Genome wide association studies (GWAS) of Cataract in type 2 diabetes patients in South India

By

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Outline…

- Work progress from October 2020- March 2021
- Introduction
- Cataract and Diabetes
- GWAS on Diabetic Cataract
- Objectives-Work Plan

Work progress from October 2020- March 2021

- Data Generation –Isolated DNA samples and Genotyped samples from Freeze 3. 80% of work in Data generation
- Undergoing hands on training for LINUX/Ubuntu
- Undergoing hands on training for PLINK, for performing QC analysis and R software
- Started working on cataract in type 2 diabetes patients

Introduction

- Lens is a avascular organ, receives nutrients and oxygen from the non-pigmented ciliary and endothelial blood vessel of Iris
- Cataract is defined as clouding of eye lens or opacity of crystalline lens, which prevents clear vision. Based on the Lens opacity, can be classified as nuclear cataract, cortical cataract and posterior capsular cataract, congenital cataract
- According to WHO report 2021, 94 million people are affected by cataract

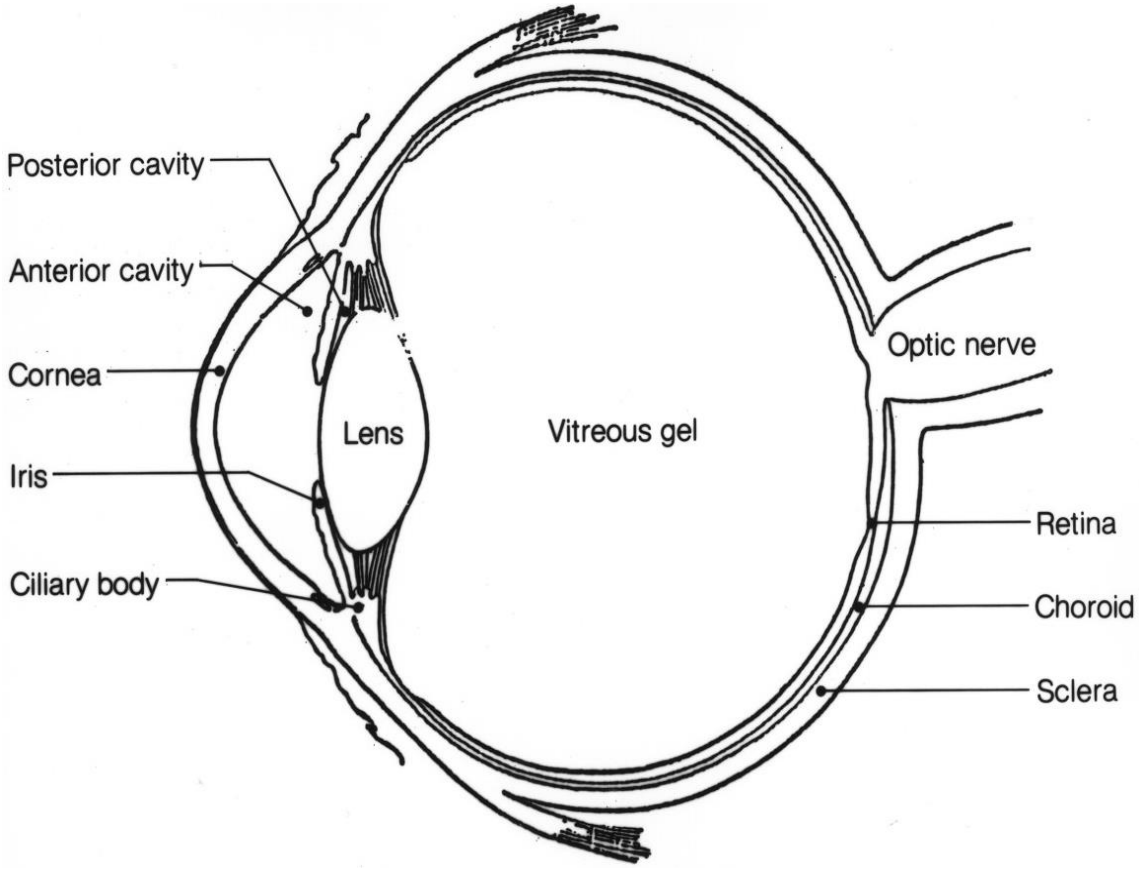

Fig 1. Cross section of eye

Cataract and Diabetes

- Cataract is a slow and progressive condition, increased incidence in Diabetic population
- Those with Diabetes mellitus are 5 times more likely to develop cataract. (Kiziltoprak *et al*,2019)
- From Wisconsin Epidemological Study of Diabetic Retinopathy, 8.3% of type 1 diabetes had cataract compared to 24.9% in type 2 diabetes (Kiziltoprak *et al*,2019)
- Diabetes increases the risk of cataract by 60%. However, by reducing HbA1c by 1%, the risk reduces by 19% (Stratton *et al*,2000)
- Hyperglycemia plays a key role in diabetes induced cataractogenesis, through, aldose reductase pathway, non-enzymatic glycation/glycoxidation and oxidative nitrosative stress
- Previous animal study on Diabetic rats have shown accumulation of sorbitol and galactitol, which leads to ‘’fast’’ opacification of lens (Obrosova *et al*, 2010)
- The prevalence of cataract in type 2 diabetes has been found to be 65.6% in South Indian population (Fathima *et al*, 2016)

Do Diabetes and Cataract share a genetic basis?

Earlier GWAS studies on diabetic cataract

- Chang *et al*(2016) reported *CACNA1c* gene to be associated with diabetic cataract based on from their GWAS studies from Scottish diabetic cohort.

- Zhang *et al*(2021) reported putative causality of *MIR4453HG* and *KCNK17* genes in an East Asian population

- Hui-Ju lin *et al*(2013) reported variants from *PPARD*, *CCDC102A*, *GBA3*, *NEDD9*, *GABRR1/2*, *RPS6KA2*, *tcag7.1163*, *TAC1*, *GALNTL1 and KIAA1671* to be associated with diabetic cataract in an Taiwanese population. These genes are involved in mechanism of regulating blood sugar in cataract formation

Objectives of this study

1. To conduct a GWAS in South Indian type 2 diabetes with cataract

2. To identify significant variants from the GWAS data analysis with diabetic cataract

3. To study, characterize and validate the effect of the identified variants in diabetic cataract by functional genomics

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