Integration of genetic colocalizations with physiological and pharmacological perturbations identifies cardiometabolic disease genes

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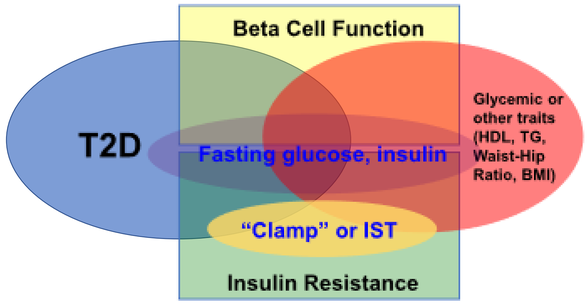
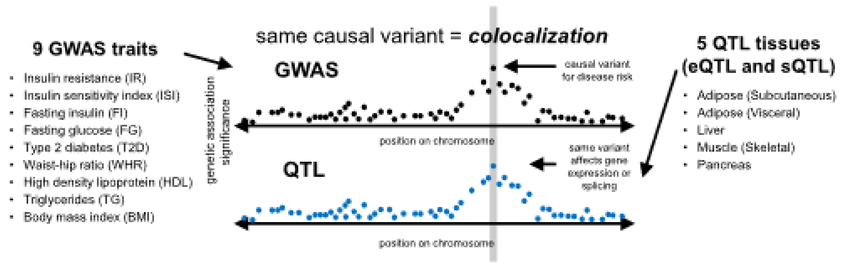
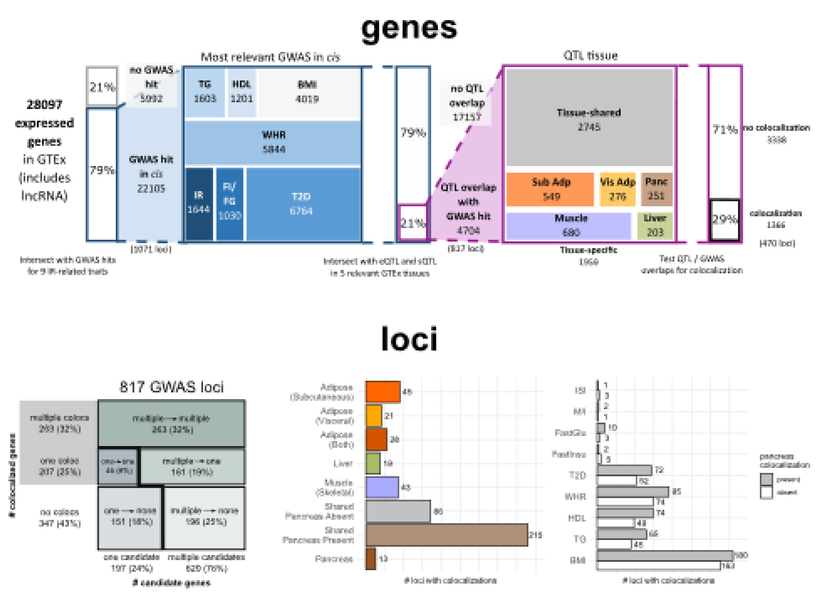
Insulin resistance (IR) leads to type 2 diabetes (T2D) and other diseases, but is hard to study directly



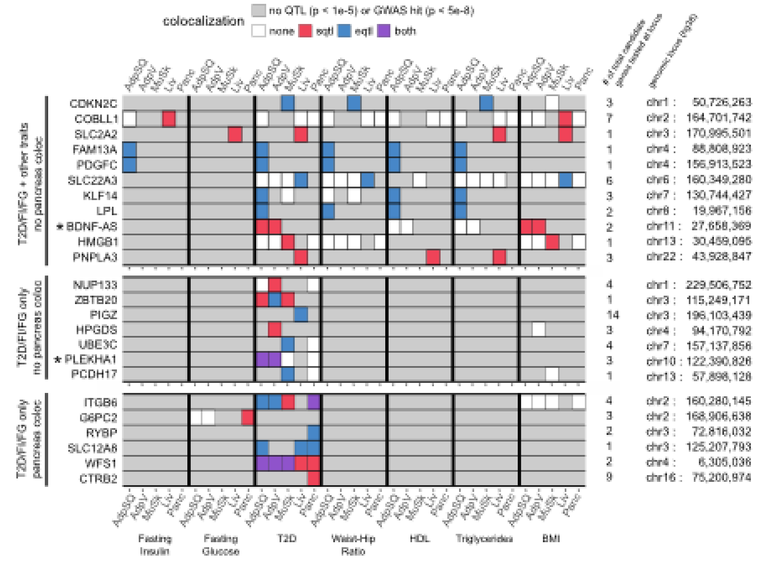
Genetic associations were integrated across 9 IR-related traits and 5 IR- or T2D- relevant human tissues



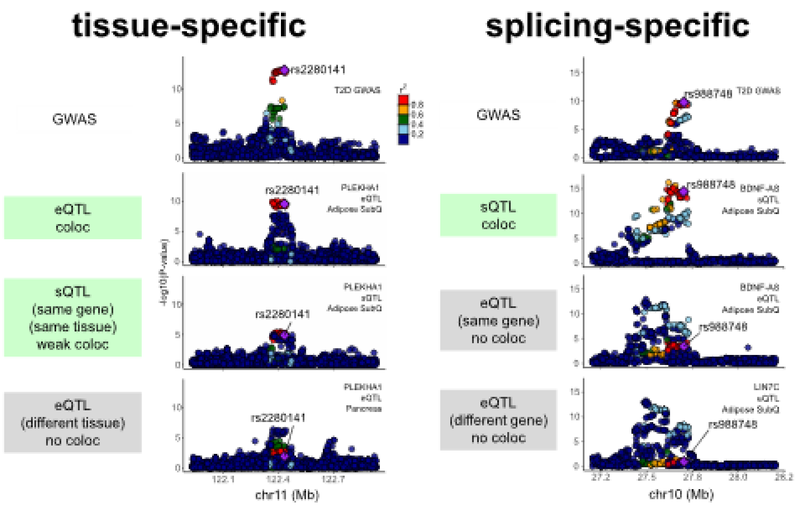
Colocalization analysis found 1366 genes associated with 470 IR-related GWAS loci



Uniquely colocalized IR and T2D loci show various patterns of tissue and trait sharing



Tissue-specific genes and splicing-specific genes exist



Funding, data, and code availability

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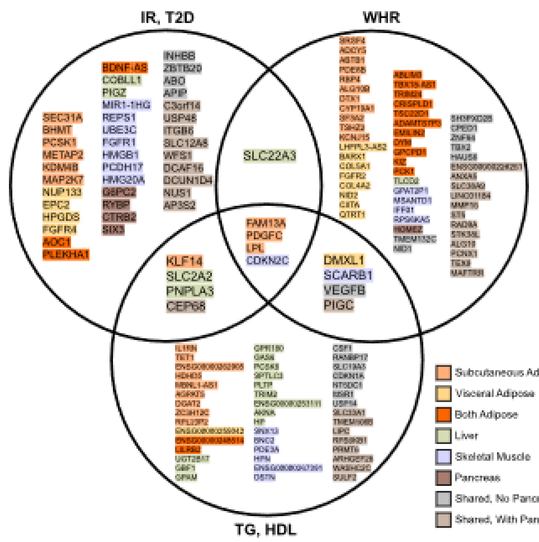
A generalized version of the heatmap-producing code is available at https://github.com/mikegloudemans/post-coloc-toolkit.

For further questions about this project or about applying the methodology to your own diseases of interest, contact me at mgloud@stanford.edu.

Loci with single colocalized genes show tissue-specificity patterns according to trait cluster



Candidate causal genes show varied patterns of response to a panel of 21 perturbagens in fat, liver, and muscle cells