# IMPACT OF SYNONYMOUS MUTATIONS ON RNA SPLICING

Although synonymous mutations have long been considered functionally neutral, this view has been progressively challenged over the past two decades. It is now well established that synonymous variants can affect gene expression by altering splicing regulatory elements, particularly when they occur near exon–intron boundaries or within exonic splicing enhancers and silencers. Several individual examples have demonstrated that such variants can lead to aberrant splicing and disease.

What  is less clear, however, is the extent to which this phenomenon operates at a genome-wide level and how frequently synonymous substitutions contribute to functional and potentially pathogenic effects. Srinivasan et al. (1) address this gap by systematically investigating the impact of synonymous variants on splicing, showing that their contribution is far more widespread than previously appreciated. These findings challenge the traditional view of synonymous mutations as largely neutral and underscore the need to reconsider their role in the interpretation of variants and in the genetics of the disease.

1. https://pubmed.ncbi.nlm.nih.gov/41436921/