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ABSTRACT BOOK

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Inhibition of FTSJ1, a tryptophan tRNA-specific 2'-O-methyltransferase as possible mechanism to readthrough premature termination codons (UGAs) of the CFTR mRNA

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Cystic Fibrosis (CF) is an autosomal recessive genetic disease caused by mutations in the CFTR gene, coding for the CFTR chloride channel. About 10 % of the mutations affecting the CFTR gene are "stop" mutations, which generate a Premature Termination Codon (PTC), thus resulting in the synthesis of a truncated CFTR protein. A way to bypass PTC relies on ribosome readthrough, that is the capacity of the ribosome to skip a PTC, thus generating a full-length protein. "TRIDs" are molecules exerting ribosome readthrough and for some of them the mechanism of action is still under debate. By in silico analysis as well as in vitro studies, we investigate a possible mechanism of action (MOA) by which our recently synthesized TRIDs, namely NV848, NV914 and NV930, could exert their readthrough activity. Our results suggest a likely inhibition of FTSJ1, a tryptophan tRNA-specific 2'-O-methyltransferase. In addition, we report that our TRIDs do not exert readthrough on natural termination codons.