

Title: Tissue Specific Ribosomes: in health and cancer

Abstract: The human ribosome is composed of two ribosomal RNA subunits (60S and 40S) and 80 structural ribosomal proteins (RPs) and usually viewed as invariant across tissue types. However, growth data from a genome-wide yeast homozygous deletion across environments showed that the ribosome is adaptive, with certain RP proteins essential in some environments but not others. Analysis of Ribosomal Protein (RP) levels in normal and cancer samples and cell lines from large mRNA, copy number variation and ribosome protein profiling datasets showed highly consistent tissue specific RP mRNA signatures and multiple RP mRNA-subtypes in cancers, with significant survival and genomic differences. In cancer cell lines, CRISPR-Cas9 knockout of specific RP genes does not affect cell viability. In human adult and fetal tissues, RP protein levels showed development stage and tissue specific heterogeneity. Our results suggest that heterogeneous RP levels play a significant functional role in cellular physiology, suggests that the human ribosome may be structurally variable, with yet undiscovered mechanisms regulating ribosome structure across tissue types. Since antibiotics target bacterial ribosomes, our results suggest the possibility to create novel “antibiotics” to target cancers.