P4.14

Prevalence of the common coding variant rs2241880 of the ATG16L1 gene in Maltese Crohn's disease patients

N. Azzopardi[1], P. Ellul[1], C. Saliba[2], G. LaFerla[3], G. Grech[2]

[1]Department of Gastroenterology , Mater Dei Hospital, Msida [2]Department of Pathology, University of Malta, Msida,

[3]Department of Surgery, University of Malta, Msida; Department of Surgery, Mater Dei Hospital, Msida

Introduction: In Crohn's disease the ATG16L1 (rs2241880) polymorphism affects Paneth cells and impairs autophagosome formation specifically after activation of nucleotide-binding oligomerisation domain 2(NOD2). Studies from Europe, Australia and New Zealand1 have shown an increased frequency of the ATG16L1 rs2241880 SNP allele in Crohn's disease patients versus controls while studies from Korea, Japan and East Asia revealed no positive association of this gene with Crohn's disease.

Aims and methods: We have studied the prevalence of the ATG16L1 (rs2241880) polymorphism among Maltese Crohn's disease patients and age-matched controls and the association between the ATG16L1 genotype and phenotype of these patients. 83 patients diagnosed with Crohn's disease through histological, radiological and endoscopic findings and 91 controls were recruited. Genotyping for the common coding variant rs2241880 of the ATG16L1 gene involved:

- DNA extraction (whole blood)
- Gradient Polymerase Chain Reaction (PCR)
- PCR
- Quantitative PCR (qPCR) and High Resolution Melt (HRM) for exon 9 (Thr300Ala) of the ATG16L1 gene with rs2241880 primers using 5x Hot FirePol® EvaGreen® qPCR Mix Plus
- Restriction Fragment Length Polymorphism (RFLP) with the SfaNI/LweI enzyme (to confirm the HRM results)

Results: 7% of the Crohn's population were homozygous, 53% were heterozygous and 40% were wild type for the rs2241880 variant versus 14%, 50% and 36% of the control population. There was no statistical difference in the prevalence of the rs2241880 mutation between control and Crohn's disease populations ($\chi^2 p$:0.328). The phenotypes of patients with different ATG16L1 polymorphisms were then compared. There was no statistically significant difference in gender ($\chi^2 p$:0.623), disease location (Fisher's exact test p:0.885), disease type (Fisher's test p:0.205), and patients on azathioprine ($\chi^2 p$: 0.394) or on biologicals ($\chi^2 p$: 0.437). Only the age at diagnosis was significantly different (Fisher's test p: 0.047) between the 3 subgroups.

Conclusion: Susceptibility genes differ among Crohn's disease populations in different geographical regions. In Malta there was no significant difference in the prevalence of ATG16L1 mutant genes between Crohn's and control populations. A similar pattern to that found among European populations would be expected in Malta, though a comparison with North African populations would be interesting to carry out.