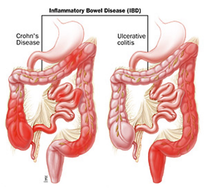
# Single cell RNA sequencing to uncover intestinal cell-type specific *cis*-eQTL driving inherited predisposition to IBD

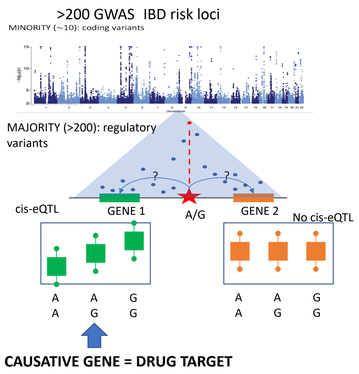
Yumie Tokunaga[1], Marie Wéry[1], Alice Mayer[2], Latifa Karim[2], Samira Azarzar[1], Viacheslav Petrov[1], Loic Demeulenaere[1], Manon Deckers[2], Emilie Detry[2], Wouter Coppieters[2], Edouard Louis[3], Michel Georges[1], Souad Rahmouni[1]

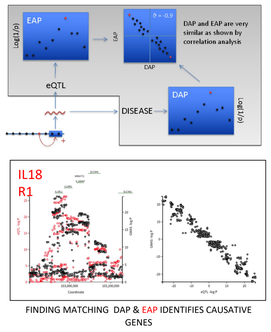
[1]Unit of Animal Genomics, GIGA-Institute, University of Liege, Liege, Belgium
[2]GIGA Genomic Platform, GIGA-Institute, University of Liège, Liege, Belgium
[3]CHU-Liège and Unit of Gastroenterology, GIGA-Institute, University of Liège, Liege, Belgium

## Summary

**IBD** is characterized by a chronic idiopathic inflammation of the gastrointestinal (GI) tract and consist of two main forms: ulcerative colitis and Crohn's disease. The importance of genetic susceptibility has been well established through Genome Wide Association Studies (GWAS), which have identified over 200 risk loci for IBD. However, the **« true causative » genes** in these loci have been identified for only few on the basis of independently associated coding variants. Fine-mapping studies suggested that most risk variants cause "cis"-eQTL in disease relevant cell types, but recent post-GWAS studies could not find matching cis-eQTLs for the majority of risk loci (137/200). This indicates that the relevant cell types were either not present amongst the analyzed cell populations or under-represented.
In this study, we performed cis-eQTL analysis with single cell RNA-seq of human gut biopsies to uncover the truly relevant cell types with higher resolution and unbiased approach.



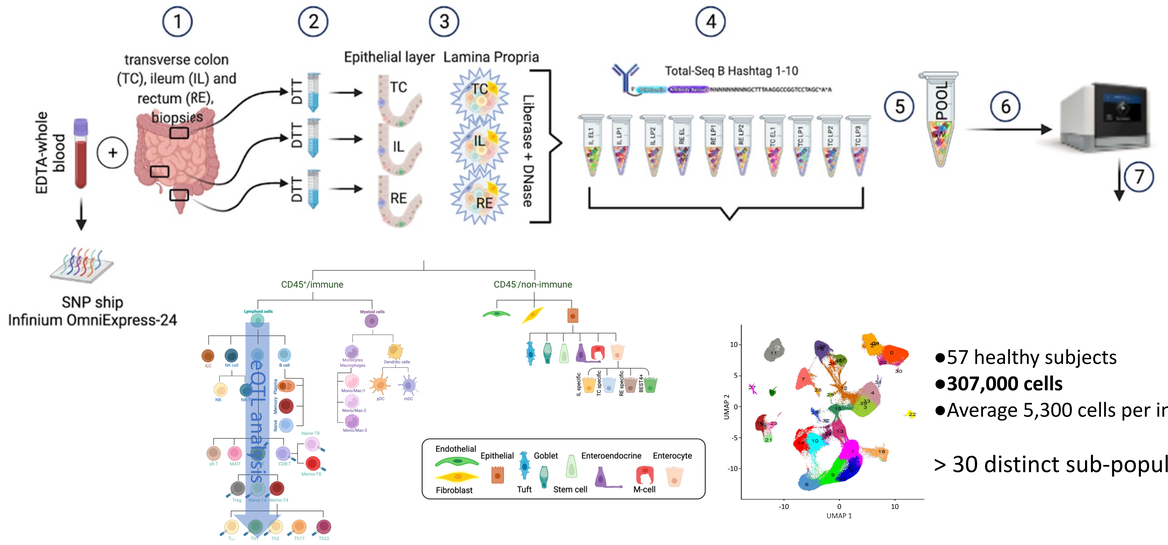


EAP: Cis-eQTL analysis
- 6 circulating immune cell types,
- intestinal biopsies, 3 locations
- 300 healthy individuals

DAP: IBD case-control FWAS
- IIBDGC
- > 30,000 individuals

Where are the matching eQTL for the remaining 150 IBD risk loci?

## ScRNAseq Workflow of Intestinal Biopsies



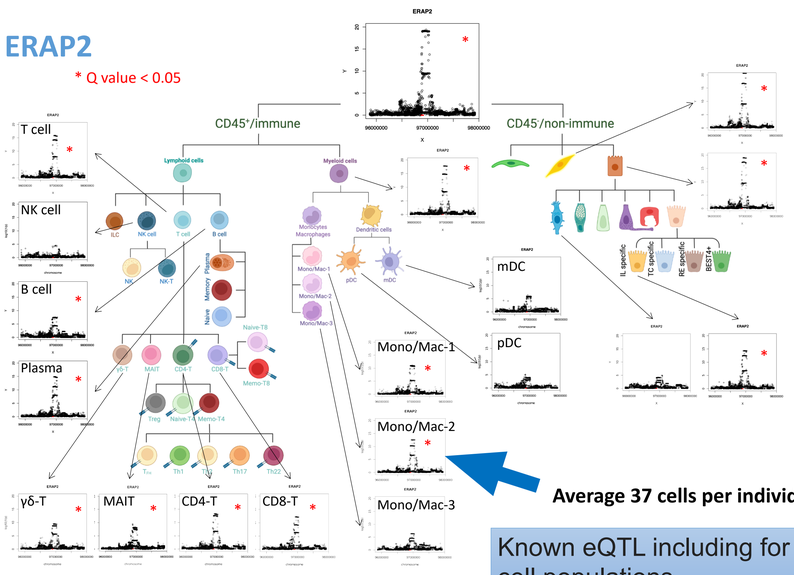

- ●57 healthy subjects
- ●**307,000 cells**
- ●Average 5,300 cells per individual

> 30 distinct sub-populations

## Cell Type Specific eQTLs by scRNAseq of Intestinal Biopsies

### ERAP2

* Q value < 0.05

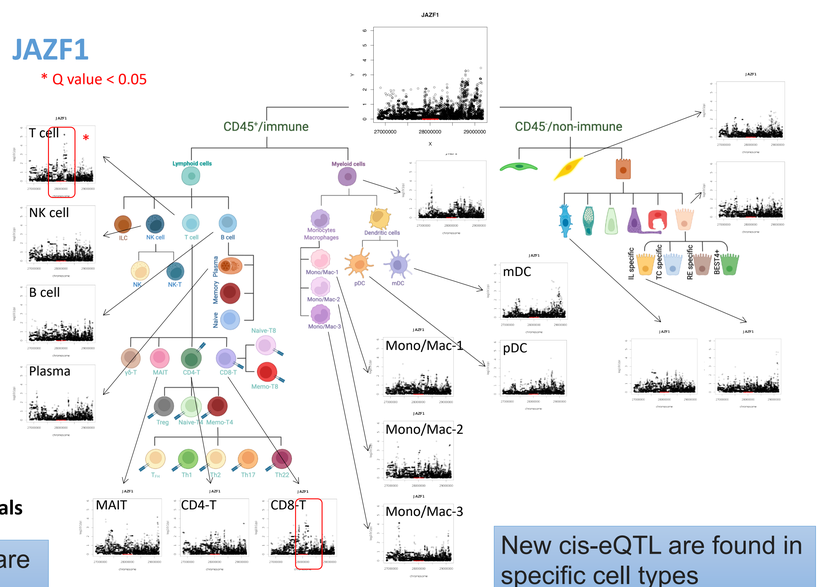



Average 37 cells per individuals

Known eQTL including for rare cell populations

### JAZF1

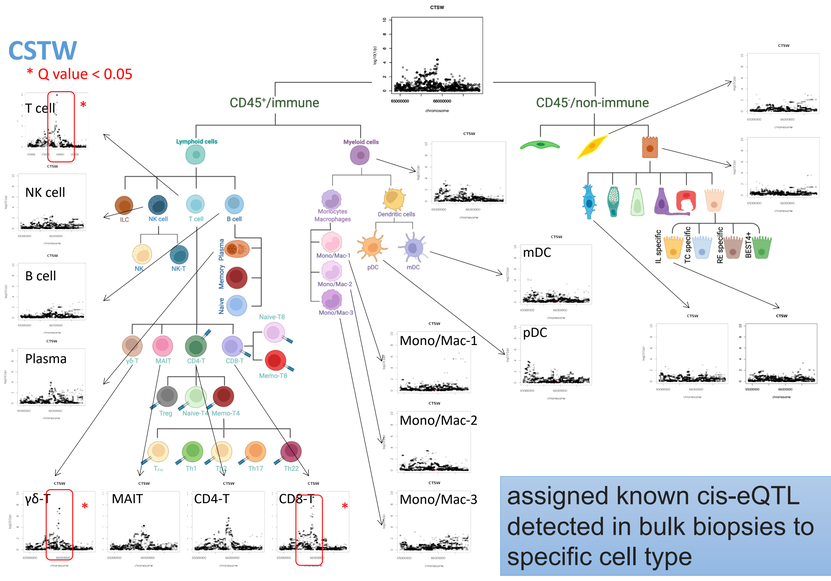
* Q value < 0.05




New cis-eQTL are found in specific cell types

### CSTW

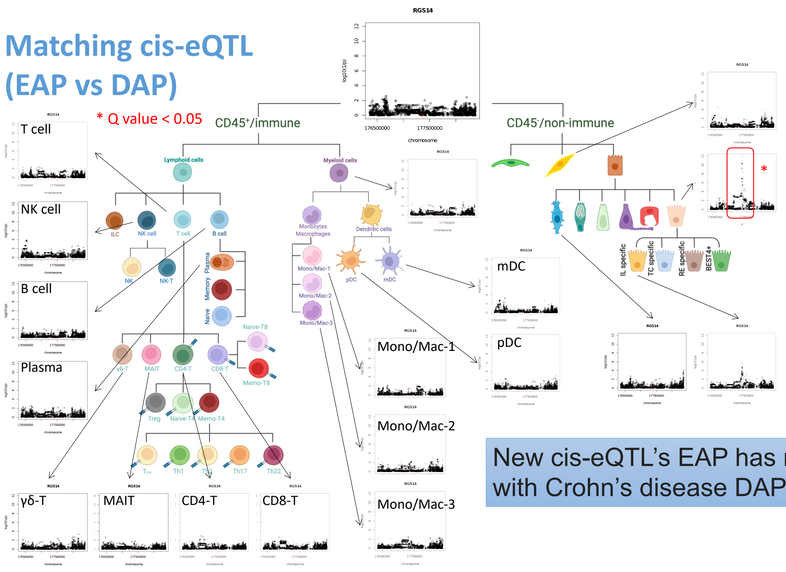
* Q value < 0.05



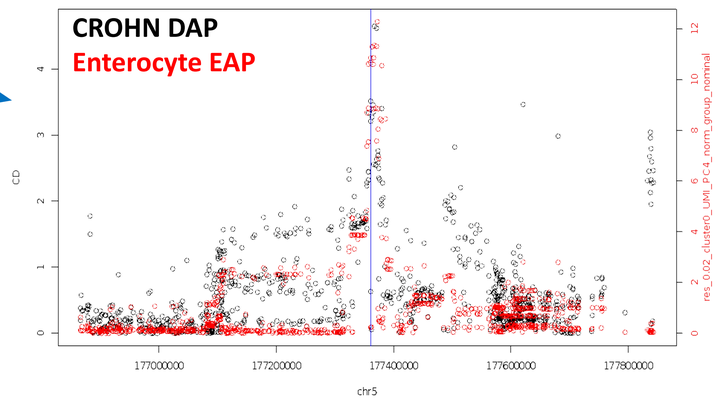

assigned known cis-eQTL detected in bulk biopsies to specific cell type

### Matching cis-eQTL (EAP vs DAP)

* Q value < 0.05




New cis-eQTL's EAP has matched with Crohn's disease DAP




## Conclusions

1. identified previously known eQTL including for rare cell populations with less than 40 cells per individual: ex; ERAP2

2. identified > 800 eQTL including new ones such as JAZL1

3. possible to assign eQTL that were previously detected in bulk biopsies to specific cell populations.

4. identified cis-eQTL in rare intestinal subpopulations with matching DAP-EAP that may point towards new causative genes for IBD

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