ARTÍCULO DE MAYOR FACTOR DE IMPACTO MARZO 2014

Romanos, Jihane; Rosen, Anna; Kumar, Vinod; Trynka, Gosia; Franke, Lude; Szperl, Agata; Gutierrez-Achury, Javier; van Diemen, Cleo C.; Kanninga, Roan; Jankipersadsing, Soesma A.; Steck, Andrea; Eisenbarth, Georges; van Heel, David A.; Cukrowska, Bozena; Bruno, Valentina; Mazzilli, Maria Cristina; **Nunez, Concepcion**; Ramon Bilbao, Jose; Mearin, M. Luisa; Barisani, Donatella; Rewers, Marian; Norris, Jill M.; Ivarsson, Anneli; Boezen, H. Marieke; Liu, Edwin; Wijmenga, Cisca. *Improving coeliac disease risk prediction by testing non-HLA variants additional to HLA variants.* GUT. 63(3): 415-422 doi: 10.1136/gutjnl-2012-304110.FACTOR DE IMPACTO: **10,732**

Enlace: http://gut.bmj.com/content/63/3/415.full.pdf+html

OPEN ACCESS

ORIGINAL ARTICLE

Improving coeliac disease risk prediction by testing non-HLA variants additional to HLA variants

Jihane Romanos,[1,2] Anna Rosén,[3,4] Vinod Kumar,[1] Gosia Trynka,[1,5] Lude Franke,[1] Agata Szperl,[1] Javier Gutierrez-Achury,[1] Cleo C van Diemen,[1] Roan Kanninga,[1] Soesma A Jankipersadsing,[1] Andrea Steck,[6] Georges Eisenbarth,[6] David A van Heel,[7] Bozena Cukrowska,[8] Valentina Bruno,[9] Maria Cristina Mazzilli,[10] Concepcion Núñez,[11] Jose Ramon Bilbao,[12] M Luisa Mearin,[13] Donatella Barisani,[14] Marian Rewers,[6] Jill M Norris,[15] Anneli Ivarsson,[3] H Marieke Boezen,[16] Edwin Liu,[6] Cisca Wijmenga,[1] PreventCD Group

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/gutjnl-2012-304110).

For numbered affiliations see end of article.

Correspondence to
Professor Cisca Wijmenga, Department of Genetics, University Medical Centre Groningen, PO Box 30001, Groningen 9700 RB, The Netherlands; c.wijmenga@umcg.nl

JR and AR contributed equally to this article.

HMB, EL, CW jointly directed

ABSTRACT

Background The majority of coeliac disease (CD) patients are not being properly diagnosed and therefore remain untreated, leading to a greater risk of developing CD-associated complications. The major genetic risk heterodimer, HLA-DQ2 and DQ8, is already used clinically to help exclude disease. However, approximately 40% of the population carry these alleles and the majority never develop CD.

Objective We explored whether CD risk prediction can be improved by adding non-HLA-susceptible variants to common HLA testing.

Design We developed an average weighted genetic risk score with 10, 26 and 57 single nucleotide polymorphisms (SNP) in 2675 cases and 2815 controls and assessed the improvement in risk prediction provided by the non-HLA SNP. Moreover, we assessed the transferability of the genetic risk model with 26 non-HLA

Significance of this study

What is already known on this subject?

- HLA-DQ2 and DQ8 provide the highest genetic risk for CD. However, these genes are present in about 40% of the population, and only a subset will develop disease. Therefore, screening for HLA-DQ2 and DQ8 alleles is helpful only to identify those at extremely low risk for CD.
- Current recommendations are to perform periodic screening of certain high-risk groups for CD, such as first-degree relatives and those with type 1 diabetes. However, the degree of risk is not uniform among all of these groups.
- Current methods of genetic testing are