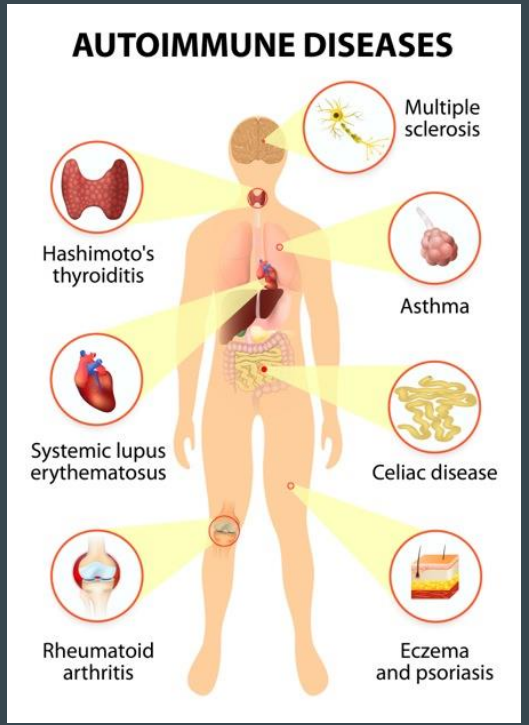
Autoimmune Diseases

Finding Commonality between Celiac, Crohn's, Hashimoto's Thyroiditis and Eczema

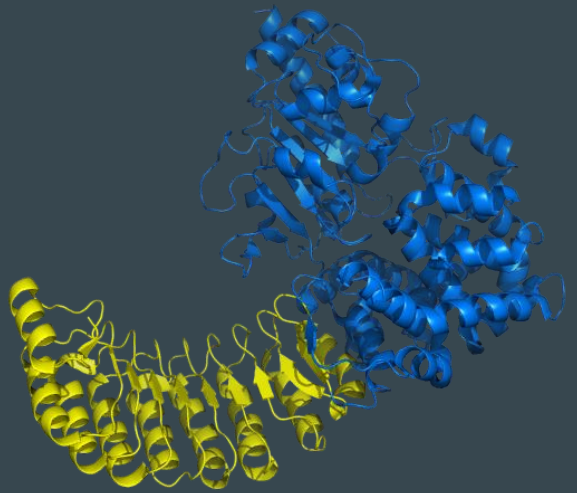
Background Autoimmune diseases

- Body attacks own healthy cells
  - Caused by overactivity in the immune system
- Common examples: Rheumatoid arthritis, lupus, IBD, MS, Type 1 diabetes
- Often linked to inflammation
- Not very well understood
  - Can run in family
  - Can be triggered by environmental factors including stress



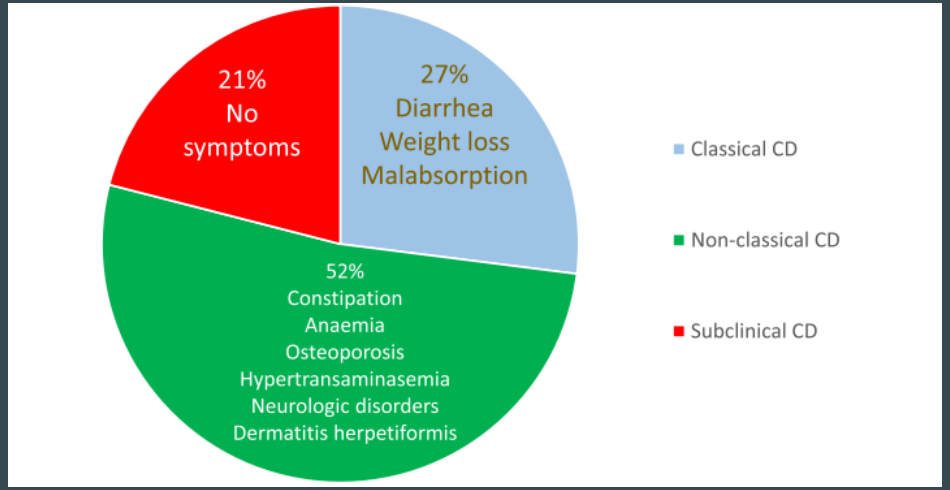
Background Crohn's

- Inflammatory Bowel Disease
- Affects entire digestive tract
  - Abdominal cramping
  - Diarrhea
  - Fever
  - Bowel obstruction
- NOD2 gene mutation
  - Sustained mucosal immune response



Background Celiac

- Immune system damages small intestine, increasing gut permeability
- Gluten is an environmental trigger
- Only seen in people who can express HLA-DQ2/HLA-DQ8
    - Human leukocyte antigen proteins, responsible for presenting antigens in immune response

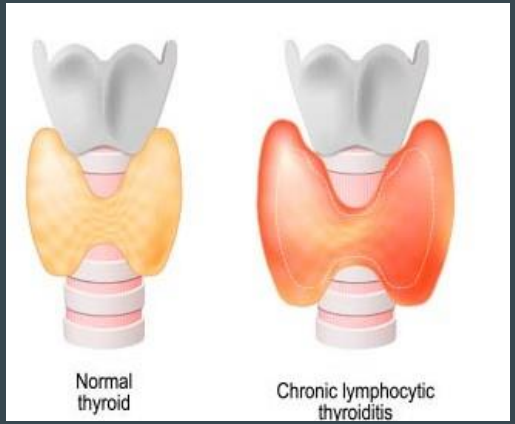


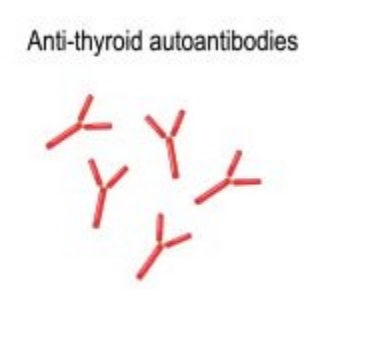
Background Eczema

- Very Common
- Complex Disease
- Genetic and Environmental
- Usually starts in early childhood

Background Hashimoto's Thyroiditis

- The body attacks the thyroid
- Much more common in women
  - Later diagnosis
- Symptoms: enlarged thyroid gland, depression, weight gain, dry skin or hair
- Known pathways affected: immune, apoptotic, metabolism, and GPCR receptor signaling

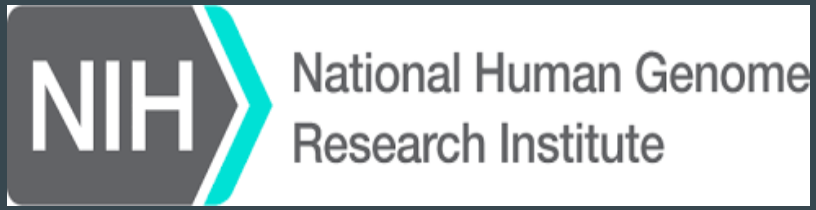




Research Question

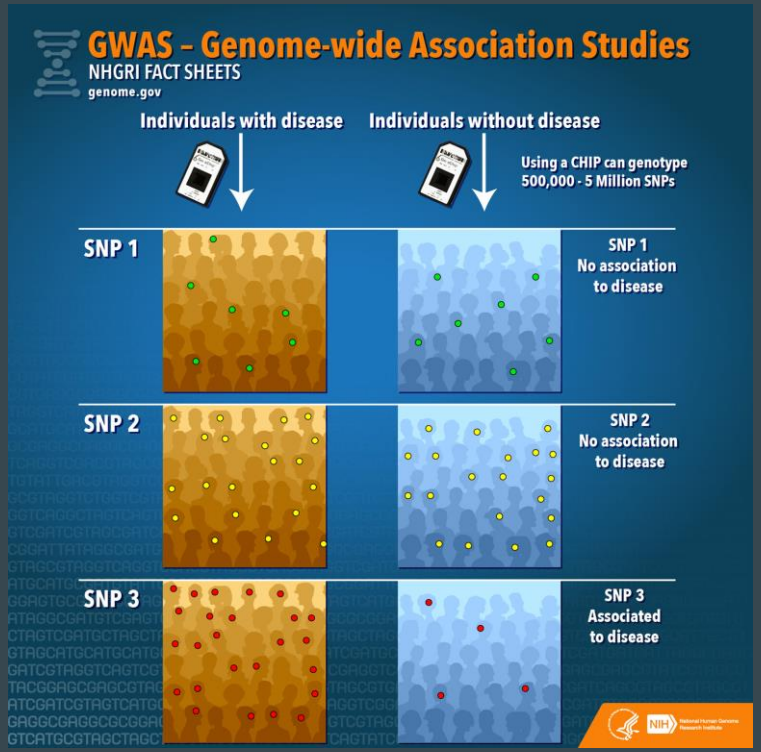
Identify genetic commonality between these four diseases

- Analyze commonly associated genes
- Look for significant genes through gene expression
- Pathway Analysis



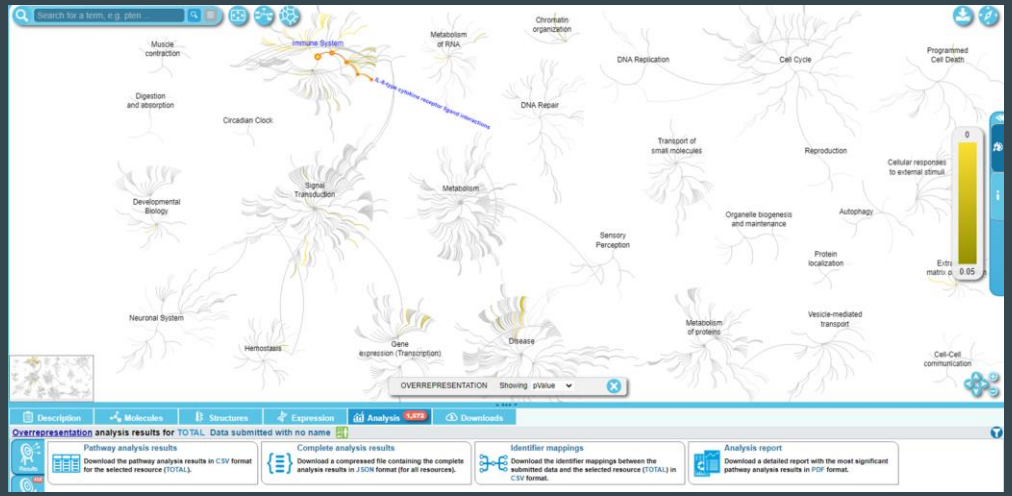
GWAS and ClinVar

- GWAS
  - Control groups Vs Experimental
  - Identify SNPs that are more common in experimental group
  - Link risk genes to common SNPs
- ClinVar
  - Archive of reports of relationships between human variation and phenotypes
  - Submissions with variants found in patient samples



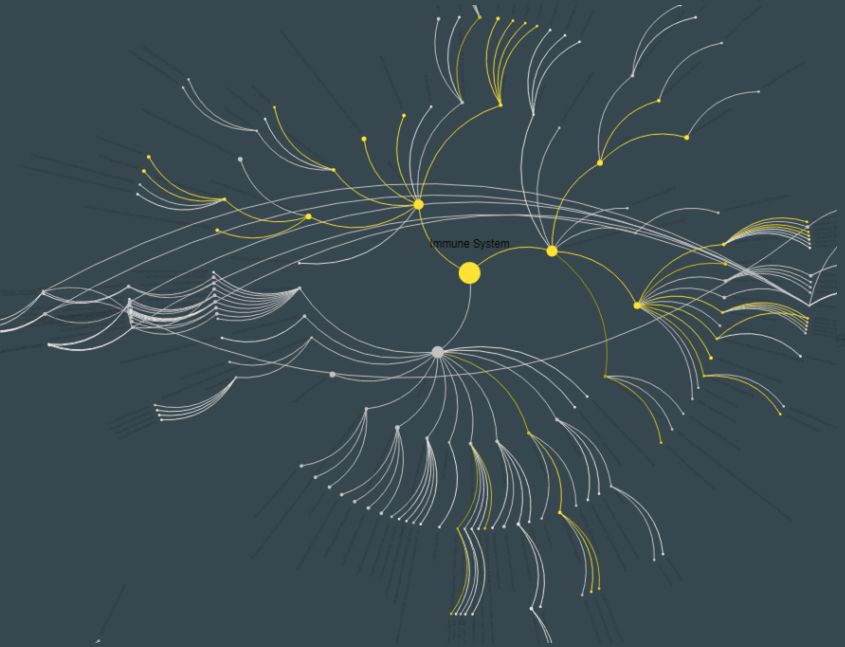
Analysis with Reactome

- Pathway Analysis
- View Pathways most related to given genes
  - Input: List of genes
  - Output: Most significant pathways

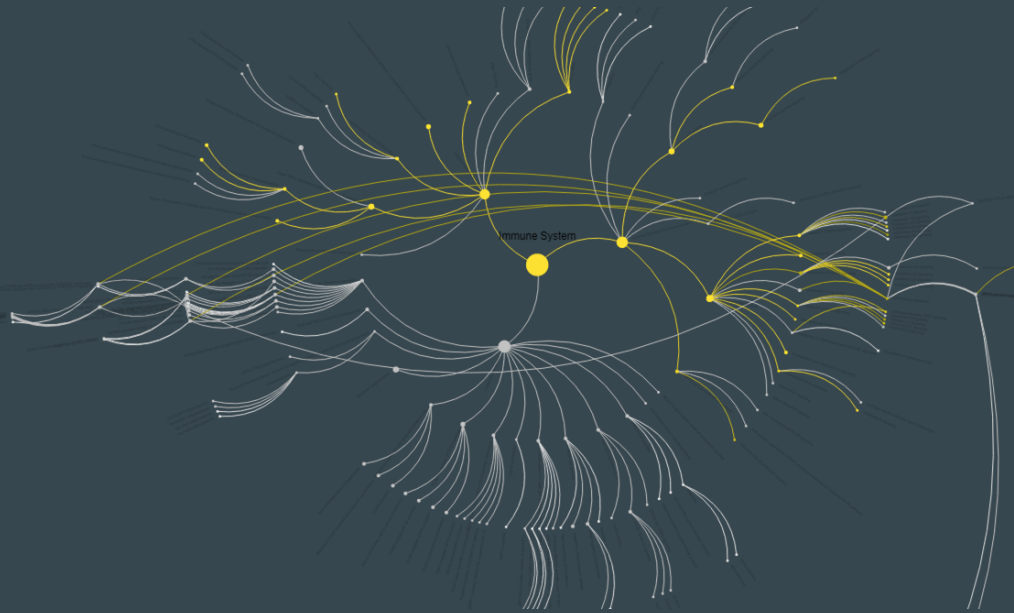


Analysis with Reactome

Eczema

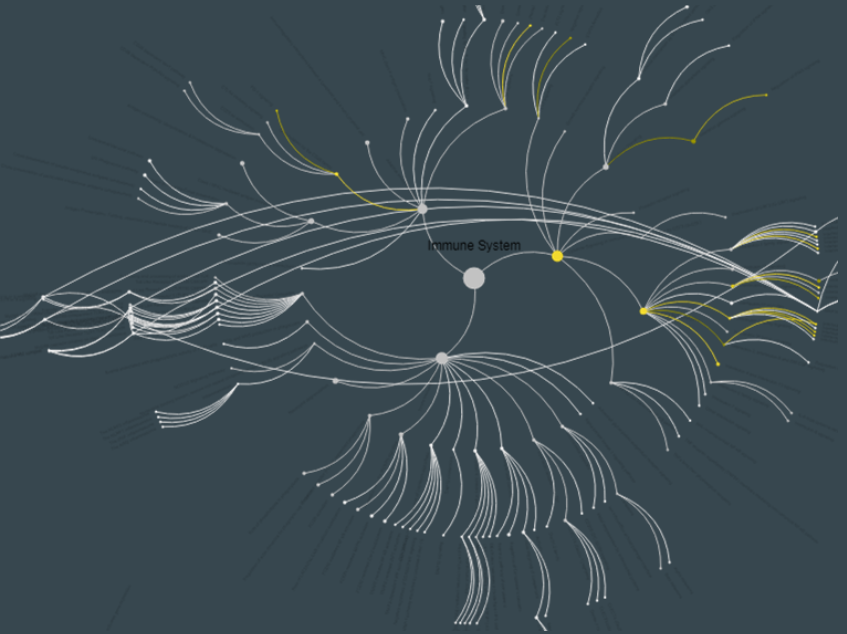


Crohns

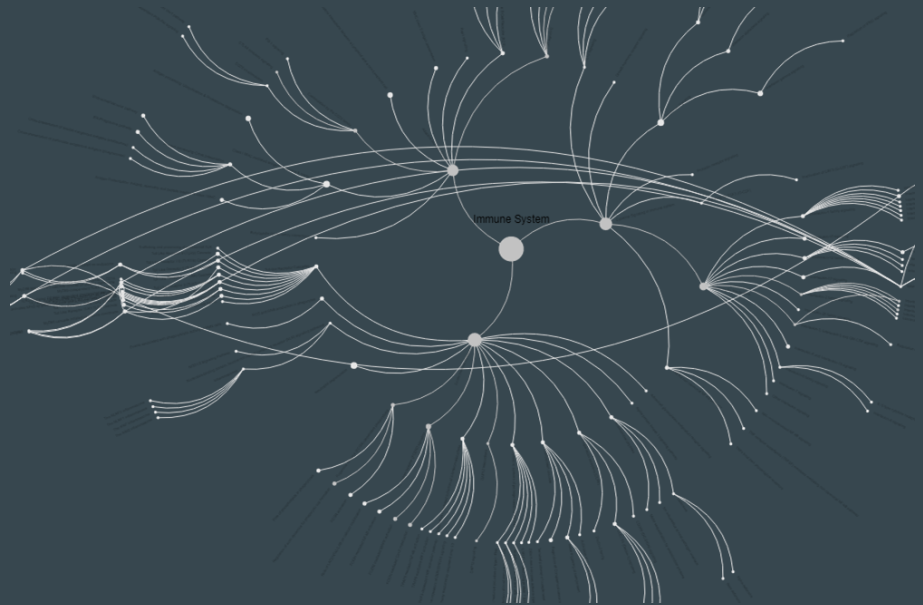


Analysis with Reactome

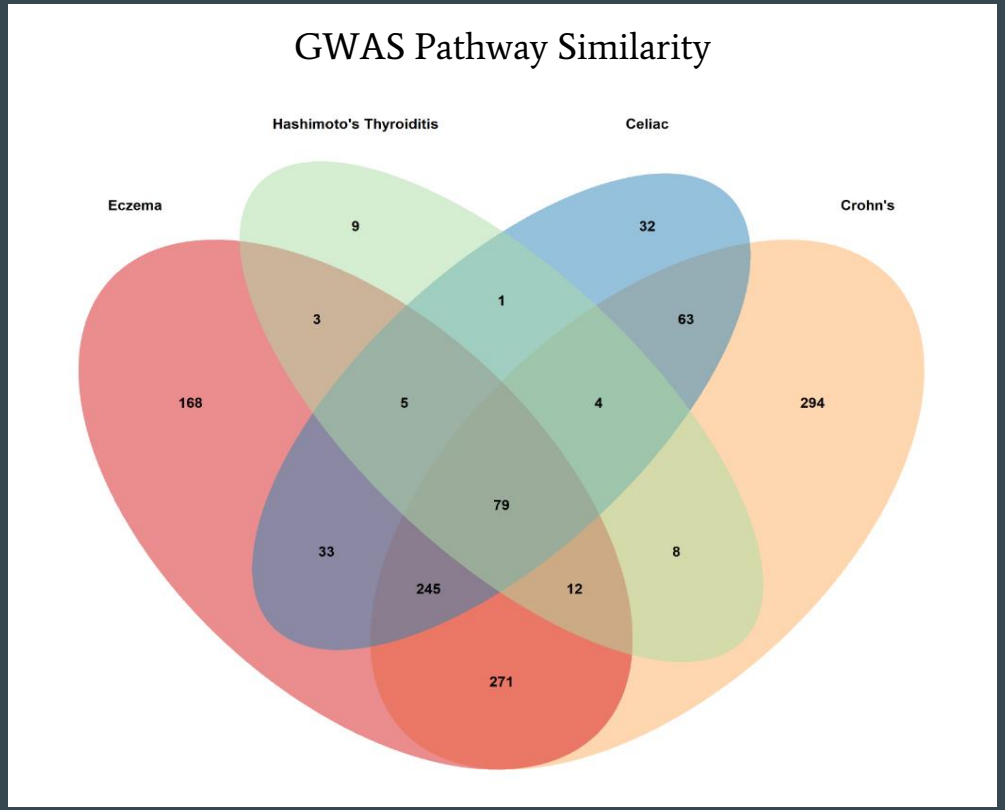
Celiac

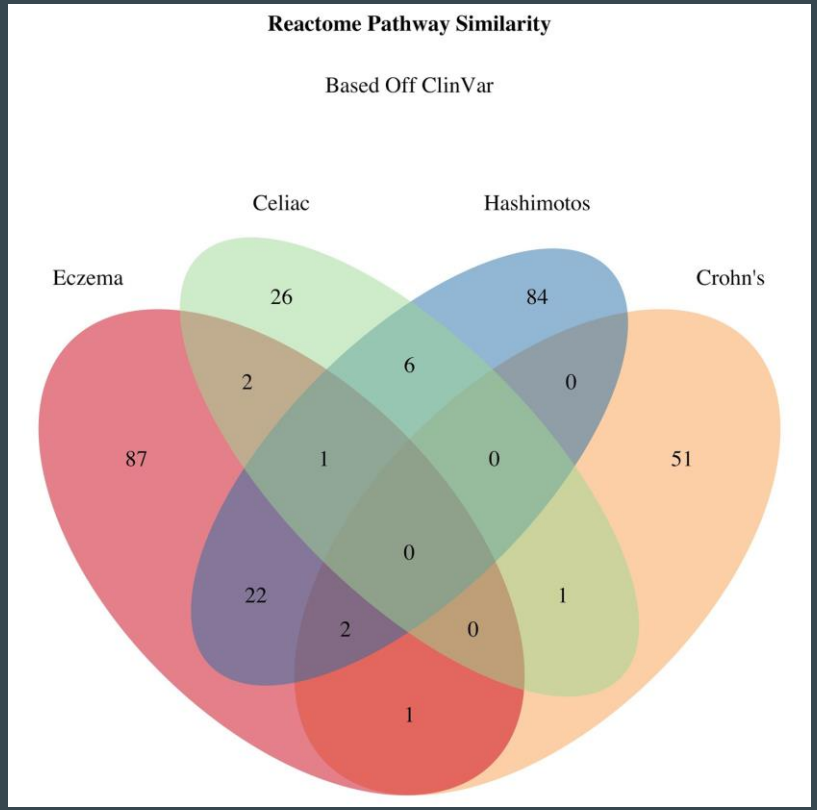


Hashimoto



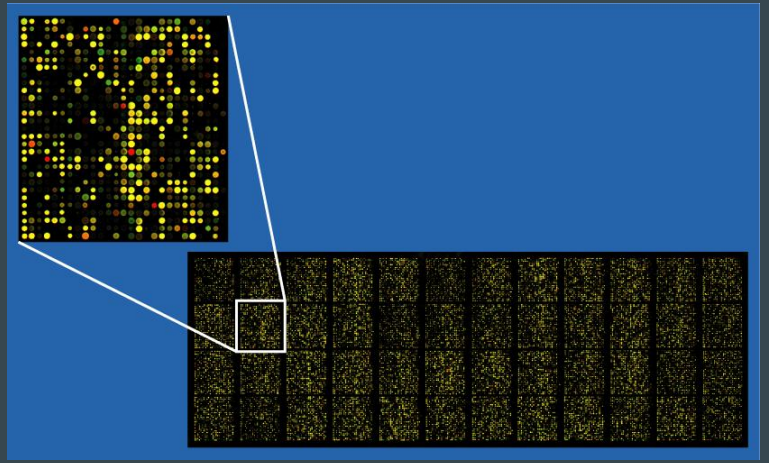
Results of GWAS and ClinVar analysis

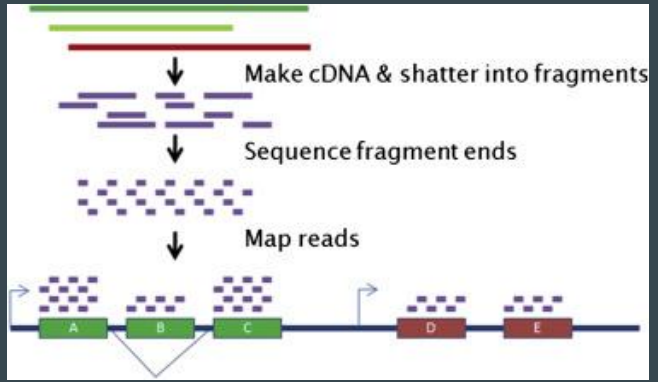




Gene Expression

- Can be measured with either microarrays or with RNA-seq
- Microarrays
  - Known sequences used to map DNA fragments and show expression of different genes
  - DNA fragmented by endonucleases
  - Fluorescent markers react to probes
- RNA-seq
  - Show the presence and quantity of RNA
  - Break into small parts
  - Sequence fragments
  - Map to DNA



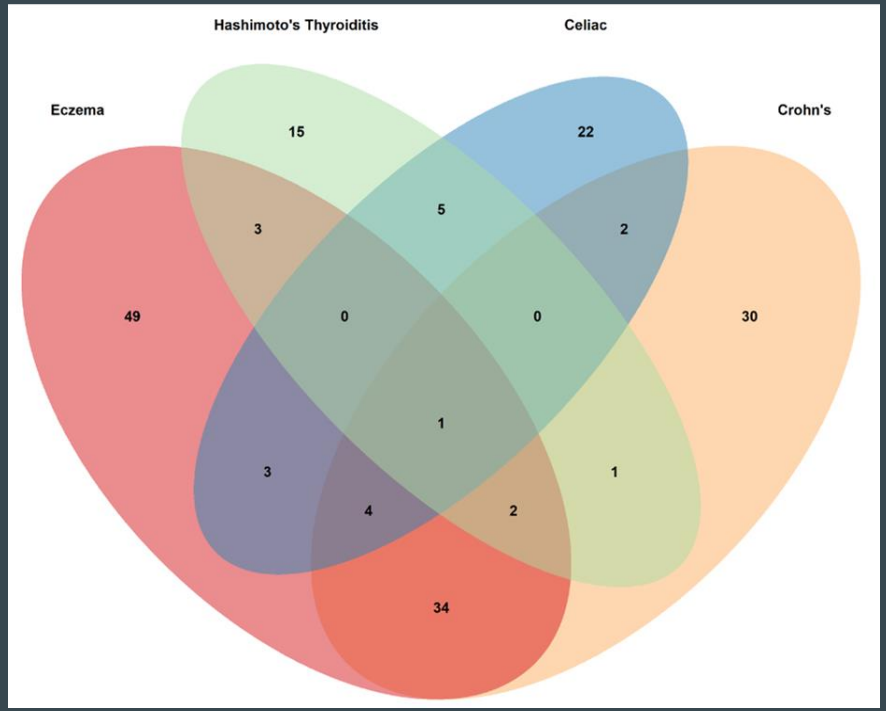


Gene Expression Results

Combined genes from GWAS, ClinVar and MicroArray Studies for pathway analysis

One Significant Common Pathway

- RUNX1 and FOXP3 control the development of regulatory T lymphocytes (Tregs)



Conclusion

- Some general similarity between the diseases, but very little specific similarity for all of them.
- RUNX1 and FOXP3 regulatory pathway is involved in all four diseases
- Hashimoto's Thyroiditis does not have nearly as much information as the rest of the diseases which make it difficult to compare them well.
- Follow up analysis could yield more results

Follow Up Questions

- Autoimmune diseases and cancer
- RNA-seq data instead of just microarray data
- Pull data from many more studies