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# Aminoglycoside-mediated promotion of translation readthrough occurs through a non-stochastic mechanism that competes with translation termination.

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## Author information

### Abstract

Attempts have been made to treat nonsense-associated genetic disorders by chemical agents and hence an improved mechanistic insight into the decoding of readthrough signals is essential for the identification and characterisation of factors for the treatment of these disorders. To identify either novel compounds or genes that modulate translation readthrough, we have employed dual reporter-based high-throughput screens that use enzymatic and fluorescence activities and screened bio-active NINDS compounds (n = 1000) and siRNA (n = 288) libraries. Whilst siRNAs targeting kinases such as CSNK1G3 and NME3 negatively regulate readthrough, neither the bio-active NINDS compounds nor PTC124 promote readthrough. Of note, PTC124 has previously been shown to promote readthrough. Furthermore, the impacts of G418 on the components of eukaryotic selenocysteine incorporation machinery have also been investigated. The selenocysteine machinery decodes the stop codon UGA specifying selenocysteine in natural selenoprotein genes. We have found that the eukaryotic SelC gene promotes the selenocysteine insertion sequence (SECIS)-mediated readthrough but inhibits the readthrough activity induced by G418. We have previously reported that SECIS-mediated readthrough at UGA codons follows a non-processive mechanism. Here, we show that G418-mediated promotion of readthrough also occurs through a non-processive mechanism which competes with translation termination. Based on our observations, we suggest that proteins generated through a non-processive mechanism may be therapeutically beneficial for the resolution of nonsense-associated genetic disorders.

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