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Topic of Research: Identification and characterization of alternatively spliced novel serpin isoforms

Abstract

Serpins are the serine protease inhibitors which are known to regulate the functions of serine proteases. The current thesis is based on the identification of alternatively spliced novel isoforms of serine protease inhibitors. In this study with the help of combined approach of computational tools and molecular biology techniques, we have successfully identified novel isoforms in human α-1-Antitrypsin, α-1-Antichymotrypsin, Protein C inhibitor and Neuroserpin.

In neuroserpin, we have identified two novel isoforms HNS-N and HNS-T. HNS-N isoform was confirmed in brain and was generated as a result of substitution of last coding exon with a novel exon N. While on the other hand, novel isoform HNS-T was confirmed in both brain and liver and produced as a result of splicing of known coding exon E7 with novel exon E7' resulting in elimination of coding exons E8 and E9. In addition to HNS-N and HNS-T, two novel shorter transcripts of Neuroserpin (HNS-S1 and HNS-S2) were also found. In α-1-antitrypsin, we have found a novel isoform (AAT-T) in liver which lacks amino acids encoded by coding exon E4 and thus reactive centre loop. We have also found two novel isoforms in α-1-antichymotrypsin (ACT). In ACT, one novel isoform (ACT-N) was confirmed in both brain and liver and has a different N-terminal due to substitution of first coding exon. While on the other hand, ACT-T lacks the amino acids encoded by coding exon E4 due to splicing of E3 with E3' and thus lacks reactive centre loop. In Protein C Inhibitor, we have identified one novel isoform PCI-N which was found to have a different N terminal and was larger as compared to its known isoform due to splicing of novel exon N with the first coding exon. The novel isoform PCI-N was confirmed in both liver and kidney. All these isoforms need to be characterized in terms of structure-function relationship for its better understanding.