Celiac disease consequences

HIGH RED BLOOD CELLS (RBC), MCV (abnormal erythropoiesis)

https://ac.els-cdn.com/S1590865800803990/1-s2.0-S1590865800803990-main.pdf?_tid=366395f2-fc2f-11e7-9168-00000aab0f27&acdnat=1516266716_c352be8f9cd3ea34fd1e60b5f40c486f

Anemia
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1785098/

THYROID ABNORMALITIES (ALSO SUPPORTS THE REVERSE LINK, from thyroid abnormalietes to CeD)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5435852/

INCREASED CD4+ Tcells

Here this studies shows that we have a decrease of CD4+ in PBMC during inflammation (Figure 1)
http://www.sciencedirect.com/science/article/pii/S1074761316301431?via%3Dihub#mmc1

HYPER-CHOLESTEROLEMIA
https://www.glutenfreesociety.org/gluten-and-high-cholesterol/
Note that your results go in the opposite direction… and also weird, because you have reduced levels of all cholesterol types
I removed **CHOLESTEROL**. IT is not significant after Q pruning

HYPERTENSION
https://www.nature.com/articles/1001404

THROMBOCYTOSIS (high platelets) and trombocytopenia (low platelets)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1785098/

OTHER AUTOIMMUNE DISEASES
https://www.ncbi.nlm.nih.gov/pubmed/29076940

Narcolepsy
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4894018/
narcolepsy has never been reported as a consequence but observed as co-occurance with CeD. We can now see the direction

more general neurological disorders:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3641836/

The link between schizoprenia however appears to be very weak, but this agree with the effect size you see in your analyses. Narcolepsy is much much stronger than schizoprenia

INCREASED EOSINOPHILS/ DECREASED LYMPHOCYTES
Firstly reported by Astle et al Cells using MR . I put it as a new because it is new connection made with MR method. Now we also see the reverse direction

Overlap with infection diseases/allergies.
I think that observation on tonsilities is quite new

QUESTION FOR MATTHIJS:

-- remind me the physical poistion of HLA region that we considered?

I am asking because it is very interesting to see that narcolepsy (in addition to other autoimmune diseases) remains significant for causality, even after removing HLA

TEXT POSTER:

Introduction:
Celiac disorder affects up to two percent of the European population, and it is hereditary. ~~People with a frst degree relative with celiac disease have 30 times higher risk of developing celiac disease.~~ The inheritance model of celiac disease is oligogenic.[1] In this model, ~~HLA-DQ2 is~~ a genetic variant in the major histocompatibility complex (MHC) region, the HLA-DQ2 haplotype, ~~that~~ accounts for 40% of the inheritable risk, b~~B~~ut~~, this genetic variant alone~~ it is not sufcient enough to develop ~~celiac disease~~the disease. 30% of the Europeans are in fact carriers of the variant, ~~however~~ but only 3% express celiac disease. Other 42 non-HLA variants have been identified, but still remains little understanding on what triggers the disease. We ~~expect to~~aimed to systematically assess ~~fnd~~ multiple ~~causal or protective~~ clinical parameters ~~or~~ and molecular mechanisms ~~that will be quantifed~~to identify ~~to understand the impact of the~~ causal ~~or~~ and protective ~~relationship~~factors, that can ~~potentially~~ explain what is triggering ~~celiac~~ disease manifestation in ~~the 3% from the 30% of the Europeans that are carriers of~~ HLA-~~t~~DQ2 carriers.

MATERIALS AND METHODS
We investigated over 500.000 ~~publicly available~~ clinical parameters and molecular phenotypes, ~~available from databases, and~~for which ~~published~~ summary statistics from genome-~~t~~wide association studies (GWAS) were available. ~~, with~~We used the concept of Mendelian Randomization[3] (MR) approach, and applied ~~. We used~~ two-~~t~~samples MR methods: Inverse ~~t~~Variance Weighted[4] (IVW) ~~method~~ and MR-~~t~~Egger method[5] to infer causality links by combining

summary statistics from GWAS. For our analyses, we discarded variants located in the MHC region to avoid over-estimation of causality for factors that also influenced by the same or other HLA haplotypes

RESULTS

We identifed 1133 signifcant (FDR < 0.05) clinical parameters ~~or molecular mechanisms~~ that cause or protect for celiac disease, and others that show feedback mechanisms . For example autoimmune diseases such as Type 1 Diabetes (T1D), ~~which~~ have been largely describe~~ds~~ ~~the~~ to co-~~t~~occur~~rence of T1D and~~ with celiac disease.[6,7] ~~A shared association between celiac disease and crohn's disease.[7] The~~We also confirmed a causative effect of eosinphils (and protective of lymphocytes) ~~is~~ in increasing the ~~a~~ risk ~~factor for~~ of celiac disease, ~~and that lymphocytes is associated as a~~which was recently described using the same approach [8]. Here we also observed that there is feedback mechanisms, with the disease also affecting, in turn, the number of eosinophils and lymphoctyes ~~protective factor for celiac disease.[8]~~ . Finally, in addition to ~~These fndings~~parameters that are ~~consistent~~supported by previous epidemiological studies, we found an interesting causative role for infection diseases and allergies.

Conclusion & Discussion

We have carried out a systematic application of Mendelian Randomization to hundred of thousands of phenotypes, making this study the largest of its kind. We have identified causal and protective factors for celiac disease, recapitulating knowledge from epidemiological studies and also highlighting new key player. We expect that application to other diseases can bring new insights in the understanding of pathophysiology as we well as of biological mechanism, especially as more genome-wide association studies on -omics measurements will be available in the future.

~~with literature~~