

#1498 - No Preferences

## Novel SERPING1 Mutations in Bulgarian Patients revealed by a Targeted Next Generation Sequencing platform

Dermatology / Hereditary angioedema

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### Background

Hereditary angioedema (HAE) is a rare autosomal dominant disease characterized by swelling of the face, lips, tongue, larynx, genitalia, or extremities, with abdominal pain caused by intra-abdominal edema. HAE is caused by mutations affecting the C1 inhibitor gene (SERPING1), resulting in low levels of C1 inhibitor (Type I HAE) or normal levels of ineffective C1 inhibitor (Type II HAE).

### Method

Genotyping was performed by means of a targeted next generation sequencing platform of the SERPING1 in 30 C1-INH-HAE type 1 patients, belonging to 13 HAE families. The newly developed and validated custom NGS platform targets the entire 11q12-q13.1 loci, including the promoter, coding, intron-exon boundary as well as intronic regions of the SERPING1 gene. Complement fractions and clinical symptoms were analyzed in relation to revealed gene mutations. Consent was obtained from all of the patients.

### Results

This is the first genetic study of the Bulgarian HAE patients. Genetic defects were identified in 10 HAE families are: 3 nonsense, 2 splice-site defects, 2 frameshift mutations, 1 indel non frameshift, 1 missense, and 1 large deletion of exon 4. Novel mutations, not previously reported in human gene mutation databases were discovered, and were predicted to be deleterious due to the expected effect on DNA transcript and protein.

### Conclusion

We identified 10 mutations of the SERPING1 gene in 13 HAE Type I families from the Bulgarian population (comprising 50% of the diagnosed HAE families in the country), revealing novel mutations, causative for C1-INH deficiency. A recently developed and validated targeted NGS platform was used for SERPING1 genotyping, presenting excellent potential for the future of HAE genetic diagnostics.