FUNCTIONAL SIGNIFICANCE OF TRANSCRIPTS EDITING BY DOUBLE-STRANDED RNA ADENOSINE DEAMINASES

Summary

Adenosine deaminases that act on RNA (ADARs) convert adenosine to inosine in double-stranded regions of RNA via hydrolytic deamination. As inosines are recognized as guanosines during translation this editing event can lead to a codon exchange in the edited mRNA. The amino acid changes introduced by this A-to-I RNA editing result in significant alterations in the physiological properties of gene products. For instance, editing of the "Q/R" site of AMPA GluR-B subunit dramatically decreases the Ca+2 permeability of the channel. Dramatic changes in the G-protein coupling efficiency of 5-HT2CR as well as in the rates of KV2K1 channel closure have been reported to be consequences of A-to-I RNA editing also. In addition, creation of an alternative splice acceptor site via editing of its own mRNA by ADAR2 has been reported. The A-to-I RNA editing mechanism requires: (1) a double-stranded RNA (dsRNA) structure, usually formed between the exonic editing site and a downstream intron sequence and (2) dsRNA-specific adenosine deaminases. The members of this ADAR gene family appear to share structural similarity, containing two to three repeats of dsRNA-binding domains and a separate deaminase or catalytic domain. Defects in ADAR are a cause of some diseases, for example dyschromatosis symmetrica hereditaria.