Dinucleoside Polyphosphate RNAs as Substrates for Decapping Enzyme DXO

Buchova, Zuzana (School: Gymnazium Praha 6 Arabska 14)

RNA has numerous roles in cells and its information is encoded by its sequence, secondary structure and chemical modifications. The least explored RNA modifications are noncanonical 5' RNA caps, such as Nicotinamide adenine dinucleotide (NAD) or dinucleoside polyphosphates (NpnNs). In the laboratory, where I worked on my project, new 5' RNA cap Ap2A was discovered in mammalian tissue cell culture employing LC-MS technique. It was also observed that the concentration of Ap2A-RNA increased under stress conditions. The role, biosynthesis and metabolism of noncanonical RNA caps still remain unexplored. To understand the role of RNA caps, RNA processing enzymes should be studied as well. In my work, I focus on decapping enzyme DXO and its unknown activity. It was described that DXO is cleaving the entire NAD moiety from RNA. I revealed that DXO is also a decapping enzyme for newly discovered eukaryotic Ap2A-RNA. Moreover, this enzyme cleaved various noncanonically capped RNA, showing a preference for diphosphates and tetraphosphates (Gp2A-, Ap2G-, Gp2G-, Gp4A-, Ap4G-, Ap4A-, Gp4G-). This finding suggests that human RNA may contain other unknown caps in addition to the canonical 7-methyguanosine (m7G) structure. Moreover, DXO may regulate concentration of Ap2A-RNA under the stress. In general, noncanonical RNA caps may play some role in biochemical and immunological processes in cells and understanding this role could bring new options in therapy for viral, bacterial and oncological diseases.