



UK Biobank Eye and Vision Consortium

Issue 12 | October 2018

Derived data from a further 7,500 brain MRI scans has been released and there is data on a total of 21,408 participants. Since the launch of genetics data, there has been exciting new eye-related publications. Some of the major publications are described in the next few pages. Some of the research findings have been featured in the press and we have highlighted a few studies which may be of interest. Serum and red blood cells assay data that were due to be released in July 2018 has been postponed due to further quality control checks. Further updates will be posted in Essential Timelines in Data Showcase in the UK Biobank website.

In this Newsletter:

- Release of a further 7,500 brain MRI scans
- Next Annual meeting
- UK Biobank in the press
- Publication news

Do you have an item for our next newsletter?

Please contact:

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UK Biobank in the press

June 2018, The Economist: [The eye's structure holds information about the health of the mind](#)

May 2018, The Guardian: [Wearing glasses may really mean you're smarter, major study finds](#)

May 2018, Evening Standard: [Genetic tests to assess glaucoma risk for children](#)

May 2018, Alzheimer's Research UK: [Big data reveals new Alzheimer's risk genes](#)

February 2018, The Washington Post: [In our eyes, Google's software sees heart attack risk](#)

Genome-wide analyses identify 68 new loci associated with intraocular pressure and improve risk prediction for primary open-angle glaucoma

Increased intraocular pressure (IOP) is the most important risk factor for primary open-angle glaucoma (POAG). In the meta-analysis of 139,555 European participants, 112 genomic loci associated with IOP were identified and 68 of them were novel. These loci suggest a strong role for angiopoietin-receptor tyrosine kinase signalling, lipid metabolism, mitochondrial function and developmental processes underlying risk for elevated IOP. Regression-based glaucoma prediction models had an area under the receiver operating characteristic curve (AUROC) of 0.76 in US NEIGHBORHOOD study participants and 0.74 in independent glaucoma cases from the UK Biobank. Genetic-prediction models for POAG offer an opportunity to target screening and timely therapy to individuals most at risk.

Khawaja AP, Cooke Bailey JN, Wareham NJ, et al. Genome-wide analyses identify 68 new loci associated with intraocular pressure and improve risk prediction for primary open-angle glaucoma. *Nature Genetics* 2018;50(6):778-82.

[Link to PDF](#)

Genome-wide association study of intraocular pressure uncovers new pathways to glaucoma

Increased intraocular pressure (IOP) is currently the sole modifiable risk factor for primary open-angle glaucoma (POAG). A combined analysis of participants from the UK Biobank (n=103,914) and previously published data from the International Glaucoma Genetic Consortium (n=29,578) identified 101 statistically independent genome-wide significant SNPs for IOP and found 53 to be associated with glaucoma. A number of previously implicated (extracellular matrix and collagen) and novel (vascular development and cell migration) pathways were associated with IOP and glaucoma. An allele score based on the IOP loci and loci influencing optic nerve head morphology was able to enhance risk stratification.

MacGregor S, Ong J-S, An J, et al. Genome-wide association study of intraocular pressure uncovers new pathways to glaucoma. *Nature Genetics* 2018;50(8):1067-71.

[Link to PDF](#)

Genome-wide association meta-analysis highlights light induced signaling as a driver for refractive error

A large GWAS meta-analysis in 160,420 participants identified 139 independent susceptibility loci through single variant analysis and 22 additional loci through post-GWAS methods. Significant biological pathways include retinal cell physiology, light processing and, specifically, glutamate receptor signalling were the most prominent mechanisms. Functional contributions to refractive-error development were determined in all cell types of the neurosensory retina, retinal pigment epithelium, vascular endothelium and extracellular matrix. Newly identified genes implicate novel mechanisms such as rod-and-cone bipolar synaptic neurotransmission, anterior-segment morphology and angiogenesis.

Tedja MS, Wojciechowski R, Hysi PG, et al. Genome-wide association meta-analysis highlights light-induced signaling as a driver for refractive error. Nat Genetics 2018;50(6):834-48.

[Link to PDF](#)

Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning

Risk stratification is important to identify and manage the risk for cardiovascular disease. New knowledge may be extracted from retinal fundus images using deep learning techniques. Deep learning models trained on data from 284,335 patients and validated on two independent datasets of 12,026 and 99 patients predicted cardiovascular risk factors age (mean absolute error within 3.26 years), gender (area under the receiver operating characteristic curve (AUC) = 0.97), smoking status (AUC = 0.71), systolic blood pressure (mean absolute error within 11.23 mmHg) and major adverse cardiac events (AUC = 0.70).

Poplin R, Varadarajan AV, Blumer K, et al. Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning. Nature Biomedical Engineering 2018.

[Link to PDF](#)

Next UKBB Eye & Vision Consortium Annual Meeting:

TUESDAY 5TH FEBRUARY 2019

WELLCOME TRUST

183 Euston Rd, London NW1 2BE

Agenda items

- If you wish to attend, please save this date -

Genome-wide association studies for corneal and refractive astigmatism in UK Biobank demonstrate a shared role for myopia

An GWAS analysis for corneal and refractive astigmatism was performed in the UK Biobank among 88,000 participants. Four loci (ZC3H11B, LINC00340, HERC2/OCA2 and NPLOC4/TSPAN10) were associated with corneal astigmatism, while the three latter loci were associated ($P < 5 \times 10^{-8}$) with refractive astigmatism. These loci were previously found to be related with axial length, myopia, spherical equivalent refractive error and eye colour. Findings support the shared genetic susceptibility of myopia and astigmatism.

Shah; RL. Guggenheim; JA

[Link to PDF](#)

Genome-wide association analyses identify 139 loci associated with macular thickness in the UK Biobank cohort

An analysis of 68,000 participants from the UK Biobank cohort identified 139 SNPs associated with macular thickness at genome-wide significance ($P < 5 \times 10^{-8}$). Most significant loci were LINC00461, TSPAN, RDH5, and SLC6A20. These genetic loci showed pleiotropic effects with myopia, neurodegenerative diseases, cancer and metabolic traits. Findings may further elucidate the pathogenesis of macular degeneration and glaucoma.

Gao; H. Huang; H. Kim

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