Beyond AGCU: Roles of Modified Nucleotides in Conformational Switching of RNA

Helix 69 (H69) from 23S rRNA is a key component of the intersubunit bridge B2a in ribosomes. The sequence, secondary structure, and pseudouridylation of H69 are highly conserved across phylogeny. Three pseudouridine residues are located in the loop region at positions 1911, 1915, and 1917 (E. coli numbering). NMR studies on oligonucleotides with and without these modifications reveal their influence on H69 structure. Chemical probing of bacterial ribosomes also reveals structural differences between modified and unmodified rRNA, which correlates with growth advantages of wild-type over pseudouridine-deficient strains. Helix 69 plays important functional roles through conformational adaptability involving association with various factors. The structures of oligonucleotides representing H69 can also be altered by changes in magnesium concentration, pH, or the presence of small molecules. Results from model systems extend our knowledge of the structural variability of H69 under different solution conditions, enhance our understanding of the functional roles of pseudouridine, and allow for the development of ligands that target H69 as potential antibiotics.

Next Generation Sequencing – A Powerful Tool for Identification of RNAs in Disease

The application of next generation sequencing has revolutionized our understanding of the functional organization of the human genome. We have applied NGS to identify non-coding RNAs expressed in breast cancer (BC), and identified a non-canonical pathway for production of microRNA-like molecules and also several hundred new human genes, among them one encoded from one intron of the ERBB2/Her2 oncogene. Since Her2 is one of the most important BC markers, our results may lead to a revision of important aspects in diagnostics and treatment of the disease.