

CHEMICAL ENGINEERING

SEMINAR SERIES



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Genomic aptamers and ribozymes: From discovery to biological functions

ABSTRACT: Ribonucleic acids are central components of many biological regulatory and catalytic complexes. We use bioinformatics and in vitro selection experiments to discover functional RNAs in a wide variety of genomes and thus find structured macromolecules that act as catalysts (ribozymes) or highly specific binders (aptamers) that may represent novel modes of gene regulation. Using secondary structure-based bioinformatics searches, we previously found that the hepatitis delta virus (HDV) and hammerhead ribozymes are widely distributed throughout nature. To date we have confirmed in vitro the catalytic activity of these ribozymes in many organisms, where the HDV ribozymes are often present in multiple copies and sequence families. The biological functions of these ribozymes include 5' processing of retrotransposons and other repeats, and likely translation initiation.

To discover new aptamers in the human genome, we have again used structure-based searches for known aptamer folds and an in vitro selection with ATP as target. We have identified several aptamers in the human genome, and single examples in mouse, frog and a bacterium. Interestingly, the ones identified using in vitro selection, which is unbiased with respect to the structure of the functional RNA, fold into the same fold as had previously been discovered in vitro using synthetic libraries. Two of the human aptamers map to introns and appear to sense ATP through a kinetic, rather than equilibrium, mechanism. Current efforts aim to test the hypothesis that the aptamers are ATP-binding domains of human riboswitches.

Overall, our aim is to describe the distribution of ribozymes and aptamers and establish their biological functions, especially in higher

RECEPTION 3:30 • LECTURE 4:00 – 5:00
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