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Background

Crohn's disease (CD) is associated with elevated anti-glycans antibody response in 60% of CD patients, and 25% of healthy first-degree relatives (HFDRs), suggesting a genetic influence for this humoral response. In mice, anti-glucan antibody response depends on the NLRP3 inflammasome. Here, we explored the effect of mutated *CARD8*, a component of the inflammasome, on anti-glycans antibody response in human.

Methods

The association between p.C10X mutation (rs2043211) of the *CARD8* gene and the levels of anti-glycans antibody response was examined in 39 CD families. The family-based QTDT association test was used to test for the genetic association between *CARD8* p.C10X mutation and anti-glycan antibodies in the pedigrees. The difference in antibody responses determined by ELISA was tested in a subgroup of CD probands (one per family) and in a subgroup of HFDRs using the Wilcoxon Kruskal Wallis non-parametric test.

Results

The QTDT familial transmission tests showed that the p.C10X mutation of *CARD8* was significantly associated with lower levels of antibody to mannans and glucans but not chitin ($p=0.024$, $p=0.0028$ and $p=0.577$, for ASCA, ALCA and ACCA, respectively). These associations were independent of *NOD2* and *NOD1* genetic backgrounds. The p.C10X mutation significantly associated or displayed a trend toward lower ASCA and ALCA levels ($p=0.038$ and $p=0.08$, respectively) only in the subgroup of CD probands. Such associations were not significant for ACCA levels in both subgroups of CD probands and of HFDRs.

Conclusion

Our results show that ASCA and ALCA but not ACCA levels are under the influence of *CARD8* genotype. Alteration of CARD8, a component of inflammasome, is associated with lower levels of antibodies directed to mannans and glucans at least in CD patients.