KEMIJSKI INŠTITUT

Vabilo na Preglov kolokvij / Invitation to the Pregl colloquium

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Velika predavalnica Kemijskega inštituta /
Great Lecture Hall
National Institute of Chemistry
Hajdrihova 19, Ljubljana, Slovenia

Synthetic RNA Chemistry – Ribozymes and Riboswitches

Methylation is a prevalent post-transcriptional modification encountered in coding and non-coding RNA. For RNA methylation, cells use methyltransferases and small organic substances as methyl-group donors, such as *S*-adenosylmethionine (SAM). SAM and other nucleotide-derived cofactors are viewed as evolutionary leftovers from an RNA world, in which riboswitches have regulated, and ribozymes have catalyzed essential metabolic reactions. We disclose the thus far unrecognized direct link between a present-day riboswitch and its inherent reactivity for site-specific methylation.[1] The key is O^6-methyl pre-queuosine (m^6preQ_1),[2] a potentially prebiotic nucleobase which is recognized by the native aptamer of a $preQ_1$ class-I riboswitch. Upon binding, the transfer of the ligand's methyl group to a specific cytidine occurs, installing 3-methylcytidine (m^3C)[3] in the RNA pocket under release of pre-queuosine ($preQ_1$). Our finding suggests that nucleic acid-mediated methylation is an ancient mechanism that has offered an early path for RNA epigenetics prior to the evolution of protein methyltransferases. Furthermore, our findings may pave the way for the development of riboswitch-descending methylation tools based on rational design as a powerful alternative to *in vitro* selection approaches.

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Vljudno vabljeni / Kindly invited