Ribonucleic acid or RNA are biological molecules that perform many functions. A common RNA function is to carry the genetic message (mRNA) for protein synthesis by translation. The process of translation can be regulated in many ways. Elements of the mRNA known as untranslated regions (UTRs) which flank the protein encoding region control the rate of translation. In eukaryotes, mRNA translation begins with the recognition of a 5´cap and scanning 5´UTR until the start codon of the protein coding sequence is detected. This is known as cap-dependent translation.

In many cancers, overall rate of translation is reduced. However, cancer cells themselves continue to proliferate and grow, requiring active protein synthesis. To overcome the reduced rate of cap-dependent translation, some cancer genes have evolved to include an RNA element in the 5´UTR known as an IRES (Internal Ribosome Entry Site) which directly recruits the ribosome for translation, skipping cap-dependent regulation. This is cap-independent translation. Like other regulatory RNA, IRES function depends on its structure.

I am interested in investigating changes in 5´UTR RNA structure that may indicate the mechanism for the switch or transition between cap-dependent and cap-independent translation. We will investigate the mRNA 5´UTR of the tumor suppressor p53, which is known to contain IRES elements. By inducing certain known triggers for cap-independent translation we anticipate to detect changes in RNA secondary structure, and we will correlate these changes with changes cellular mRNA levels and translation efficiency.

Activating wild-type p53 mRNA cap-independent translation is of particular therapeutic importance in certain pediatric cancers, breast cancer, and prostate cancer.