUT Teaching Hospital Parklane, Enugu, Nigeria.

19 Shiley Eye Institute, Hamilton Glaucoma Center, Department of Ophthalmology, University of California,

San Diego, La Jolla.

20 Institut d'Ophthalmologie Tropicale de l'Afrique, Bamako, Mali.

21 Université des Sciences des Techniques et des Technologies de Bamako, Bamako, Mali.

22 Service Spécialisé d'ophtalmologie, Hôpital Militaire de Région No1 de Yaoundé, Yaoundé, Cameroun.

23 Center for Diabetes Research, Department of Biochemistry, Wake Forest School of Medicine, Winston-Salem, North Carolina.

24 Center for Human Genetics, Bar Harbor, Maine.

25 Department of Ophthalmology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.

26 University of Nigeria Teaching Hospital, Ituku Ozalla, Enugu, Nigeria.

27 Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, Ohio.

28 Institute for Computational Biology, Case Western Reserve University, Cleveland, Ohio.

29 Department of Ophthalmology, Faculty of Medical Sciences, University of Campinas, Campinas, Brazil.

30 Department of Psychiatry and Behavioral Sciences, Duke University, Durham, North Carolina.

31 Clayton Eye Care Center Management Inc, Marrow, Georgia.

32 Kathleen Price Bryan Brain Bank and Biorepository, Department of Neurology, Duke University, Durham, North Carolina.

33 McGovern Medical School, Ruiz Department of Ophthalmology & Visual Science, The University of Texas Health Science Center at Houston, Houston.

34 The Emmes Corporation, Rockville, Maryland.

35 Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor.

36 Department of Ophthalmology and Visual Sciences, University of Alabama at Birmingham.

37 Section of Academic Ophthalmology, School of Life Course Sciences, FoLSM, King's College London, London, United Kingdom.

38 Department of Epidemiology and Biostatistics, University of California at San Francisco.

39 Institute for Human Genetics, University of California at San Francisco.

40 Sheikh Zayed Regional Eye Care Centre, Kanifing, The Gambia.

41 Division of Research, Kaiser Permanente Northern California, Oakland.

42 Department of Ophthalmology, St Joseph Hospital, Kinshasa, Limete, Democratic Republic of the Congo.

43 The Eye Specialists Hospital, Enugu, Nigeria.

44 Department of Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee.

45 Clinique Spécialisée en Ophtalmologie Mohammedia, Mohammedia, Morocco.

46 Genome Institute of Singapore, Singapore.

47 Bernard and Shirlee Brown Glaucoma Research Laboratory, Harkness Eye Institute, Columbia University Medical Center, New York, New York.

48 Cellular Biology and Anatomy, Augusta University, Augusta, Georgia.

49 James & Jean Culver Vision Discovery Institute, Augusta University, Augusta, Georgia.

50 Center for Biotechnology & Genomic Medicine, Augusta University, Augusta, Georgia.

51 The Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, New York.

52 The Mindich Child Health and Development Institute, Icahn School of Medicine at Mount Sinai, New York, New York.

53 Center for Molecular Biology and Genetic Engineering, University of Campinas, Campinas, Brazil.

54 Lions Sight-First Eye Hospital, Kamuzu Central Hospital, Lilongwe, Malawi.

55 Division of Nephrology, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York.

- York.
- 56 Nigerian Navy Reference Hospital, Ojo, Lagos, Nigeria.
 - 57 Department of Ophthalmology, University of Ibadan, Ibadan, Nigeria.
 - 58 Department of Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York.
 - 59 Channing Division of Network Medicine, Brigham and Women's Hospital, Boston, Massachusetts.
 - 60 Instituto de Glaucoma y Catarata, Lima, Peru.
 - 61 John P Hussman Institute for Human Genomics, University of Miami Miller School of Medicine, Miami, Florida.
 - 62 Duke Molecular Physiology Institute, Duke University, Durham, North Carolina.
 - 63 Sydney Brenner Institute for Molecular Bioscience, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa.
 - 64 Brien Holden Vision Institute, Sydney, Australia.
 - 65 School of Optometry and Vision Science, University of New South Wales, Sydney, Australia.
 - 66 Department of Epidemiology, University of Michigan, Ann Arbor.
 - 67 Hoftalon Hospital, Londrina, Brazil.
 - 68 San Antonio Eye Health, San Antonio, Texas.
 - 69 Eyes of Africa, Child Legacy International (CLI) Hospital, Msundwe, Malawi.
 - 70 Nuffield Department of Public Health, University of Oxford, Oxford, United Kingdom.
 - 71 Harvard University Medical School, Boston, Massachusetts.
 - 72 Massachusetts Eye and Ear Hospital, Boston.
 - 73 Department of Ophthalmology, Radboud University Medical Center, Nijmegen, the Netherlands.

IMPORTANCE: Primary open-angle glaucoma presents with increased prevalence and a higher degree of clinical severity in populations of African ancestry compared with European or Asian ancestry. Despite this, individuals of African ancestry remain understudied in genomic research for blinding disorders.

OBJECTIVES: To perform a genome-wide association study (GWAS) of African ancestry populations and evaluate potential mechanisms of pathogenesis for loci associated with primary open-angle glaucoma.

DESIGN, SETTINGS, AND PARTICIPANTS: A 2-stage GWAS with a discovery data set of 2320 individuals with primary open-angle glaucoma and 2121 control individuals without primary open-angle glaucoma. The validation stage included an additional 6937 affected individuals and 14,917 unaffected individuals using multicenter

EXPOSURES: Genetic variants associated with primary open-angle glaucoma.

MAIN OUTCOMES AND MEASURES: Presence of primary open-angle glaucoma. Genome-wide significance was defined as **RESULTS:** A total of 2320 individuals with primary open-angle glaucoma (mean range age, 64.6 http://56-74 years; 1055 http://45.5% women) and 2121 individuals without primary open-angle glaucoma (mean range age, 63.4 http://55-71 years; 1025 http://48.3% women) were included in the discovery GWAS. The GWAS discovery meta-analysis demonstrated association of variants at amyloid-? A4 pre

CONCLUSIONS AND RELEVANCE: In this genome-wide association study, variants at the APBB2 locus demonstrated differential association with primary open-angle glaucoma by ancestry. If validated in additional populations this finding may have implications for risk assessment and therapeutic strategies.

JAMA. 2019 Nov 5;322(17) :1682-1691. doi: 10.1001/jama.2019.16161.

<http://www.ncbi.nlm.nih.gov/pubmed/31688885>