FASSBERG SEMINAR SERIES

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Ribozymes meet RNA modifications

Nearly all classes of RNA are decorated with post-transcriptional modifications, which play important functional roles in all kingdoms of life. Methylated nucleotides belong to the most evolutionary conserved RNA modifications that could have influenced the evolutionary path of catalytic RNA. Primordial ribozymes may have installed modifications to enhance catalysis, or mediated their removal to facilitate replication and storage of genetic information. In vitro evolution in the laboratory offers the possibility to reconstruct analogues of such potentially extinct ribozymes.

Using in vitro selection from random nucleic acid libraries, we identified RNA-cleaving DNA enzymes that specifically recognize modified adenosines, including N^6-methyladenosine (m^6A) and N^6-isopentenyladenosine (i^6A), and strongly discriminate modified from unmodified RNA. To find nucleic acid enzymes that install RNA modifications, we took advantage of a selection strategy that resulted in ribozymes for RNA-catalysed labelling of RNA, by attachment of fluorescent ATP or re-purposed antiviral nucleotide analogues at internal ribose hydroxyl groups. We followed a similar route to enrich RNAs that catalyse the site-specific installation of RNA modifications on the nucleobase. This presentation will discuss the recently discovered methyltransferase ribozyme that catalyses the site-specific installation of 1-methyladenosine (m^1A) in a substrate RNA, utilizing O^6-methylguanine (m^6G) as a small-molecule cofactor. The ribozyme shows a broad RNA sequence scope, as exemplified by site-specific adenosine methylation in tRNAs. These findings provide fundamental insights into RNA's catalytic abilities, serve synthetic tools to install m^1A in RNA, and may pave the way to *in vitro* evolution of other methyltransferase and demethylase ribozymes.

Host: Marina Rodnina

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zoom access data will be mailed before the seminar!