TYPE 2 DIABETES KNOWLEDGE PORTAL NEWSLETTER

Upcoming webinars

Join us on Thursday September 26 at noon EDT for our next webinar. Watch our home page for information on the agenda and connection instructions.

Future webinar dates:

Thursday, November 14
Thursday, January 16
Thursday, March 12

New videos available

We've released two new videos:

- a short video introduction to the table of predicted T2D effector genes
- a recording of our July webinar, featuring gene-specific resources in the T2DKP

Both are available from the T2DKP Resources page and the Broad Institute YouTube channel.

Stay up to date with the T2DKP

Contact us:

help@type2diabetesgenetics.org

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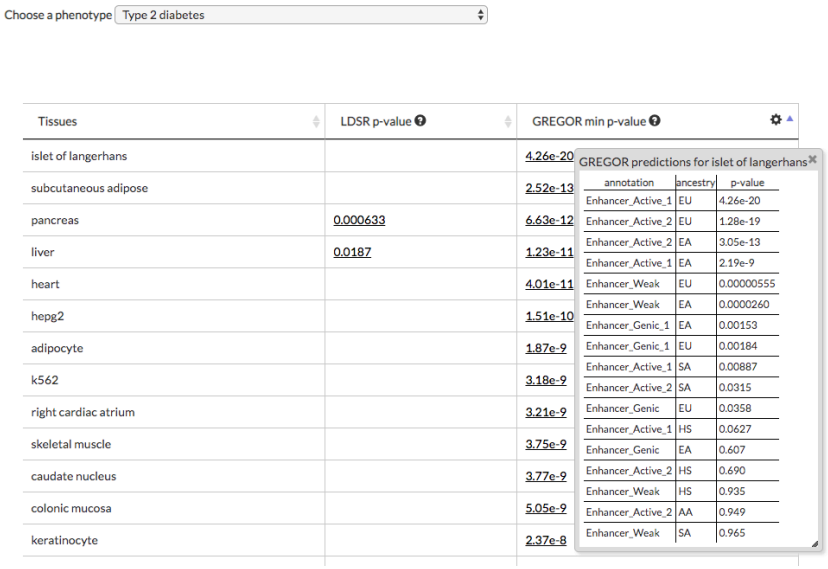
T2D Knowledge Portal

FOCUS on methods that mine genomic data for clues about disease



Tissue FOCUS table

Identifying the gene products that are directly involved in disease processes is essential for a better understanding of disease risk and progression. But it is rarely straightforward to make these identifications from variant genetic associations.

To help researchers make the connection between risk-associated variants and disease genes, we are assembling a toolkit of cutting-edge computational methods and applying them to all of the genetic association data in the T2DKP. The methods integrate GWAS data with transcriptomic data, tissue-specific gene expression results, eQTL data, and more to predict the probability of associations between variants, genes, phenotypes, and tissues. We present these results in interactive FOCUS (Find Orthogonal Computational Support) tables.

New datasets

IVGTT-based Insulin Secretion GWAS: genetic associations for first-phase insulin secretion, as measured by intravenous glucose tolerance tests in over 5,500 multi-ethnic non-diabetic individuals

GIANT 2018 BMI, Height exome chip analysis: genetic associations for BMI and height, determined in over 718,000 individuals

GIANT 2018 Body Fat Distribution exome chip analysis: associations for waist/hip ratio adjusted for BMI, determined in over 344,000 individuals

GLGC exome chip analysis: associations for plasma lipid levels in over 347,000 multi-ancestry participants

Chronic Inflammation GWAS: genetic associations with plasma C-reactive protein, a measure of chronic inflammation, in more than 312,000 individuals

COGENT-Kidney Consortium eGFR GWAS: associations with estimated glomerular filtration rate (eGFR) in over 204,000 subjects

All of these datasets are described in detail on the T2DKP Data page.

We previously added to the Gene page a Gene FOCUS table that presents results to help researchers evaluate candidate causal genes around a genetic association signal (read our blog post describing this interface). Now, we have added a Tissue FOCUS table presenting results that can suggest which tissues or cell types may be relevant for a disease or trait of interest.

To use the table, choose a phenotype of interest to see p-values for different tissues, denoting the significance with which variants associated with that phenotype are enriched in each tissue. The methods used for these predictions are DEPICT, GREGOR, and LD score regression (LDSR). Find complete details about the table and methods in our downloadable documentation.

This table is part of a triad of FOCUS tables, along with the Gene FOCUS table and the in-development Variant FOCUS table. Our aim is to help researchers prioritize genes, variants, and tissues for further investigation. These interfaces are under active development, and we welcome your feedback.

Speedy new analysis pipeline gets revved up

Part of the responsibility of the Accelerating Medicines Partnership in Type 2 Diabetes (AMP T2D) Data Coordinating Center (DCC) at the Broad Institute is to perform association analysis on genetic association data received from AMP T2D collaborators. At the outset of the project, quality control and analysis of these data were performed in a largely manual manner that was very time-consuming. To increase its efficiency, speed, and reproducibility, the T2DKP team at the DCC has developed an automated genomic analysis pipeline, termed LoamStream.

LoamStream is now up and running, and we have used it to re-analyze, in a small fraction of the time, several sets of individual-level genetic association data from AMP T2D collaborators that were previously analyzed manually. Updated analyses were performed for the BioMe AMP T2D GWAS, CAMP GWAS, Diabetic Cohort - Singapore Prospective Study GWAS, FUSION exome chip analysis, FUSION GWAS, FUSION Metabochip,

Connect with us at ASHG 2019

The T2DKP team will be attending the American Society of Human Genetics meeting in October, and we'll be presenting in multiple venues.

- Our **booth** (#131) in the exhibit hall will be open on Wednesday October 16 and Thursday October 17 from 10am-4:30pm, and on Friday October 18 from 10am-3:30pm. Come meet us, have your questions answered and get a hands-on tutorial!
- We will be presenting at the **Broad genomics booth** (#714) on Wednesday October 16 from 3-4pm and on Friday October 18 from 10-11am. We'll cover the latest developments in the Knowledge Portal Network.
- Join our **Ancillary session** to learn about a new initiative integrating multiple genetic, genomic, and epigenomic data types:

Translating Variant Associations to Functional Insights Using the Knowledge Portal Network
Wednesday, Oct. 16, 12:45-2:00 pm
Marriott Marquis Houston,
Tanglewood room

- Attend **talks** from the T2DKP team:

Marcin von Grotthuss, "Public programmatic access to GWAS summary statistics and analytical methods."

Lokendra Thakur, "Calculating principled gene priors for genetic association analysis."

- View **posters** from theT2DKP team:

Ben Alexander, "Systematic comparison of different evidence sources for predicting GWAS effector genes."

Peter Dornbos, "The functional impacts of rare coding variants in 46,000 individuals on 23 quantitative phenotypes."

and METSIM GWAS datasets.

The LoamStream software allowed T2DKP analysts to run these analyses rapidly and to determine associations for many more phenotypes than were analyzed previously. Each dataset was analyzed for associations with glycemic, lipid, renal, anthropometric, and blood pressure phenotypes, and in addition, the type 2 diabetes cases in the BioMe AMP T2D GWAS set were analyzed for associations with three diabetic complications: chronic kidney disease, end-stage renal disease, and neuropathy. The Loamstream pipeline generates detailed Quality Control and Analysis reports, available for download from the dataset-specific sections of the T2DKP Data page.

Results from these re-analyses are integrated into the T2DKP and may be viewed on Gene and Variant pages and in Manhattan plots. They may be searched using the Variant Finder, and the individual-level data from the GWAS sets may be securely accessed for custom association analysis using the Genetic Association Interactive Tool (GAIT) on Variant pages.

LoamStream is currently being modified so that it can be applied to exome sequencing data as well as GWAS data. We anticipate that going forward, it will greatly streamline the quality control and analysis processes at the DCC.

Custom burden test now handles multiallelic variants

Some sequence variants are biallelic or multiallelic: that is, the reference nucleotide may be substituted by two or more different nucleotides or indels. Previously, in the custom burden test (found on T2DKP Gene pages) these variants were treated as a single allele. Now, the software underlying the custom burden test has been updated so that it treats multiple alleles separately, offering the ability to choose whether each allele of a multiallelic variant should be included in or excluded from the custom burden test. Stay tuned for other major improvements to the burden test, including the ability to use several different aggregation test methods, coming to the T2DKP in the near future!