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Minireview

Transglycosylation: A mechanism for RNA modification (and editing?)

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Abstract

The vast majority of the ca. 100 chemically distinct modified nucleosides in RNA appear to arise via the chemical transformation of a genetically encoded nucleoside. Two notable exceptions are queuosine and pseudouridine, which are incorporated into tRNA via transglycosylation. Transglycosylation is an extremely efficient process for incorporating highly modified bases such as queuine into RNA. Transglycosylation is also a requisite process for "isomerizing" an N-nucleoside into a C-nucleoside as is the case for pseudouridine formation. Finally, transglycosylation is an attractive possibility for certain RNA editing events (e.g., pyrimidine to purine conversions) that cannot occur via the known, more straightforward enzymatic reactions (e.g., deaminations). This review discusses what is known about the mechanisms of transglycosylation for the queuine and pseudouridine RNA modifications and will speculate about a potential role for transglycosylation in certain RNA editing events.

Keywords: RNA; Modification; Editing; Pseudouridine; Queuosine; Transglycosylation

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1. Introduction

One characteristic of all RNAs is the occurrence of modified nucleosides throughout the primary structure. Modified nucleosides are incorporated into the polynucleotide chain by specific RNA-modifying enzymes during all stages of the post-transcriptional processing of nascent RNA transcripts. To date, ca. 100 chemically distinct nucleosides have been identified, spanning a wide range of chemical complexity [1]. "Simple" modifications (e.g., methylations, thiolations, etc.) are generally the result of a single enzymatic activity, while the more "complex" modifications are characterized by the presence of multiple modifications (e.g., methylation and thiolation) or the requirement for multi-step biosynthetic pathways to achieve the desired transformation. With few exceptions, modified nucleosides arise from the chemical transformation of a genetically encoded nucleoside [2]. One notable exception is queuosine, which is incorporated into tRNA via transglycosylation (in this case, cleavage/reformation of the glycosidic bond, exchanging one base for another). Pseudouridine is also introduced into various RNAs via intramolecular transglycosylation. We will review what is known about the mechanisms of transglycosylation for these two RNA modifications and will speculate about a potential role for transglycosylation in certain RNA editing events.

2. tRNA-guanine transgylcosylase

Of the known tRNA modifications, queuosine (Q, 7-(((4,5-*cis*-dihydroxy-2-cyclopenten-1-yl)amino)methyl)-7-deazaguanosine) and archaeosine (G^+, 7-formamidino-7-deazaguanosine) represent two of the most complex that have been identified thus far (Fig. 1). Both feature a heterocyclic base moiety that is structurally unique from other nucleosides [3,4]. In each case, the nucleosides consist of neither a purine nor pyrimidine but rather a pyrrolopyrimidine heterocyclic backbone. Furthermore, each of these modifications possesses an exocyclic side-chain extending from the 5-position (analogous to the purine 7-position) carbon of the pyrrolopyrimidine ring. Archaeosine appends an amidino functionality at this position, while queuosine possesses a much more elaborate aminomethyl cyclopentenyl diol side-chain (Fig. 1).

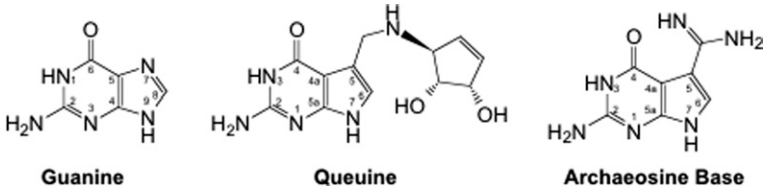

Fig. 1. Structures of guanine, queuine, and archaeine (the base of archaeosine). Note that the N^7 of the purine ring system corresponds to the C^5 of the pyrrolopyrimidine ring system.