2.22 An Investigation of Rare Genetic Variants for COPD: Evaluating the Mmalton Mutation

[1] Mohamed Abdulkadir

[1] Royal College of Surgeons in Ireland, Dublin, Ireland

Background: Alpha-1 antitrypsin deficiency (AATD) is a genetic disorder caused by mutations in the SERPINA1 gene, resulting in a reduced level or function of the alpha-1 antitrypsin (AAT) protein. M_{malton} is an underdiagnosed mutation causing severe AATD that manifests with emphysema and liver cirrhosis This article aims to provide a comprehensive overview of M_{malton}, its molecular mechanisms, clinical implications, and diagnostic considerations.

Methods: Blood samples (n = 12) were collected from individuals with low AAT levels showing an MM phenotype on isoelectric focusing (IEF). An assay for the rapid detection of M_{malton} was optimised using PCR-based genotyping and patient data were extracted from the national AATD registry and medical charts in Beaumont Hospital, creating a case study describing the clinical consequences of M_{malton}.

Results: Using the new assay, a novel case of M_{malton} heterozygote was diagnosed in a patient who showed a normal MM phenotype IEF. (Figure 1)

Conclusion: Despite increasing awareness for testing at-risk populations for AATD, there is a discrepancy between identified cases and expected cases within the population due to the multi-layered approach required to achieve a conclusive diagnosis. The case study and the table showing the various genotypes outlined a correlation between having M_{malton} and developing pulmonary and hepatic complications.

Disclosures:

Funding: The authors declare that there was no funding granted

Conflict of Interest: The authors declare that they have no conflict of interest.

Figure 1. M_{malton} genotype assay melting peaks.

Using the newly-optimised assay, a novel case of M_{malton} heterozygote (Genotype: M/M_{malton}) was identified using PCR-based genotyping.