Clin Lymphoma. 2005 Mar;5(4):253-6.

Potential impact of a single nucleotide polymorphism in the hyaluronan synthase 1 gene in Waldenstrom's macroglobulinemia.

Adamia S, Treon SP, Reiman T, Tournilhac O, McQuarrie C, Mant MJ, Belch AR, Pilarski LM.

Departments of Oncology and Medicine, University of Alberta and Cross Cancer Institute, Edmonton, Alberta T6G 1Z2, Canada.

The hyaluronan synthase 1 (HAS1) gene encodes a plasma membrane protein that synthesizes hyaluronan, an extracellular matrix molecule. Previously, in patients with Waldenstrom's macroglobulinemia (WM), we detected upregulation of HAS1 transcripts and identified aberrant splice variants of this gene. Aberrant splicing of HAS1 results from activation of cryptic splice sites. In turn, activation of cryptic donor and acceptor splice sites can be promoted by mutations occurring upstream of these sites and/or at the branch point of slicing. We measured the frequency of the HAS1 833A/G polymorphism (ie, single-nucleotide polymorphism; SNP) in patients with WM and healthy donors. Additionally, HAS1 gene expression was evaluated in the same group of patients. Our observations so far suggest that HAS1 833A/G SNPs contribute to aberrant splicing of this gene; this idea is supported by the fact that 833A/G SNP is located on an exonic splicing enhancer motif. Based on the results obtained thus far, we speculate that individuals with HAS1 833G/G genotype are predisposed toward aberrant HAS1 splicing and expression of HAS1 variants, resulting in an enhanced risk of developing WM. Study of a larger group of patients and healthy donors is needed to confirm these speculations and to evaluate the prognostic significance of these findings.