GWAS analysis of type 2 diabetes with and without Diabetic Kidney Disease (DKD) in South Indians

By

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Outline…

- ❑ Work Progress
- ❑ Background
- ❑ Definition and Characterization of Diabetes Kidney Disease
- ❑ Study Design
- ❑ Clinical Parameters for the study
- ❑ Workflow

Work done so far...

DNA Extraction >2500 Samples

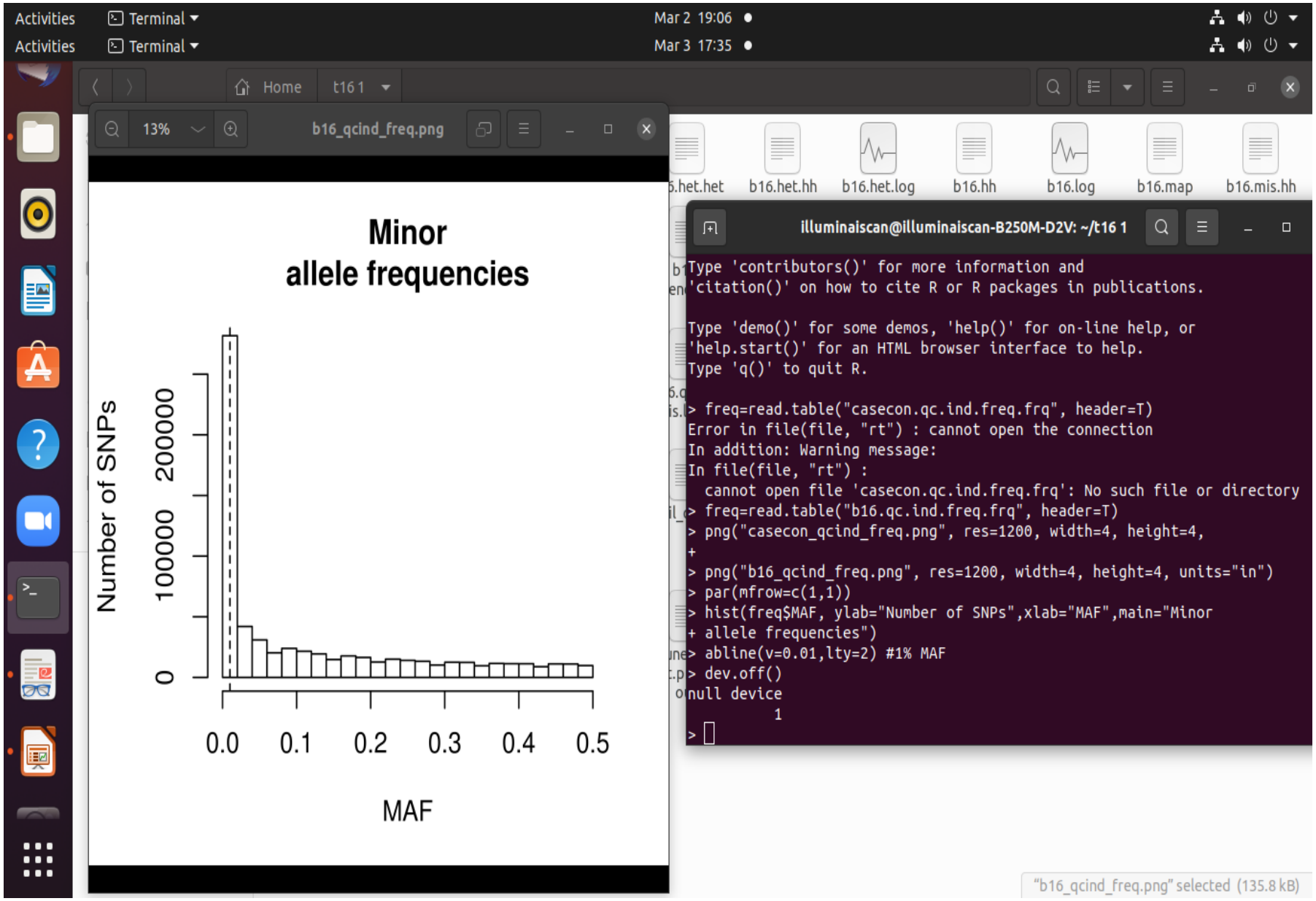
GWAS >25 Batches

Fundamentals of Bioinformatics

Linux/Ubuntu Platforms

Bioinformatics tools:

- ❖ PLINK
- ❖ R



Background

- Chronic Kidney Disease is "progressive," which means it gets worse over time. An estimated 750 million people have **chronic kidney disease** globally **. (Bello *et al*)**

- **Diabetic Kidney Disease** (earlier called **Diabetic nephropathy)** results when diabetes damages the blood vessels and other cells in kidney **.** Over time uncontrolled diabetes can cause damage to blood vessels in the kidney.

- Kidney disease in diabetic patients is clinically characterized by increasing rates of urinary albumin excretion, starting from normalbuminuria, which progresses to microalbuminuria, macroalbuminuria, and eventually to **end-stage renal disease** (ESRD).

- Studies conducted in migrant Asian Indians in the U.K. and European have reported increased prevalence of diabetic nephropathy compared with white Caucasians. Diabetic kidney disease is the leading cause of an ESRD worldwide, and it is estimated that 20% of type 2 diabetic patients reach ESRD during their lifetime. (**R Unnikrishnan *et al* 2007)**

Definition and characterization of Diabetic Kidney Disease

Diabetic Kidney disease is defined as:

- Albuminuria (albumin-to-creatinine ratio ≥3.4 mg/mmol [30 mg/g])
- Estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73m^2.
- Diabetes is defined as fasting glucose ≥7 mmol/L (126 mg/dL) and/or use of medications for diabetes;
- Hypertension as systolic BP ≥140mmHg and diastolic ≥90mmHg and/or use of medications for hypertension. **(Anand *et al* CAARS STUDY 2017)**

There are no data on the GWAS of diabetic kidney disease in Indians.

Broad objectives of my Study

1. To identify the genetic markers associated with Diabetic Kidney Disease in South Indian population using Genome-wide association studies.

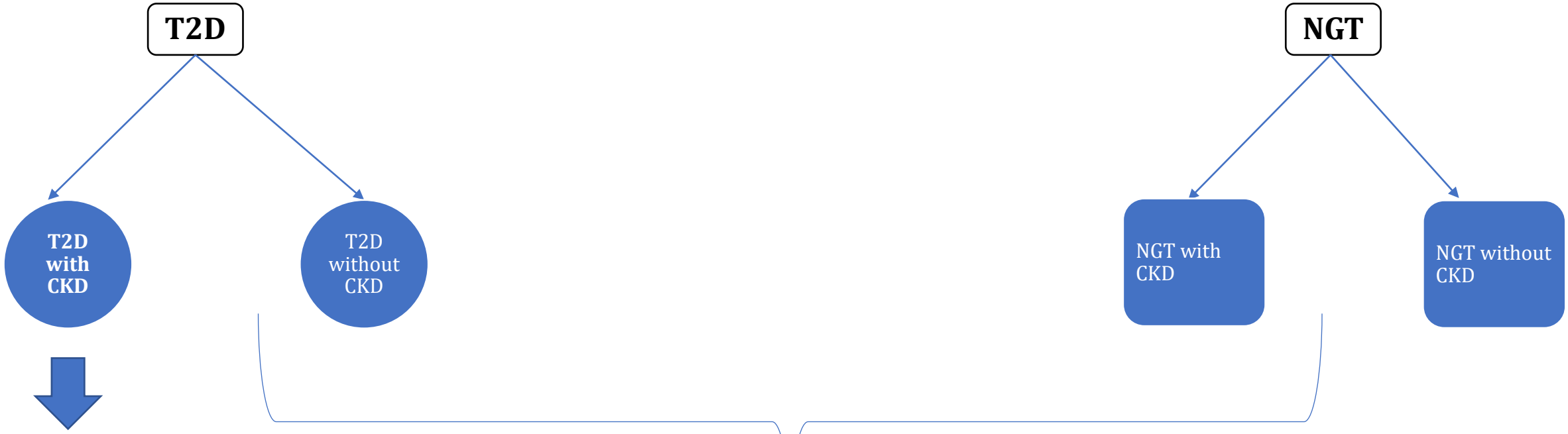
2. To carry out functional validation for the rare variants from GWAS Analysis.

3. To construct a Polygenic Risk Score (PRS) for DKD in South Indian population.

CLINICAL VARIABLES that will be considered for the study

- Age
- Gender
- Waist measurement
- BMI
- Blood pressure
- Lipid levels
- Retinopathy /Cardio vascular disease
- HbA1c
- Microalbuminuria (30 – 299 mg/mmol)
- Macro albuminuria (>300 mg/mmol)
- eGFR rate

GWAS Analysis-Work flow



Different variables

- Microalbuminuria
- Macroalbuminruia
- eGFR rate
- High blood pressure

Susceptible variants

Functional validation and Polygenic Risk Score

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