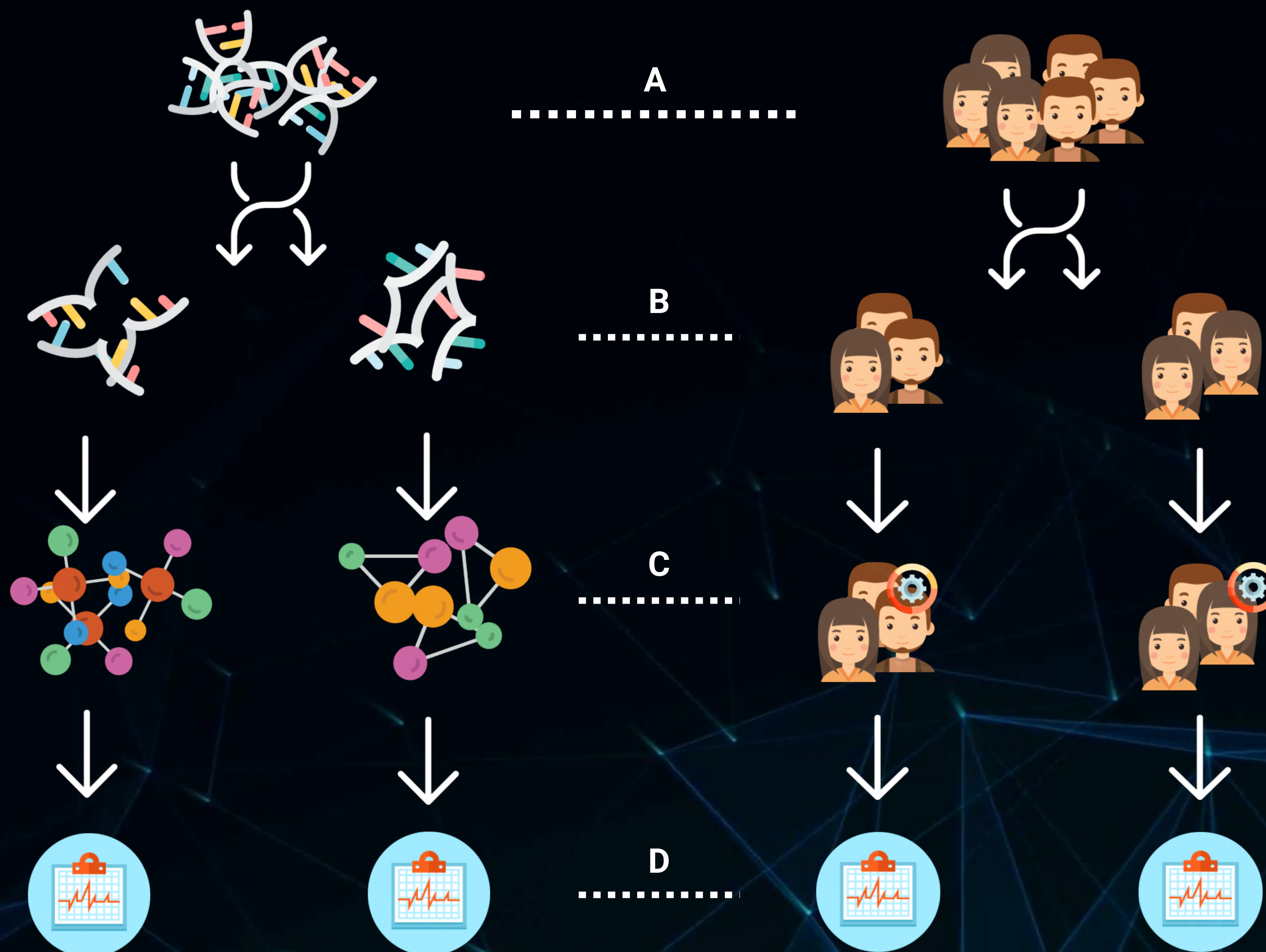


Celiac Disease Triggers

Using Mendelian Randomization to infer causality

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INTRODUCTION

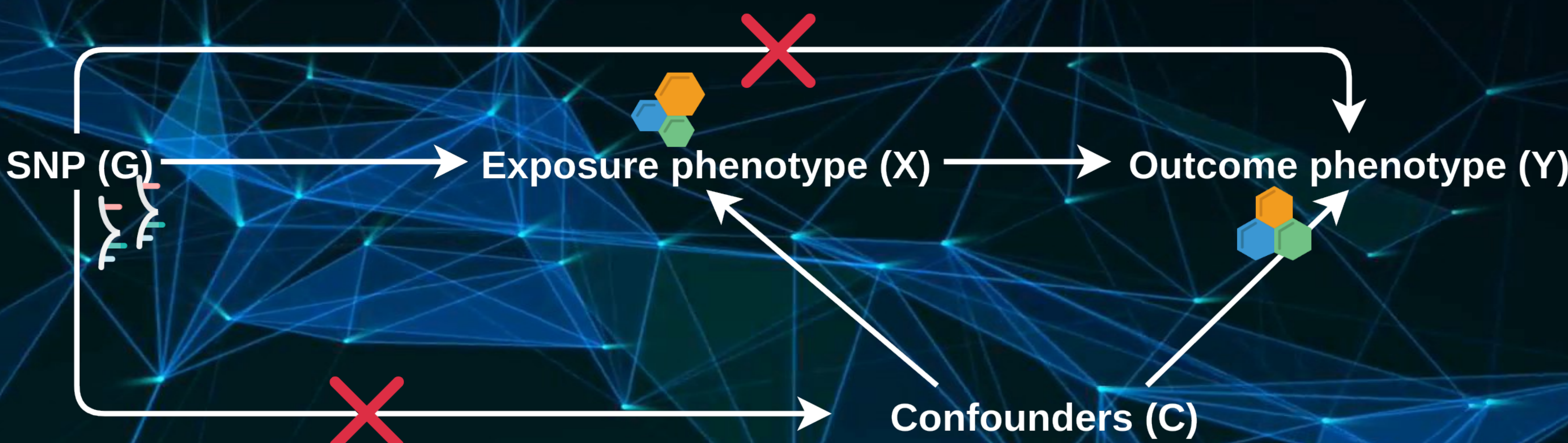
Celiac disorder affects up to two percent of the European population, and it is hereditary. People with a first-degree relative with celiac disease have 30 times higher risk of developing celiac disease. The inheritance model of celiac disease is oligogenic.^[1] In this model, HLA-DQ2 is a genetic variant in the major histocompatibility complex (MHC) region that accounts for 40% of the inheritable risk. But, this genetic variant alone is not sufficient enough to develop celiac disease. 30% of the Europeans are carriers of the variant, however 3% express celiac disease. We expect to find multiple causal or protective clinical parameters or molecular mechanisms that will be quantified to understand the impact of the causal or protective relationship, that can potentially explain what is triggering celiac disease in the 3% from the 30% of the Europeans that are carriers of HLA-DQ2.^[2]

MATERIALS AND METHODS

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

RESULTS

We identified 1133 significant ($FDR < 0.05$) clinical parameters or molecular mechanisms that cause or protect for celiac disease. For example Type 1 Diabetes (T1D), which describes the co-occurrence of T1D and celiac disease.^[6] A shared association between celiac disease and crohn's disease.^[7] The effect of eosinophils is a risk factor for celiac disease, and that lymphocytes is associated as a protective factor for celiac disease.^[8] These findings are consistent with literature.



OTHER (NON-AUTOIMMUNE) DISEASE OF DIGESTION SYSTEM

WHITE BLOODCELLS
EOSINOPHILS, LYMPHOCYTES

INFECTIONS,
ALLERGIES

OTHER AUTO-
IMMUNE DISEASES

ABNORMAL
ERYTHROPOIESIS
ANEMIA

BONE-RELATED
DISORDERS

SKIN
DISORDERS

NEUROLOGICAL
DISORDERS

REDUCED BODY
FAT/MASS

THROMBOCYTOSIS

THYROID
ABNORMALITIES

HYPERTENSION

PBMC
NATURAL KILLER CELLS, CD4+

CELIAC DISEASE

