**Supplementary discussion: Meta-Analysis**

 A series of twelve meta-analyses of the three individual AIDs with the four individual NHL subtypes demonstrated seven regions which passed a genome-wide threshold of significance in the meta-analysis, which would not have been discovered in analysis of the individual diseases (Table 3). Effect sizes are modest and total risk explained is low, however, the genes in these regions are worth discussion.

 From the CLL and MS meta-analysis, rs140522 is in the 5' untranslated region of *ODF3B*, and rs6793295 is in the *LRRC34* gene, which were identified in recently published meta-analyses of multiple CLL GWAS (Law, et al., 2017) and MS GWAS (International Multiple Sclerosis Genetics Consortium, 2011) (Patsopoulos, et al., 2017). (Note: in that 2011 study (2), the SNP reached a p-value of 10-6, but additional validation targeting this SNP was performed in that study.

 From the DLBCL and MS meta-analysis, rs2425752 is in the *NCOA5* gene, a nuclear receptor coactivator. This SNP has also been reported in the latest MS meta-analysis (Patsopoulos, et al., 2017). The gene is reported in solid cancers such as hepatocellular carcinoma (Liu, et al., 2017), luminal breast cancer (Ye, Huang, & Luo, 2017), squamous cell carcinoma (Chen, et al., 2014), and in the Hodgkin lymphoma versus MS meta analysis (Khankhanian, et al., 2016).

 From the CLL and RA meta-analysis, rs3731714 lies on an intron of *CASP10*, a member of the cysteine-aspartic acid protease family, a cascade of enzymes which play a central role in the execution-phase of apoptosis. An ENCODE query (ENCODE 2017 -- https://www.encodeproject.org/) revealed significant DNase enrichment in multiple blood and small intestinal cell lines and evidence for altered motifs, including multiple forkhead box binding motifs. CHiP-seq data from ENCODE demonstrated binding of *GATA1*, a hematopoiesis-associated transcription factor, in peripheral blood-derived erythroblasts. Further, rs3731714 has been associated with *CASP10* expression in esophagus mucosa (Consortium, 2015). Mutations in *CASP10* have been associated with autoimmune lymphoproliferative syndrome (ALPS) type II(Wang, et al., 1999). Previous candidate gene studies have suggested that common variants in *CASP10* may be associated with NHL (Lan, et al., 2007) and gastric cancer (Hyland, et al., 2014). Other genes in the region include *PPIL3* and *CFLAR*. *PPIL3* (Peptidylprolyl isomerase like 3) encodes a member of the cyclophilin family. Cyclophilins catalyze the cis-trans isomerization of peptidylprolyl imide bonds in oligopeptides and are thought to act either as catalysts or as molecular chaperones in protein-folding events. *CFLAR* (CASP8 and FADD like apoptosis regulator) encodes a protein that is a regulator of apoptosis and is structurally like *CASP8*; however, the encoded protein lacks caspase activity. Rs3731714 has been associated with *PPIL3* expression in lymphoblastoid cell lines (Lappalainen, et al., 2013), peripheral blood monocytes (Zeller, et al., 2010) and with *CFLAR* expression in blood (Fehrmann, et al., 2011). Thus, the observed association between rs3731714 and the CLL-RA phenotype raises an intriguing possibility for a single allele to be associated with multi-genic consequences resulting in failure of apoptosis of leukocytes.

 From MZL and RA, rs16947122 is in the intronic region of *FBXW8* (F-box and WD repeat domain containing 8), which belongs to the Fbw class in the f-box protein family. The F-box proteins function in phosphorylation-dependent ubiquitination and antigen processing. *FBXW8* has also been reported to play an essential role in cancer cell proliferation through proteolysis of cyclin D1(Okabe, et al., 2006). Association with disease endpoints have been reported with this SNP; however, *FBXW8* along with its adjacent genes, *HRK* and *TESC*, were recently suggested to be related to cognition and psychoses (Bulayeva, et al., 2015).

 Also from MZL and RA, a group of three SNPs (rs1364229, rs7192064, rs2131402) are found in a gene desert, 500K base pairs upstream from the *CDH8* gene, and over 2M base pairs from the next closest documented human gene. These do not seem to be on any obvious regulatory region (ENCODE 2017 -- https://www.encodeproject.org/ ; and UCSC genome browser, regulatory tracks, 2017 -- https://genome.ucsc.edu/). A PubMed search returned no results for these SNPs (PubMed 2018 -- https://www.ncbi.nlm.nih.gov/pubmed/).

 From CLL and SLE, rs1439112 resides on an intron of the *MGAT5* gene which encodes the enzyme mannosyl (alpha-1,6-)-glycoprotein beta-1,6-N-acetyl-glucosaminyltransferase V. This enzyme catalyzes the decisive step in the generation of tetra-antennary N-glycans attached to the cell surface, and of secreted glycoproteins. These are key molecules in innate as well as adaptive immunity. For example, some are implicated in the discrimination between “self” and “non-self” (Rudd, 2001). Thus, genetic variability of this enzyme could perturb glycosylation processes instrumental for maintaining immune system tolerance and recognition of foreign antigens such as cancer cells. Of interest, the glycosylation pattern of immunoglobulins contributes to their affinities for Fc and other immune receptors, linking these molecules to the pathogenesis of immune-based diseases. In a mouse model study, loss of *MGAT5* expression lowered the threshold needed for T cell activation, and *MGAT5* deficient mice presented a variety of autoimmune phenotypes (Demetriou, Granovsky, Quaggin, & Dennis, 2001). In humans, GWAS identified variants in *MGAT5* as susceptibility factors for psoriasis (Aterido, et al., 2016), and variants in this gene were associated with the plasma N-glycome (Huffman, et al., 2011). The psoriasis-associated variant impacted N-glycosylation levels as well as activity of CD8+ and CD4+ T cells (Aterido, et al., 2016). In the cancer context, *MGAT5* mRNA and glycan products are upregulated in tumor cells and correlate with poor prognosis (Taniguchi & Kizuka, 2015). *MGAT5* knockout mice showed reduced cancer growth and metastasis (Granovsky, et al., 2000). Blocking expression of MGAT5-modified glycans in breast cancer cell lines led to suppression of tumor progression with activation of Th1 cytokine production and macrophages (Li, et al., 2008). Additionally, rs1439112 affects binding of several transcription factors including *GATA3*(Enciso-Mora, et al.), a regulator of T-helper-Type 2 (Th2) cell development, and EP300, a histone acetyltransferase frequently mutated in lymphoma subtypes (Pasqualucci, et al., 2011). Further, the SNP is predicted to affect an enhancer region in primary B-cells as well as primary T helper memory cells.

A group four SNPs (rs10936599, rs1317082, rs13069553, and rs7621631) at the *TERC-ACTRT3-MYNN* locus were also associated in the meta-analysis of SLE versus CLL. These four SNPs are in high LD with one another (r2 ≥ 0.88 for all pairwise comparisons). This locus was associated with the risk of bladder cancer (Figueroa, et al., 2014), colorectal cancer (Houlston, et al., 2010), multiple myeloma (Chubb, et al., 2013), CLL (Speedy, et al., 2014), MGUS (Weinhold, et al., 2014), pulmonary fibrosis (Fingerlin, et al., 2013), and telomere length (Codd, et al., 2013) at genome-wide significance. Additionally, suggestive associations have been observed for multiple sclerosis (International Multiple Sclerosis Genetics Consortium, 2011) and celiac disease (Dubois, et al., 2010). Several of these variants are located with the *MYNN* (myoneurin) gene, which encodes a member of the *BTB/POZ* and zinc finger domain-containing protein family that is involved in the control of gene expression. Other genes in this region include *ACTRT3* (actin related protein, formerly *ARPM1*), *TERC* (telomerase RNA component), and *LRRC34* (leucine rich repeat containing 34). *TERC* is an attractive biological candidate due to its role in telomere maintenance. Telomerase is a ribonucleoprotein polymerase that maintains telomere ends by the addition of the telomere repeat TTAGGG. The enzyme consists of a protein component with reverse transcriptase activity and a RNA component, encoded by *TERC*, that serves as a template for the telomere repeat. Telomerase expression plays a role in cellular senescence, as it is normally repressed in postnatal somatic cells resulting in progressive shortening of telomeres. Deregulation of telomerase expression in somatic cells may be involved in oncogenesis. Studies in mice suggest that telomerase also participates in chromosomal repair, since *de novo* synthesis of telomere repeats may occur at double-stranded breaks. The C allele at rs10936599 was associated with increased telomere length in genome-wide association studies (from SNPedia July 2018 -- https://www.snpedia.com/), while the alternate allele was found to be the risk allele in our study. Interestingly, patients with SLE had shorter leukocyte telomere lengths than controls in cross-sectional studies (Haque, et al., 2013).

The final SNP of interest in the meta-analysis of CLL versus SLE was rs10069690, an intronic variant in the *TERT* gene (telomerase reverse transcriptase). *TERT* encodes the reverse transcriptase subunit of telomerase, hTERT. The SNP variant has been associated with CLL (Berndt, et al., 2016) (Speedy, et al., 2014) and multiple solid cancers, including breast (Haiman, et al., 2011), testicular (Turnbull, et al., 2010), ovarian (Kuchenbaecker, et al., 2015) and prostate cancer(Kote-Jarai, et al., 2011). Other variants in this region have been associated with other cancer types (Wang, et al., 2014), underscoring the importance of this region in cancer risk. The A (minor) allele of rs10069690 has been shown to result in a splice site variant of hTERT which acts as a dominant negative inhibitor of telomerase (Killedar, et al., 2015). Specifically, the alternatively spliced, INS1b, transcript does not encode the reverse transcriptase domain required for telomerase enzyme activity, but retains its ability to bind to the telomerase RNA subunit, hTR, resulting in decreased telomerase activity and telomere shortening (Killedar, et al., 2015).

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